コミュニケーション行動の生涯発達についての
分野横断的研究拠点の形成

平成２７年度～平成３１（令和１）年度私立大学戦略的研究基盤形成支援
研究成果報告書

令和2年4月

学 校 法 人 名 慶應義塾

大　　学　　名 慶應義塾大学

研 究 組 織 名 日吉心理学研究室

研 究 代 表 者 斎藤　太郎

（慶應義塾大学 文学部 ）

目次

（１）はしがき

私が慶應義塾大学日吉心理学研究室に着任した 2013 年以降，研究室メンバーも入れ替わりが続き，心理学領域の潮流も変わったこともあいまって研究室メンバーの研究も以前とは異なる内容になりつつあった。そのような状況で研究室や装置を整備し，研究環境を整えることが心理学研究室の喫緊の課題となっていた。これに対し研究環境を物質的に整えるばかりでなく，共同研究体制をも整えながら「研究拠点を形成する」本事業は我々にとって願ってもない貴重な機会であった。ところが実際には願っても容易には叶うはずはなく，1 度目の申請では塾内申請の段階で非採択であった。しかし，その後に日吉研究室メンバーを含め，多くの先生方のお力添えで大学理事にも状況をご理解いただくことができ，2 度目は塾内通過，文科省通過と無事に採択され現在に至った。

本研究プロジェクトでは「コミュニケーション行動の生涯発達」というテーマを軸として，（１）子供研究，（２）障害研究，（３）加齢研究をそれぞれのメンバーで分担しつつ，それぞれのメンバーが医学部や理工学部との共同研究を通して分野横断的研究を実施し基礎研究ばかりでなく，臨床や工学的応用などを試みてきた。幸い研究室メンバーはもとより医学部等との共同研究を進める素地があったこともあり，更なる共同研究体制の拡大も比較的スムーズであった。特に日吉キャンパスは理工学部の矢上キャンパスに隣接することもあり，研究室同士の連携もうまく進み，学生達も夏場は汗水たらしながら矢上から谷を下り，日吉の丘へ登り NIRS 実験や脳波実験を心理学研究室で行ってくれた。当初の予想以上に理工学部との有機的な連携体制も構築することができた。整備した実験室等を心理実験実習の教育にも活用できたことも利点の１つであった。また，2020 年 3 月に本事業は終了したが，結果として今後 5 年程続く本拠点を中心とする比較的大型の外部研究資金を複数獲得することができ，本事業の研究を継続発展することが可能となった。

本プロジェクトを完遂することができたのもひとえに日吉心理学研究室の先生方，嘱託職員，戦略ＰＤ研究員，事務担当職員，日吉学術研究支援課のみなさま，三田心理学研究室の先生方，医学部，理工学部をはじめとする戦略の共同研究員の先生方の本事業へのご尽力の賜物である。そして，採択当時に文学部日吉主任であった斎藤太郎先生には，文学部長に代わって快く研究代表者となっていただき，本事業を監督いただいた。みなさまへ心より感謝の意を表したい。

2020 年 5 月 1 日　皆川泰代　（研究プロジェクトリーダー）

（様式 2）

法人番号	131015
プロジェクト番号	S1511005

平成 27 年度～平成 31（令和1）年度「私立大学戦略的研究基盤形成支援事業」
研究成果報告書概要

1　学校法人名　慶應義塾　　2　大学名　慶應義塾大学

3　研究組織名　日吉心理学研究室

4　プロジェクト所在地　神奈川県横浜市港北区日吉４－１－１

5　研究プロジェクト名　コミュニケーション行動の生涯発達についての分野横断的研究拠点の形成

6　研究観点　研究拠点を形成する研究

7　研究代表者

研究代表者名	所属部局名	職名
斎藤太郎	文学部	教授

8　プロジェクト参加研究者数　２４　名

9　該当審査区分　理工・情報　生物・医歯　人文・社会（○印）

10　研究プロジェクトに参加する主な研究者

研究者名	所属・職名	プロジェクトでの研究課題	プロジェクトでの役割
文学部・教授	斎藤太郎	(1)子供研究：乳幼児の発達障害の言語、視覚、嗅覚刺激に対する行動指標や脳機能指標による早期診断法、発達障害児のコミュニケーションスキル支援技術の開発	斎藤から梅田まで 14 名は心理学を中心とした人文社会科学研究を行う。本プロジェクトは(1)子供研究(2)障害研究(3)加齢研究の 3 つに分かれ、特に太字で示した日吉心理学研究室の研究者が各分野の統括を行う。各分野において、本研究の中核となる認知機能、感情、精神の発達について実験心理学、社会心理学、認知神経科学的研究を医学部、理工学部との連携により押し進め、学術的な統括を行う。各分野の医、理工との提携先を(1)-(3)の数字で示す。
文学部・教授	**皆川泰代**		
文学部・教授	山本淳一		
文学部・教授	川畑秀明		
文学部・准教授	伊澤栄一		
経済学部・教授	**中野泰志**	(2) 障害研究：視覚障害者研究に基づく支援技術の開発、聴覚障害児のコミュニケーション能力の解明、発話障害者の会話補助ツールの研究開発	
文学部・教授	坂上貴之		
文学部・助教	大森貴秀		
言語文化研究所・准教授	川原繁人		
理工学部・教授	**髙山緑**	(3) 加齢研究：高齢者の性格やコミュニケーション能力が QOL（生活の質）、幸福感そして寿命に与える影響を検討。記憶や推論などの認知機能が感情理解やストレス度に与える影響、およびそれらの脳内基盤の解明。	
商学部・准教授	木島伸彦		
文学部・助教	**寺澤悠理**		
文学部・教授	伊東裕司		
文学部・教授	梅田聡		
理工学部・教授	岡田英史	(1,3)NIRS による計測と解析手法開発	信頼性高く、革新的なデータ解析手法を提供し、研究全体の質を高める。研究結果を効果的な技術として形にし、社会へ効果的に波及させる。
理工学部・名誉教授	岡田謙一	(1)発達障害児の嗅覚計測と応用	
理工学部・教授	青木義満	(1,3)大規模動画データの計測、解析、応用	

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法人番号	131015
プロジェクト番号	S1511005

大学院 SDM 研究科・教授	前野隆司	(2)視覚障害者の支援技術開発	
医学部小児科・教授	高橋孝雄	・正期産児、早期産児の NIRS を用いた脳機能研究、アイカメラ等の行動研究を実施	生涯発達の初期段階（新生児）についての貴重なデータの提供、臨床への応用
医学部小児科・講師	池田一成		
医学部小児科・助教	有光威志		
医学部精神・神経科学・教授	三村將	・認知神経科学的手法を用いた精神医学研究、コミュニケーション障害疾患例に対する効果的な訓練プログラムの開発	研究成果を臨床的に応用し、認知症、老年期うつ病、ストレス性疾患などの早期判断、治療への活用
（共同研究機関等）			
大阪大学大学院　・教授	佐藤眞一	高齢者の精神状態についての社会心理学研究	高齢者の気分や性格について信頼性の高い評価法を提供
大阪大学大学院・准教授	権藤恭之		

＜研究者の変更状況（研究代表者を含む）＞

旧

ﾌﾟﾛｼﾞｪｸﾄでの研究課題	所属・職名	研究者氏名	プロジェクトでの役割
(1)子供研究	文学部・准教授	伊澤栄一	コミュニケーション行動の発達・進化研究

（変更の時期：平成 31 年　4 月　1 日）

新

変更前の所属・職名	変更（就任）後の所属・職名	研究者氏名	プロジェクトでの役割
文学部・准教授	文学部・教授	伊澤栄一	コミュニケーション行動の発達・進化研究

旧

ﾌﾟﾛｼﾞｪｸﾄでの研究課題	所属・職名	研究者氏名	プロジェクトでの役割
高齢者の精神状態についての社会心理学研究	大阪大学大学院・准教授	権藤恭之	高齢者の気分や性格について信頼性の高い評価法を提供

（変更の時期：平成 30 年 4 月 1 日）

新

変更前の所属・職名	変更（就任）後の所属・職名	研究者氏名	プロジェクトでの役割
大阪大学大学院・准教授	大阪大学大学院・教授	権藤恭之	高齢者の気分や性格について信頼性の高い評価法を提供

旧

ﾌﾟﾛｼﾞｪｸﾄでの研究課題	所属・職名	研究者氏名	プロジェクトでの役割

（様式 2）

法人番号	131015
プロジェクト番号	S1511005

（2）障害研究	文学部・教授	坂上貴之	意思決定研究

（変更の時期：平成 31 年 4 月 1 日）

新

変更前の所属・職名	変更（就任）後の所属・職名	研究者氏名	プロジェクトでの役割
文学部・教授	文学部・名誉教授	坂上貴之	意思決定研究

旧

ﾌﾟﾛｼﾞｪｸﾄでの研究課題	所属・職名	研究者氏名	プロジェクトでの役割
（3）加齢研究	文学部・助教	寺澤悠理	高齢者の感情制御

（変更の時期：平成 31 年 4 月 1 日）

新

変更前の所属・職名	変更（就任）後の所属・職名	研究者氏名	プロジェクトでの役割
文学部・助教	文学部・准助教	寺澤悠理	高齢者の感情制御

旧

ﾌﾟﾛｼﾞｪｸﾄでの研究課題	所属・職名	研究者氏名	プロジェクトでの役割
正期産児、早期産児の NIRS を用いた脳機能研究、アイカメラ等の行動研究を実施	医学部小児科・講師	池田一成	生涯発達の初期段階（新生児）についてのデータの提供、臨床への応用

（変更の時期：平成 30 年 4 月 1 日）

新

変更前の所属・職名	変更（就任）後の所属・職名	研究者氏名	プロジェクトでの役割
医学部小児科・講師	さいたま市立病院・周産期母子医療センター所長	池田一成	生涯発達の初期段階（新生児）についてのデータの提供、臨床への応用

（様式 2）

法人番号	131015
プロジェクト番号	S1511005

11　研究の概要（※　項目全体を10枚以内で作成）

（１）研究プロジェクトの目的・意義及び計画の概要

本プロジェクトは乳幼児，小児，成人，高齢者，障害者という様々な対象についてコミュニケーション行動の生涯発達を脳科学的，心理学的に明らかにすることで統合的な理解を進め，理解に基づくコミュニケーションの補助や促進のツール，システムの開発を行う。具体的には，音声，言語，視線，表情，ジェスチャーなどを含めコミュニケーション行動における様々な信号処理およびそれらの複数者間相互作用についての心的，神経的システム，その生涯発達を明らかにする。同時に，コミュニケーション行動が困難になる自閉スペクトラム症（自閉症）といった非定型的発達との比較により，ヒトのコミュニケーションの発達について多面的な検討を進める。自閉症以外にもヒトが行うコミュニケーション行動の「困難さ・つまずき」(他者の気持ちの理解や自分の気持ちの表現の難しさ，視聴覚情報処理における困難さ，発達や加齢に伴う変性など)に注目するので対象者は，視覚障害者や精神疾患患者も含める。さらに本研究では，この「困難さ・つまずき」を埋める訓練法，ツールやシステムの開発を学際的な枠組みで行う。以上の目的のために本プロジェクトでは次の５つのテーマを設定して研究を進めた。

1）fNIRS(functional Near-Infrared Spectroscopy：近赤外分光法)ハイパースキャンニングを用いた 2 者間の社会的相互作用の脳機能研究

2）感情情報処理の脳機能と生理指標

3）音声コミュニケーションにおける音韻，プロソディーの役割

4）効果的なコミュニケーション活動を目指すツールについての研究

5）発達障害スクリーニングを目指すシステムの研究

（２）研究組織

本プロジェクトではコミュニケーション行動の様態理解に関する研究と，その理解に基づくモデルや仮説を検証し，応用する研究を心理，理工・医学部で循環的に実施する(図 1 参照)。領域は⑴子供研究，⑵障碍研究，⑶加齢研究に分かれる，日吉心理学研究室の教員６名を中心として，そして文学部心理学研究室や言語文化研究所教員８名に協力を得つつ（1）～（3）を分担し，心理学的・認知神経科学的見地から研究を行う。本事業で雇用したPD研究員（毎年３－４名）RA（毎年１名）が心理学教員と協働しながら研究を進める。（1）～（3）の3グループ各々に研究内容と関係の深い理工学部（４名）・医学部（４名）との連携研究を行う。

（1）子供研究では新生児研究については特に医学部の小児科との共同研究を行う。この他に乳幼児や子どもの二者間の社会的相互作用コミュニケーションの研究については，まず神経学的定型者の成人について表情や音声を介したコミュニケーションの様態を明らかにするために NIRS や脳波を用いてリアルタイムの脳活動や生理指標の測定を行う。この場合に，心理の分野の研究者が実験計画を行い，行動指標や脳活動を含める生理データも取得するが，その多量なデータの解析やモデリングは理工学系の特に情報学系のPD研究者と協働する。一方で二者間同時計測のより効果的な脳波計測電極などハード面での開発は理工学系の機械学の研究者と協働する。（2）障碍研究では共同研究者である工学系研究者の画像工学的技術を援用しつつ，発達の様子を客観的に計測し，発達障害スクリーニングを目指すシステムの研究や効果的なコミュニケーション活動を目指す療育を見出すことを目指してきた。（3）高齢者研究ではPD研究員とも協働しながら脳科学的研究を行ったり，高齢者学を専門とする共同研究期間の研究者（2 名）と研究を行ってきた。同時に感情情報処理の脳機能と生理指標の研究については，医学部精神科との共同研究を進め成果をあげてきた。（1）－（3）いずれのグループも以前より共同研究を行っていた場合と本研究プロジェクトを通じて共同研究を開始したパターンがあったが，いずれも円滑な共同研究を進め，学会発表および論文出版という形で成果をあげてきた。特に理工学部（矢上キャンパス）に近い日吉心理学研究室で研究設備を整えたので，学生や研究者も行き来がしやすく実験室および装置の効果的な使用ができた。

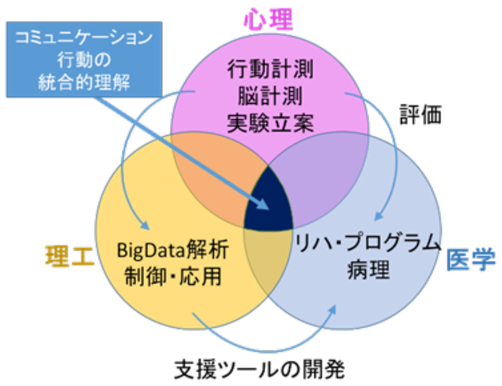

図１　共同研究体制

（３）研究施設・設備等

本研究プロジェクトにて日吉心理学研究室実験室６（約34m²）に実験キャビンや脳機能計測装置 NIRS を

（様式 2）

法人番号	131015
プロジェクト番号	S1511005

設置した。実際 NIRS 装置を 1 台購入する本資金の補助が充分得られなかったため，それを補填する資金を獲得し整備を進めた。使用人数は実験の有無により大きく変更するが，研究および実験授業の教育にも使用してきたので，平均すると 1 週間あたりのべ 25 人，NIRS，キャビンの使用時間はそれぞれ約 10 時間である。そしてこれまで機材室として使用していた部屋を改修し，共同研究室（約40m^2）として研究員等のデスクスペースとした。使用人数は 1 週間でのべ 30 人である。電気生理室（約15 m^2）の古いシールドルームを新しいキャビンに変え，他資金で脳波計も購入した。脳波導入後の使用人数は 1 週間でのべ 10 人，キャビンの使用時間は約 10 時間である。これらの日吉キャンパスの fNIRS 実験施設，共同研究室や脳波シールドルームは共同研究を行う理工学部や医学部にも施設を開放し，共同研究を行った。三田キャンパスにある心理学実験研究施設および慶應義塾大学病院でも本プロジェクトの研究を各々のグループで実施した。

（４）研究成果の概要　※下記、13及び14に対応する成果には下線及び＊を付すこと。

＜現在までの進捗状況及び達成度＞

1. fNIRS ハイパースキャンニングを用いた 2 者間の社会的相互作用の脳機能研究

1-1 母子相互作用 （理工学部，医学部連携）

ハイパースキャンニングとは複数者が何かしらの認知活動を伴うタスクを行っている際に，複数者の脳活動を同時に計測し，脳の同期性や関連性を検討する手法であり，コミュニケーション行動の脳機能を明らかにするための重要な手法である。fNIRS は頭部に測定プローブのキャップを装着するだけで計測ができるので，自然なコミュニケーション時の脳活動を測定するのに適している。

母子コミュニケーションにおいて運動や生理信号の同期活動という現象が知られている。本研究ではそれら潜在的な活動を脳活動のレベルで客観的に明らかにすることを目指している。さらには同様な同期活動の成人版も1－2で検討し，相互作用脳活動の発達を明らかにすることを目指す。さらに中間報告後に（1）子供研究であった本研究は（2）障害研究での発達障害スクリーニングの研究とも併せて検討することとし発達障害のリスク児を実験参加者に加えることで，母子脳同期指標が発達障害を予期する因子になるかを検討することとした。これらの目的のために，母子抱っこ条件，授乳条件，他人抱っこ条件での二者間での脳活動の同期や相互作用を定型発達児約 80 組，発達障害リスク児の母子 20 組で計測し（総計 200 名），分析を行った。授乳条件で前頭前野の背内側部や右の上側頭部など社会信号処理の部位にて同期性が確認された。これら定型発達児と母親との間に見られた同期性が発達障害リスク児に観察されるかを同様な方法で検討した。その結果，授乳条件で強くみられる同期性は見られず，リスク児は母親との間の愛着や社会関係において異なる傾向があることが示唆された。（定型発達児研究：達成度 95%，発達障害研究：達成度 80%）(*i, F, G, I)

1-2 自然な社会相互作用場面での脳活動，生理指標計測 （理工学部連携）

人間の社会的な活動は動的な情報交換に基づく。それを支える脳機能を明らかにするためには，二者が動的に相互作用する様子を時間連続的かつ同期的に捉える必要がある。また情報交換のイベントも課題依存的に決定されるものではなく，実験参加者の社会的意図に基づく自発的なものであることが望ましい。

以上の要件を満たすため，本研究では社会的相互作用場面を模した PC ゲームを作成し（図2），拘束性が低く実環境での計測が可能である fNIRS を用いて，協調作業条件及び独立作業条件の脳活動を二者間で同時計測した。このとき行動履歴のほか，心拍及び皮膚電位生理指標，ビデオ動画を同期的に取得した。さらに，自発的なイベントに関わる脳活動変化を捉えるための解析手法を考案した。

図2　ゲーム課題の協調作業条件における画面例。参加者2人は交互に画面下側に並んだ候補の中から家具類を選んで部屋の中へドラッグして配置する。独立作業条件では半分のサイズの部屋に一人で家具を配置する。

合計 39 組（78 名）の fNIRS データを取得した。まず脳活動の時間周波数領域における同期の大きさを示す指標

（様式 2）

法人番号	131015
プロジェクト番号	S1511005

であるウェーブレット・トランスフォーム・コヒーレンス(以下，WTC)をすべての二者間のチャンネル組み合わせ及び個人内のチャンネル組み合わせについて計算した。協調作業条件と独立作業条件についてWTC の時間平均値の比較を行ったところ，二者の右側頭領域と右前頭前野間をはじめとして多くの領域で協調作業条件における有意な活動同期の増加が確認できた。こうした同期活動には課題条件差に由来する様々な活動が混在している。そこで自発的な社会的相互作用の観測変数として顔面の向きに着目し，顔面が対面する相手の顔方向を向いている状態を積極的な情報交換を行うための行動と見做すことで更なる分析を行った。実験時の映像データから顔特徴トラッキングツールである OpenFace 2.0 を用いて顔向きの角度を推定し Z スコアに正規化した。手元の PC のゲーム画面を見る頻度が最も高くなることから，標準偏差の2倍以上顔を上げているタイミングを正対する相手の顔を見ているイベントとして検出し，協調作業条件において有意に同期活動が増加した WTC のうち自分だけが顔を上げているときよりも自分と相手の両方が顔を上げている（見合わせている）イベントにおいて活動が大きくなるものを回帰分析によって求めた。その結果，二者の側頭頭頂接合部(TPJ)間と背外側前頭前野(dlPFC)間，各個人の TPJ と内側前頭前野(mPFC)間の計３つのチャンネル間において有意な同期が認められた（図３）。特に TPJ と mPFC 間の結合は相手との協調に対する意思のアンケート結果とも有意な相関が認められた。これらの領域は相手の状態を推し量る”メンタライジング”と呼ばれる脳機能と深く関わっており，本課題においても同機能が重要な役割を果たしていたと考えられる。以上，本研究は社会行動を半自動的に抽出し，その行動と脳活動の関係を検討する手法を新たに開発すると共に，相互作用時の脳内機構を明らかにした。本研究は新しい解析方法や実験結果などを論文にすべく準備中であるが，実験結果について一度投稿し，現在査読コメントに対し改定中である。（達成度：80％）(*c, u, D, F, G, I)

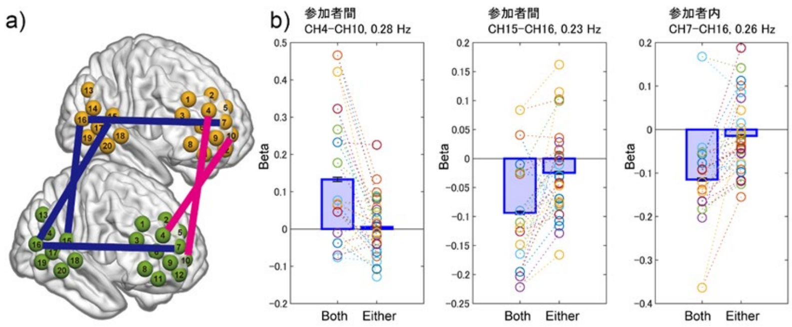

図3 社会的協調行動に関係する a)脳内・脳間ネットワークと b)各ネットワークの回帰係数のプロット。Both は顔を見合わせる行動、Either は単独で顔を向けた行動の回帰変数を示す。

また共同実験として，理工学部三木研究室が開発した微小針による小型ドライ型電極を用いて(4-1 も参照)，計 11 組の脳波データも取得した。計測部位は左右側頭部(T3，T4)と後頭部（Oz）の 3 か所とし，fNIRS 計測と同様の実験を行った。相互相関関数やパワースペクトル密度を用いた同期解析を行ったが，本計測では脳波における明瞭な同期活動は確認できなかった。現在，微小針による小型ドライ型電極を使った本研究を含めた脳波研究への応用をまとめた論文は投稿し，major revision で改訂中である。（達成度：90％）(*h, j)

2．感情情報処理の脳機能と生理指標

2-1 パーソナリティと感情情報処理の脳機能

個人の気質・性格特性と感情情報処理際の脳反応との関連を検討するため，成人 22 名を対象に，感情刺激図（90 枚）を提示した際の前頭前野活動を fNIRS で計測し，TCI 気質・性格特性尺度と脳活動の関係を検討した。複数の気質・性格特性項目と感情刺激に対する前頭葉反応との間に有意な相関がみられた。個人の気質・性格によって，感情刺激に対する反応が異なることが示唆された。さらに前頭前野内での脳部位結合も検討し，結合の強さと気質・性格特性の関係を検討し，一部で相関がみられた。以上は個々の気質・性格には前頭前野における感情制御能力も関与することを示した。現在論文作成中である。(達成度 95%) (*n)

2-2 母子の感情刺激に対する脳反応

母子コミュニケーション特徴と母子のパーソナリティ，感情制御の関係を検討するために，乳幼児をもつ母

法人番号	131015
プロジェクト番号	S1511005

親を対象に fNIRS を用いて，4 つのカテゴリの感情刺激の画像に対する脳活動を測定した。その際に刺激を見ながら感情を制御するタスクを果たした。各カテゴリの感情刺激に対する脳反応と母子遊びの特徴，パーソナリティを計測しそれらの関係性を検討した。ただし本研究は母親以外の成人にてどのような前頭前野反応が得られるか不明であったため，追加で大学生 20 名の実験を行い，現在データ解析中である（達成度：60％）

2-3 高齢者の感情情報処理の脳機能と生理指標 （医学部連携）

研究Ａ：自己の感情状態の認識が正確にできるか否かには個人差があり、この差が不安や抑うつといった精神的な健康と関連することが明らかになってきた。本研究では、感情を喚起する動画を視聴している間の脳活動(NIRS)や生理指標(心拍など)の測定を行う。その際に主観的な感情状態の報告を求め、客観的指標と主観的指標の関連性を測定し、客観的データから主観的指標を予測する際の成功率を個人における感情認識の正確さとして扱うことを目指す。この他にも認知症や精神疾患を持つ成人や高齢者に対して感情情報処理と脳活動や心拍などを含める生理指標についての基礎的な研究を医学部精神科と連携しながら進めていく。

この目的の下、悲しみ、怒り、喜び、恐れを引き起こす動画セットの作成および標準化を行い、ターゲットとする感情を適切に喚起するための刺激のセットを作成した。また、健常成人を対象に、この動画を鑑賞している際の NIRS と生理指標を測定の測定を行った。健常成人の結果については学会発表を終えている。今後は高齢者における検証を目指す。この他に別途，精神疾患者や認知症をもつ成人，高齢者の感情情報処理について生理指標を用いた研究では，医学部との連携により学会発表や論文など成果をあげてきた。

研究 Ｂ：加齢に伴う感情の平板化の認知神経基盤を検討するための研究を実施した。感情認識の鋭敏さを測る課題におけるパフォーマンスと、灰白質のボリュームの関係性を検討した所、怒りに対する鋭敏さと両側の腹側島皮質および被殻のボリュームに関係性が観察された。島皮質は、環境情報と様々なモダリティの感覚情報を統合し、覚醒度の調整に関わる場所であることから、このような心的機能の変化が感情の平板化に関与していることが示唆された。

さらに、彼らの安静時脳活動と認知機能の関連性についての詳細な分析を行った。時間的変化コネクティビティ解析(Time Variant Connectivity Analysis)の手法を用いて、安静時の脳活動の変化を観察し、デフォルトモードネットワーク、セイリエンスネットワーク、遂行機能ネットワークといった複数の機能的ネットワークの活動の持続時間や変化の個人差を検討した。その結果、自己に関わる処理に関連するデフォルトモードネットワークの一部のネットワークの生起頻度や活動持続時間が記憶や判断などの認知機能を強い関連を示すことがあきらかになった。感情の制御能力との関連については、今後さらなる検討を行う予定である。(達成度：80％) (*b, d, e, s, v, B)

2-4 高齢者のコミュニケーションにおける視聴覚情報の役割

本研究は中間報告にて高齢者について充分な研究がなされていないという，外部評価と自己評価に基づき，新たに着手した研究である。ここでは，視覚情報が若年者（成人）と高齢者の雑音下の発話理解に与える影響を脳波と行動指標により検討した。

日常のコミュニケーション環境には，多少の雑音が含まれている。我々はこうした雑音下で情報を伝達し理解している。これまでの研究によれば，発話に付随して生じる唇の動きや身振りが，雑音下における発話理解を助けることがわかっている。しかし，先行研究では，英語やオランダ語など，日本語と比べ音素数の多い言語を対象に行われてきた。それらの言語では音韻弁別に微細な口唇の動きが大きな影響を及ぼすことを考えると，日本語話者にとって口唇の動きがどの程度影響を与えているかを検討する必要がある。また，発話理解に及ぼす視覚情報の影響が，成人や高齢者でどの程度異なっているかはわかっていない。聴力の低い高齢者は，聴覚情報処理の低下を補うため，視覚情報を成人よりも多く利用する可能性がある。そこで本研究では，20 代の成人と高齢者において，視覚情報が雑音下の発話理解に与える効果を検討した。この目的を遂行するため，視覚情報（口唇と身振り動きの有無）と聴覚的ノイズ（SNR）の要因

法人番号	131015
プロジェクト番号	S1511005

を統制したビデオ刺激を作成し，ビデオ視聴中の研究参加者の脳波と行動指標を取得した。結果として，成人も高齢者も，雑音のある発話の場合，身振りがその理解を助けるが，口唇の動きは，影響がないことがわかった。発話の意味理解には，口唇は影響を及ぼさないことが示唆された。（達成度 80%）

3．音声コミュニケーションにおける音韻，プロソディーの役割

3-1 新生児の音韻，プロソディー刺激に対する脳反応 （医学部連携）

音韻処理とプロソディー処理は大脳のそれぞれ左側頭，右側頭部優位に処理され機能が側性化している。本研究は在胎週数 30 週の早産児から 41 週までの新生児を対象として，機能側性化と音声誘発反応の血行動態（HRF）の反応パターンの発達を修正月齢（PMA）別に検討した。その結果，PMA38 週までは酸素化ヘモグロビン上昇という一般的な HRF 反応が逆転しており，39 週で正期産児群と有意差のない一般的パターンがみられ，同時に左右側頭部の機能側性化の傾向がみられた。左右半球機能差や脳活動の血行動態は聴覚野がほぼ完成する在胎 30 週より徐々に発達することが明らかになった。論文も採択された（達成度：100%）（*f, g, r）

3-2 音韻配列規則に関与する音韻知覚についての研究 （海外連携）

日本語話者は abna の様に母音が存在しない場合でも、bn の子音間に母音/u/を知覚することが知られている。この現象は日本人の英語コミュニケーション向上についても重要な問題である。本研究では、この音韻配列規則による知覚のゆがみについて実験的に検討しフランス ENS と論文発表を行った。（達成度：100%）（*m, H）

3-3 フレーズプロソディー知覚についての対照言語研究 （海外連携）

イントネーションなどの言語プロソディーはコミュニケーションの中で重要な役割を果たす。本研究はプロソディーには言語普遍性があるという予備的データに基づいて、日本語話者とフランス語話者の日本語プロソディー知覚について比較する。80 名の実験が終了し、フランス EHESS と分析を進めた。（達成度：80%）（*l）

3-4 遠隔コミュニケーション事態における視聴覚間相互作用

インターネットを介したビデオ通話などの対人コミュニケーション事態について，映像と音声のずれが動画や音韻の知覚処理に及ぼす影響について検討した。視聴覚間相互作用と視聴覚間の時差に対する主観的同時性知覚との関連について，時間統制の容易な図形運動刺激と聴覚刺激を用い，両者の知覚が同一の時間情報処理に基づくものであるか実験的検討を行った。刺激間時差への順応により主観的同時性が変容するパラダイムを用い，視聴覚間相互作用および主観的同時性の判断分布について，最大 400 ミリ秒程度の時差への順応前後での変化パターンを比較した。両判断分布は互いに反対方向へ変化し，視聴覚間相互作用と主観的同時性が異なる時間情報処理に基づく事が示唆された。（達成度：60%）（*w, A）

4．効果的なコミュニケーション活動を目指すツールについての研究

4-1 子どもと高齢者にも装着しやすい脳波電極の開発 （理工学部連携）

脳波計測に一般的に用いる皿電極はインピーダンスを下げるため装着時に不快な皮膚処理を施す必要がある。本研究では、皮膚処理を不要にすることで子どもや高齢者にも簡便に装着できる脳波電極の開発を行った。本電極は微小針の付いたピラーを敷き詰めた形状をしており、被験者は痛みを感じない。電極の性能を検証するために、音声によるオドボール課題を用い、脳波成分の P300 や MMN の事象関連電位を測定した。その結果、逸脱刺激の MMN 及び P300 の振幅が、標準刺激と比較して、統計的有意に大きいことが認められた。以上より、簡便に装着可能な本電極が事象関連電位を計測できることが示された。1－2 でも先述したが，現在，本研究を含めた脳波研究への微小針の応用をまとめた論文は投稿し，major revision で改訂中である。（達成度：90%）（*j, x）

4-2 発話困難者の会話補助ツール「マイボイス」の研究 （理工学部連携）

本研究は，(1) 「マイボイス」の再生音声の質の向上，(2)「マイボイス」の更なる普及，及び (3)「マイボ

法人番号	131015
プロジェクト番号	S1511005

イス」が大学教育に有効であることを実証的に示すことを目標とした。(1)に関しては，録音方法の改善や，音声学的知見に基づいてマイボイスの改良に関する提言を行った。具体的には，日本語のピッチアクセントや促音を，より正確に実現させることを達成することができた。同時に，マイボイスの実際の作成も積極的に行い，多くの患者様にマイボイスを届けることができた。(2)に関しては，2018 年 6 月から 2020 年 3 月の間に 4 回のワークショップを開催した(プロジェクト全体で計 12 回)。それぞれの集まりで，最新マイボイスの紹介，初心者を対象とした実習，実際の介護現場でのマイボイスの使用報告，研究発表，自由議論を行った。近年，AI ひばりに象徴されるように，AI ベースの音声合成の普及も見られるが，ワークショップを通じ，自分の声そのものを録音しておくことの重要性を改めて議論し直した。また，(3)にも関わるが，この 2 年間のワークショップには学生も多く参加し，学生からのフィードバックがマイボイスの改善にそのまま繋がる事例が少なからず見られた。たとえば，ある学生から SNS で使われるようなスタンプ機能が提案され，その機能はすぐに搭載された。また，著作権問題を回避するために，マイボイス用のスタンプを自ら描いて提供してくれた学生も 2 名いた。その他，拍手機能やうなずき機能など，学生ならではの発想が，マイボイスの機能をより豊かにしてくれた。さらに第 11 回のワークショップでは，基金室の広報から取材をうけ，実際の記事として紹介された。これらの成果を踏まえ，2020 年の 6 月に行われる予定の日本言語学会において，特別シンポジウムの招待講演としてマイボイスの紹介を行う。(3)に関しては，上記の成果に加え，実際にマイボイスの試みを授業で紹介し，アンケートを通してマイボイスの教育への有効性を客観的に検証した。これらの成果は 2 本の論文にて発表されている。このように，授業や研究成果の発表を通して，マイボイスとその有用性について，多くの患者様，介護者様，医療従事者，研究者，教育者，学生に伝える機会を与え続けてきた。マイボイスを使用する患者様は増え続け，現在では総計約 350 名の方がマイボイスを作成・使用している。(達成度：90%)(*k, p, z, C)

4-3 子どもの対人相互作用を促進するためのデバイスの検証 (理工学部連携)

他の共同研究で開発された対人相互作用を促進するためのデバイス Facelooks を用いて，実際の遊びのコミュニケーション活動時の Facelooks の人工的な随伴信号(光)に対する脳活動とヒトによる社会的随伴信号(例，笑顔，発声)の脳活動の差を検証した。6ヶ月乳児を対象にした研究では，人工的信号の場合は注意に関与する前部の TPJ，ヒト信号の場合は社会性に関与する TPJ が強く反応した。更に背内側前頭前野と TPJ の結合が見られたのはヒト信号のみであり，人工的な光による信号は，注意を促す随伴信号にはなり得るが，意図や感情を伝えるには充分でない可能性が示唆された。この研究ではコミュニケーションのデバイスやツール評価に脳機能計測が有用であることを示した。本研究の基礎となる実験についての研究論文が採択された(達成度：95%) 。(*a, y, I, J)

4-4 弱視者のためのタブレット教材や閲覧アプリの開発

近年教科書や資料のデジタル化が進んでいるが，弱視者にとってタブレットでの閲覧にどのような利点，欠点があるのかが不明であった。本研究ではタブレット教材を作成し弱視者に使用してもらった上でインタビュー調査を行うことで，デジタル教科書の特徴を客観的に明らかにした。さらにはそのようなタブレットの閲覧の視認性の低さを明らかにした上でそれを改善させるための閲覧アプリを開発した。(達成度：100%)(*q, t)

5. 発達障害スクリーニングを目指すシステムの研究

5-1 嗅覚刺激に対する脳反応計測によるスクリーニング法の検証 (医学部・理工学部連携)

自閉症スペクトラム(ASD)児は嗅覚の鈍麻と過敏性があるとされている。これら嗅覚を利用して ASD の診断補助を目指し，岡田らの開発したインクジェット方式の嗅覚ディスプレイ装置を用いて脳機能計測を行った。ASD 群は個人差が大きいが嗅覚閾値別に二分した ASD 鈍麻群は，嗅覚刺激中の背側前頭前野の活動が定型発達児群と比較すると有意に小さかった。さらにこの背外側前頭前野の活動は嗅覚刺激に対する弁別閾値との有意な正の相関が認められた。嗅覚処理において認知的な要因が嗅覚障害に関連することが示唆された。嗅覚機能に関連する脳活動は捉えられ，他の手法とあわせた診断補助としての

法人番号	131015
プロジェクト番号	S1511005

1 つの可能性にはなりえると考えられた。現在投稿した論文が major revision となり改訂中である（達成度：90%）（*E）

5-2 発達障害早期発見のための微細運動の自動評価システムの開発 （理工学部連携）

ASD の乳児期の早期スクリーニングを目指し，乳児の 12 ヶ月時点からの微細運動，粗大運動を計測し，連携者の最新の画像工学技術を用いて定量化している。現在も 12 ヶ月から 36 ヶ月までの縦断データを収集中であるが，既に 24 ヶ月までの運動統合能力はらせん状に発達することなどを明らかにし報告している。（達成度：50%）（*o, J）

＜優れた成果が上がった点＞

本プロジェクトの目的の1つである医学系，工学系との分野横断的研究の拠点形成という目的は達成された。例えば分野横断研究により発達支援ツールや生理指標計測デバイスの成果は着実に得られた。この他の具体的な優れた成果は下記の通りで，第一に新しい複数者間コミュニケーション計測の解析手法を開発し，新しい知見を得てきた点，第二に会話補助ツール「マイボイス」の啓発活動が挙げられる。

1-1，1-2 複数者間コミュニケーションの脳活動の関係を検討するハイパースキャンニング研究： 我々は、3つのハイパースキャンニングデータの分析手法を確立した。1）独立成分分析を用いた手法では、共通する同期的な脳活動成分を具体的な形で抽出することができる。共通成分が複数のチャンネルに渡って存在するときにも、その分布を知ることが可能であり、従来行われてきた単一のチャンネル同士の比較よりも多くの情報を得ることができる。2）さらなる発展版として fNIRS 信号を時間周波数領域に分解したのち、そのパワー変動について非負値行列因子分解を適用し、同期的な変動を抽出する手法も確立した。乳児と成人である母とでは脳の血流動態が厳密には異なっており、独立成分分析が仮定するような同じ周波数における同期が観測されるとは限らない，本手法で母子の授乳時には異なる周波数の動機がみられることを明らかにした。3）コミュニケーション行動を画像解析で半自動的に特徴抽出を行い，行動データと脳活動同期指標（WTC）との関係を検討するGeneral Linear Model を応用した手法を開発し，適用した。この結果，成人が視線を合わせている際の脳活動同期と片方がコミュニケーション相手を見ている場合では脳活動の同期が異なる脳部位でみられることが明らかになった。

4-2 発話困難者の会話補助ツール「マイボイス」の研究：2016 年には、研究発表『マイボイス：難病患者様の失われる声を救う』（代表者：川原繁人）が、業績・活動を評価され、2015 年度日本音声学会学術研究奨励賞を受賞した。（戦略研究者：皆川泰代も共同受賞）

＜課題となった点＞

本プロジェクトは複数者間のコミュニケーション行動の脳活動同期について，上述したとおり様々な解析手法を開発し，成果をあげてきた。しかし，これらは招待講演やシンポジウムなどを通して発表し，公開をしてきたが，論文は一部のみの発表であり，充分に成果を論文発表出来ている状況ではない。

＜自己評価の実施結果と対応状況＞

本プロジェクトが狙いとする心理学と医学部，理工学部との分野横断的研究は充分になされ，それぞれ共同研究の成果が得られている。本プロジェクトは主に本事業で雇用されたPD研究員が，日吉心理学研究室教員との協働の元に推進するものである。このためにPD研究員に目標管理シートを配布し，それぞれの研究プロジェクトについて評価を行っている。その結果，各研究員は概ね計画通りに研究を遂行しているが，現時点で国際的な学術雑誌に第一著者として採択された論文が少ない。今後，多くのPD研究員が継続して別研究資金で研究を進めるので成果について出版や公開を促す予定である。また加齢研究を担当するPD研究員が少なかったこともありやや進捗が遅れていたが，2018 年度に加齢研究担当のPDを雇用し専任教員と研究を推進することで高齢者の脳波研究を進めることができた。

（様式 2）

法人番号	131015
プロジェクト番号	S1511005

＜外部（第三者）評価の実施結果と対応状況＞

中間評価では外部評価者 2 名，幕内充氏（国立リハビリテーションセンター研究所高次脳機能研究室室長），吉村優子氏（金沢大学教育学部准教授）に外部評価を依頼した。幕内氏には本事業での設備を整えた実験室を含め，研究活動を見学の上で，進捗報告書や研究業績書の評価をお願いした。4 段階評価（A+,A,B,C）では「A：順調に研究成果を上げつつあり、現行のまま推進すればよい」の評価を頂き，「分野横断的な研究が進められ成果もあがっているが，できれば同じ研究テーマについての生涯発達を検討するとなおよい」とのコメントを頂いたので，2－4 の若年者と高齢者の比較研究など対応を行った。同実験を子供で実施する予定であったが，そこまでには至っていないので今後継続予定である。

吉村氏には進捗報告書や研究業績書を送付し，評価をお願いした。同じく「A」評価を頂き，「子供研究や成人研究に比較して高齢者研究の成果が少ないので今後対応すればバランスがとれより良いプロジェクトになると思われる。」とのコメントを頂いたので上記の通り追加実験と同時に専任教員に fMRI を用いた高齢者の脳機能実験を遂行してもらうことで対応を行った。

最終年度におけるこれまでの活動の外部評価として熊崎博一氏（国立精神・神経医療研究センター・児童・青年期精神保健研究室　室長）にお願いし，A評価を頂いた。コメントとしては，「子供研究，障害者研究が大変充実している分，高齢者研究についてはやや成果が少ない印象を受けるが，まだ進行中の高齢者研究もあり今後の進展が期待できる。」とのことであった。今後も継続していくので本プロジェクト後半で進めた高齢者研究も引き続き発展させる予定である。

＜研究期間終了後の展望＞

心理学と医学部，理工学部との分野横断的研究を進めることができ，今後の外部資金応募のためにも充分な体制ができたので今後の研究に発展させたい。実際に，この体制を活用し，本プロジェクトの研究者が 2019 年度に JST/CREST に筑波大学の工学系研究者および本学の理工学部研究者と共に応募し採択された。本研究拠点をもとにこれまでのテーマ1の相互作用の研究内容やテーマ4のデバイス開発をさらに継続させる研究提案であったので，今後学外の研究者と協働しながら更なる研究の発展が期待される。同時に本プロジェクトの（1）子供研究，（2）障害研究に関連する，発達障害リスク児の縦断研究を提案した科研費・基盤研究Sに 2019 年度に採択された。この提案も本拠点を活用する研究内容であるので，実験設備や装置の有効活用ができる。

＜研究成果の副次的効果＞

日吉心理学研究室に研究設備や装置を整備し成果を出したことで，競争的研究資金を獲得しやすくなったばかりでなく，研究教育にも効果が出た。実験心理学を教える授業がここ数年で 4 コマ増加したが，ここでは NIRS を使った脳機能研究の実習なども取り入れることが可能になった。

本プロジェクトで行った 4－1 微小針電極の脳波計，4－3 コミュニケーションを円滑にするデバイス開発については引き続き別資金で継続していくので，適宜特許取得などを行っていく。

12　キーワード（当該研究内容をよく表していると思われるものを8項目以内で記載してください。）

（1）コミュニケーション　（2）生涯発達　（3）社会的相互作用
（4）高齢者　（5）母子　（6）感情情報処理
（7）脳機能　（8）ハイパースキャンニング

13　研究発表の状況（研究論文等公表状況。印刷中も含む。）

上記、11(4)に記載した研究成果に対応するものには＊を付すこと。

法人番号	131015
プロジェクト番号	S1511005

＜雑誌論文＞

[雑誌論文（査読有）]　本事業のPD研究員と研究者（教員）に下線を付す。

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法人番号	131015
プロジェクト番号	S1511005

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法人番号	131015
プロジェクト番号	S1511005

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＜研究成果の公開状況＞（上記以外）

シンポジウム・学会等の実施状況、インターネットでの公開状況等

・定期的に本プロジェクトにおける研究手法の中心となる fNIRS についてのセミナーを 4 回実施した。本プロジェクトのテーマであるコミュニケーション行動に関する研究についての海外からの講師を含むコミュニケーション行動の専門家による LSDCOM 講演会も定期的に行ってきた。
・本プロジェクトの１のテーマである 2 者間の脳機能計測について名古屋大学, 生理学研究所の招待講演者を含み本プロジェクトの成果を発表する LSDCOM シンポジウムを開催した。
・4ー2 のマイボイスプロジェクトにおいては 4 回（全 12 回）のワークショップで成果の発表, 普及に努めてきた。
・内部の研究会はPD研究員とほぼ毎週開催している。
・これまでに 14 件の研究会, セミナー, 3件の国内学会, 2018 年 5 月に 1 件の国際学会を共催している。以上の研究成果公開を含む定期的なセミナー, シンポジウム, 研究会はウェブサイトにて案内している。
・アウトリーチ活動として 2 回の子育て支援講演会「大切にしたい子どもの育ち」,「いまどきの子育てで大切なこと一幸せ子育てのコツ」を実施し日吉近隣の多くのご家族や保育者に参加いただいた。

（様式 2）

法人番号	131015
プロジェクト番号	S1511005

＜既に実施しているもの＞
http://lsdcom.keio.ac.jp/event/index.html

＜これから実施する予定のもの＞
コロナウィルス感染予防のためしばらくはシンポジウム等を行わない予定であるが，今後本プロジェクト関連のシンポジウム，研究会を行う計画はあるため下記に随時掲載予定
http://lsdcom.keio.ac.jp/event/index.html

14 その他の研究成果等

本プロジェクトのテーマ1である 2 者間の脳機能計測やテーマ3の音声コミュニケーションにおける音韻，プロソディーの役割について国際学会 NIR2019 基調講演として行った。

(*F) Minagawa, Y. (2019) "What optical imaging tells us about typical and atypical neurocognitive development" Keynote speech, NIRStralia 2019, NIR 2019, Gold Coast convention and exhibition center, Australia (Sep.17th).

本プロジェクトの１のテーマである 2 者間の脳機能計測について，国際会議 Organization of Human Brain Mapping にてシンポジウム"Brain-to-brain synchrony early in life"を提案し，採択された。イタリア，ドイツからの研究者を交えての研究成果の公開とともに討論を行った。下記は本プロジェクトからの代表者の同シンポジウムの発表。

(*G) Minagawa, Y. (2017) Exploring the neural evidence of mother-infant entrainment: Inter-brain synchronized hemodynamic activity Symposia "Brain-to-brain synchrony early in life", Annual Meeting of Human Brain Mapping, Vancouver, June.

PD 研究員や本プロジェクトメンバーと共に行った本プロジェクト成果についての招待講演を行った。

(*H) Minagawa, Y. (2019) "How has Broca's area played a role in the neuroimaging data of early language acquisition?" Symposium of the Japanese Society for Language Sciences, the 21st annual meeting. Tohoku University (July, 6th).

Minagawa, Y. (2019) "Several topics from fNIRS studies: Social interactive neuroscience and language acquisition." RWTH Aachen University (June 17th).

Minagawa, Y. (2019) "What did optical imaging reveal about Broca's area for early language development?" Colloquium of the Institute of Cognitive Science, University Osnabrueck (June 19th).

(*I)皆川泰代「社会的相互作用における二者間・内の脳機能結合：行動の自動推定と GLM の適用」日本心理学会第 83 回大会，日立製作所冠シンポジウム「心理学における脳科学―基礎と臨床をつなぐ fNIRS 研究」，立命館大学（2019 年 9 月 12 日）

(*J) Minagawa, Y. (2018) "Development of social interactive brain: Behavioral and neurocognitive evidence" Workshop "Understanding developmental disorders: from computational models to assistive technologies" ICDL-EPIROB 2018, Waseda Univ. Tokyo. (Sep. 17th)

皆川泰代（2018）「自閉症スペクトラム障害児とリスク児の音声コミュニケーション」スペシャルセッション「音声コミュニケーションと障害者 II」日本音響学会秋季大会，大分大学（9 月 15 日）

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（様式 2）

法人番号	131015
プロジェクト番号	S1511005

Minagawa, Y. (2016) Neuroimaging the developing brain from the neonatal period to adolescence. Invited Talk, Biennial Conference of the Society for functional Near-Infrared Spectroscopy, Université Paris Descartes, (Oct. 14th).

皆川泰代（2016）「乳幼児のことばの獲得における知覚情報の役割について」第 38 回視覚障がい乳幼児研究会，教育講演，慶應義塾大学（8 月 21 日）

皆川泰代（2016）「fNIRS で評価する学習による脳の可塑的変化」大会会長講演，第 19 回光脳機能イメージング学会，星稜会館（7 月 23 日）

（様式 2）

法人番号	131015
プロジェクト番号	S1511005

15 「選定時」及び「中間評価時」に付された留意事項及び対応

＜「選定時」に付された留意事項＞

関係する研究分野間における連携，分担等の関係性が具体的示されておらず、 総論的で具体性に欠ける。研究装置・設備費用が突出している点について是非を問うコメントも出ており研究装置の申請は見送る。

＜「選定時」に付された留意事項への対応＞

研究領域について下記 5 つのテーマを定め，生涯発達として（1）子供研究，（2）障害研究，（3）高齢者研究の3グループがそれぞれ5つのテーマのうち３－５つに取り組む体制を構築し，研究を進めた。

1）fNIRS ハイパースキャンニングを用いた 2 者間の社会的相互作用の脳機能研究
2）感情情報処理の脳機能と生理指標
3）音声コミュニケーションにおける音韻，プロソディーの役割
4）効果的なコミュニケーション活動を目指すツールについての研究
5）発達障害スクリーニングを目指すシステムの研究

研究装置費用申請が認められなかったため，他外部あるいは内部資金に申請し，脳波計や fNIRS 装置を購入し，研究を進めた。

＜「中間評価時」に付された留意事項＞

該当なし

＜「中間評価時」に付された留意事項への対応＞

該当なし

（3） 研究概要報告書に述べた研究内容の詳細と補足資料

1． fNIRS ハイパースキャンニングを用いた
2 者間の社会的相互作用の脳機能研究

1-1. 母子相互作用

1-2. 自然な社会相互作用場面での脳活動，生理指標計測

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Japanese Psychological Research
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Invited Review

Toward Interactive Social Neuroscience: Neuroimaging Real-World Interactions in Various Populations[1]

YASUYO MINAGAWA[2,*], MINGDI XU, and SATOSHI MORIMOTO *Keio University*

Abstract: Human social activity is a continuous dynamic behavior consisting of live social signal exchanges; thus, studying interactions among multiple humans is critical to understanding social cognition. Indeed, social neuroscience focusing on such aspects—*interactive social neuroscience*—is an emerging field of interest. Functional near-infrared spectroscopy (fNIRS) has played a significant role in accelerating this field by enabling real-world neuroimaging for various populations. The present paper will first review previous hyperscanning studies using functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), and electroencephalography (EEG). We will then summarize attempts and findings of fNIRS hyperscanning studies on social interaction in adult populations. Finally, we will review recent investigations of interactive social neuroscience in young populations and show preliminary results from a mother–infant hyperscanning study. These studies have predominantly revealed synchronized brain activities between humans and have identified conditions in which such inter-personal connectivity was found to be increased. Furthermore, these studies suggest possible mechanisms of inter-brain coupling: a process that recruits both mirror system and mentalization networks. Although fNIRS hyperscanning of infants remains limited, the reviewed literature demonstrates significant potential for fNIRS to disclose the interactive social brain and its development.

Key words: hyperscanning, functional near-infrared spectroscopy, synchronization, entrainment, social neuroscience.

Studying the single human brain places limitations on identification of human social cognition capacity, as social cognition is a psychological process to cope with another's mind, such as inferring another's intentions, feelings, and thoughts (Adolphs, 2009). Human social activity is a dynamic process that is triggered by others and is initiated to others by way of eye gaze, facial and body expressions, language, speech, and various perceptual signals. Thus, the presence and/or relationship of other agent(s), whether visible or not, with a targeted human is a prerequisite to social cognition. Previous neuroimaging studies have attempted to

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investigate the human social brain using prerecorded stimuli that simulate other individuals. For instance, cerebral activities and connectivity have been measured in response to facial stimuli, emotional stimuli, and social stories. Indeed, these cerebral responses reflect part of the social cognitive process, and such findings are vital to our understanding of social cognition at present. Nonetheless, such methods only allow for observation of certain brain mechanisms and provide a snapshot of social behavior.

Social activity is a continuous interactive behavior consisting of live social signal exchanges. Such interaction is core to human social behavior. Its significance is exemplified by a hypothetical mode called *we-mode*, which is realized exclusively through person-to-person interaction. During interactive we-mode, the cognitive subject is shifted from *me* to *we*, and information processing for others is highly accelerated (Gallotti & Frith, 2013). In the field of social neuroscience, the emergence of unique terms, such as *second-person neuroscience* and *two-in-one* systems, underscores the increasing significance of studying the brain correlates of social encounters (Konvalinka & Roepstorff, 2012; Schilbach et al., 2013). Therefore, capturing such social cognitive processing from real continuous interaction between agents is crucial to advancing the field, as it may uncover novel evidence for social neuroscience. In particular, simultaneous recording of two brains (i.e., hyperscanning) during such interaction provides the most accurate means by which to clarify the two-in-one system of the human social brain.

A series of functional magnetic resonance imaging (fMRI) and electroencephalography (EEG) studies has been conducted investigating human interaction primarily via hyperscanning, as reviewed in the next section on adult populations. However, since 2011, functional near-infrared spectroscopy (fNIRS) neuroimaging in a live social setting or hyperscanning of human interaction has been stably expanding and appears to provide unique insights into social neuroscience. The fNIRS technique is innocuous, portable, and silent (Hoshi, 2007; Minagawa-Kawai, Mori, Hebden, & Dupoux, 2008) and enables ecological experimental settings for performing interactive tasks in the real world (Figure 1). In particular, it provides the opportunity to measure the developing brain in infants and children, including those with atypical development, and may provide information crucial to understanding the origin and development of human social ability. The present paper chiefly reviews fNIRS studies on person-to-person interaction, focusing on the hyperscanning method performed on adult and young child populations. We will discuss advancements in this field and summarize the available literature with regards to the methodology and neuroscientific findings. In the

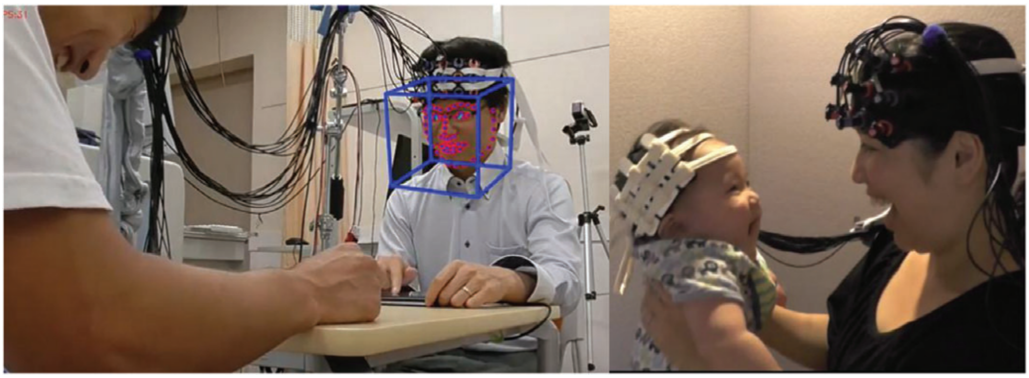

Figure 1 fNIRS measurement during face-to-face interaction task (left) and mother–infant interaction (right). For the adult experiment, automatic estimation of gaze and facial movement was applied to analyze with fNIRS data. We obtained permission from photographic subjects.

next subsection, the significance of live interactive stimuli in social neuroscience is discussed in terms of current literature on the development of social cognitive abilities. In the second section on studies on adult populations, we first review the hyperscanning studies performed by fMRI, magnetoencephalography (MEG), and EEG in comparison to fNIRS studies. EEG studies in particular have accumulated and provide various insights for those who will try fNIRS hyperscanning. After reviewing the hyperscanning studies with adults, we will focus on fNIRS studies on young populations using live social stimuli, in order to discuss the significance of live stimuli and the novel findings. Although infant–infant hyperscanning has not yet been performed, we will discuss recent findings obtained from hyperscanning of mother–infant interaction. These reviews may offer a view of fNIRS usage beyond the conventional fields, in addition to the potential of fNIRS in interactive social neuroscience. Finally, we will wrap up the review by discussing the mechanism of inter-brain coupling and current problems in this field to suggest future directions.

Interactive Live Stimuli and Their Significance

The use of live stimuli in social neuroscience is crucial to the advancement of the field in many ways. As mentioned above, non-live stimuli offer only a snapshot of social behavior. Even if the stimulus is a continuous video clip, researchers are only able to examine participants' responses to the unidirectional social stimuli. From the literature on developmental psychology, a phenomenon called *video deficit*, which pertains to difficulties of learning or performing via unidirectional video, is well known. While video deficit is observed in various behavioral processes, including language learning tasks, such as phoneme category and word, object searching task, and imitation task (Kuhl, Tsao, & Liu, 2003), this deficit may be explained by the differences between live and non-live stimuli, namely interactive and unidirectional stimuli. An alternative interpretation of video deficit is that perceptual and cognitive learning by young children and infants is facilitated by social interaction situations.

The advantages of performing either hyperscanning or single recording to determine the impact of live interactive stimuli involves four factors (a–d), categorized based on whether they are interactive or non-interactive and live or non-live. The factors and their respective amplitudes are recorded in Figure 2. Firstly, (a) enhanced sensory and perceptual amplitude of live stimuli is one of the advantages, as real humans usually provide stronger impressions in terms of size, three-dimensional information, and haptic and olfactory information than the monitor-presented ones. Employing live versions of stimuli does not merely positively affect this factor (Figure 2), but this factor (a) is influential enough to enhance the other three factors. (b) Contingency of live stimuli is also a crucial factor, as contingency provides rich social responsiveness that often serves as a reward. Quick response is a prerequisite to induce the experience of contingency. This may relate to a sense of ownership or agency as an immediate reaction to the initiator's behavior elicits the sense of "I control something," which may also induce a sense of unity. (c) The third factor, bidirectionality, is rather broad and includes various interpretations and consequences. Bidirectionality of live stimuli increases the stimulus impact, as a response signaled from the self somehow alters the behavior of others, resulting in elicitation of emotion and/or attention by him/herself. Its impact may differ

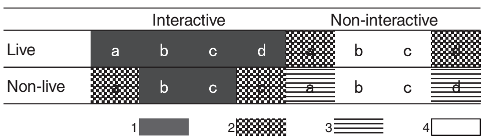

Figure 2 Amplitude of four factors contributing to experiments on social brain in different settings (live vs. non-live, interactive vs. non-interactive). Four factors are (a) sensory and perceptual characteristics, (b) contingency, (c) bidirectionality, and (d) presence of mind. The darker each square is, the higher each factor's amplitude (four levels, 1–4).

depending how and what the initiator (self) expects from the other's reaction. Hence, one important aspect of bidirectionality involves exchanges of feedforward and feedback. Previous studies on entrainment also suggest that there may be implicit bidirectional exchanges of sensory signals between agents. These sensory signals could be a visual cue (such as an eye blink, gaze movement, or body movement) or an auditory cue (such as speech). It is assumed that such implicit processing of perceptual cues contributes to the entrainment or synchronization phenomena (Chartrand & Bargh, 1999; Koike et al., 2016; Shockley, Santana, & Fowler, 2003). This implicit process may also relate to the mirroring system (e.g., contagious yawning). Depending on their quality of spatial and temporal resolutions, factors (b) and (c) can be effectively implemented using non-live stimuli. The fourth factor, (d) human presence, refers to a presence of mind that encompasses intention and emotion; it does not require the individual to react, and the experimental task need not involve any mentalization (Schilbach et al., 2010). Its impact differs depending on the relationship (e.g. *boss* or *friend*) and autobiographical background. The presence of mind itself serves as a high influential factor as has been extensively studied in the field of social psychology. *Social facilitation effect* and *social pressure* are typical examples of such studies. Such a state of the human mind may diminish in response to non-live stimuli, particularly non-interactive stimuli. However, as indicated by Figure 2, non-live stimuli still function effectively if they are interactive. Thus, hyperscanning—employing either live or non-live stimuli—demonstrates potential for exploring the two-in-one system.

Neuroimaging Social Interactions of Adult Populations

Hyperscanning Technique

The hyperscanning technique is a valuable method for observing neural activity underlying social cognition during person-to-person interaction. Although the word *hyperscanning* was first coined by Montague et al. (2002) in an fMRI study, the first hyperscanning study can be traced back to over 50 years ago using EEG (Duane & Behrendt, 1965). This dual-EEG study was designed to prove the existence of extrasensory perception between twins by calculating the correlation between their EEG traces. This paper has been criticized for poor statistical analysis and spatial resolution, but was the pioneering study that raised the notion of simultaneous acquisition of cerebral data from multiple participants (F. Babiloni & Astolfi, 2014). Hyperscanning does not necessarily pertain to simultaneous recording of persons in a live real-world setting; therefore, our review includes hyperscanning studies of adult populations using non-live stimuli, as these reports provide background information underlying current real-world interaction experiments.

fMRI Hyperscanning

After lying dormant for a long period of time, the multi-subject recording technique underwent a renaissance led by Montague et al. (2002), who were the first to apply hyperscanning to study multi-participant interaction using fMRI devices. In this seminal study, two players involved in a simple deception game were scanned simultaneously using two different fMRI devices situated over a long distance and connected via the Internet. This interactive game involved one sender and one receiver. Common activity was identified in the supplementary motor area of both players, but was observed to be stronger in the sender's brain. While this study demonstrated the technical feasibility of dual-fMRI scanning and first advocated the idea that simultaneous recording of both interacting brains could measure social interaction best, it suffered from small sample size (only three pairs) and significant time delays between the stimuli and the responses (Hari & Kujala, 2009).

Subsequently, Montague's group extended their hyperscanning fMRI techniques, using a set of turn-based neuroeconomic trust games, to reveal the neural underpinnings of various social cognitions, such as reciprocity (King-Casas et al., 2005) and agency (Chiu et al., 2008; Tomlin et al., 2006). Another study also applied fMRI hyperscanning to record two-brain activities related to the comparison of received rewards with partners (Fliessbach et al., 2007). Using recorded videos of each other's body gestures, speech, or facial expressions, other fMRI studies tackled unidirectional offline interaction by scanning two participants consecutively (Anders, Heinzle, Weiskopf, Ethofer, & Haynes, 2011; Schippers, Roebroeck, Renken, Nanetti, & Keysers, 2010; Stephens, Silbert, & Hasson, 2010). These studies utilized innovative experimental designs to investigate the neural activity underlying social interactions, and yielded impressive results. However, these experiments defined social interactions in the context of an information flow between the brains of senders and receivers in the order of seconds, and occasionally the paradigms were somewhat rigid with regard to the roles that each participant had to take (i.e., no changing roles during the experiment). These paradigms either focused on the single side (i.e., the receivers) of information flow, or failed to capture the moment-to-moment interactions between two persons. As a result, the automatic and instantaneous influence of mutual information exchange on joint actions, an important element in social interaction, cannot be examined using such paradigms (Konvalinka & Roepstorff, 2012).

Four fMRI hyperscanning studies challenged real-time interaction by creating scenarios enabling mutual gaze between two persons in joint attention paradigms (Bilek et al., 2015; Koike et al., 2016; Saito et al., 2010; Tanabe et al., 2012). Saito et al. (2010) set up a complex experimental paradigm allowing live video images of the participants' eyes and eyebrows, therefore one partner could follow the direction of the other's gaze towards the target object. After 2 years, the same group (Tanabe et al., 2012) utilized this paradigm to study patients with autism spectrum disorder (ASD). Prominent pair-specific interpersonal neural correlations were found in the right inferior frontal gyrus (IFG) of normal–normal dyads, but were reduced in ASD–normal dyads, indicating the right IFG's involvement in shared intention during eye contact. Recently, the group further expanded their fMRI hyperscanning research by investigating the neural underpinnings of shared attention in the context of learning (Koike et al., 2016). They adopted a 2-day experimental paradigm in which unknown dyads performed a mutual gaze task (MG1) followed by a joint attention (JA) task on the first day (Day 1); several days later (Day 2), the dyads performed a mutual gaze task (MG2) followed by a control gaze task (VIDEO, gazing at recorded video of the partner during MG1). Inter-brain synchrony was found in various brain regions (e.g., right middle temporal gyrus, bilateral IFG) during the real-time mutual gaze period, but not during the video period. Moreover, inter-brain synchrony in the right IFG featured a significant increase during MG2 relative to MG1 (enhanced by the JA task); no enhancement of inter-brain synchrony was found without JA (Experiment 2), or in cases where JA was administered when the partner was changed (Experiment 3). These findings indicate the possible role of the right IFG in generating and preserving shared attention. Another group (Bilek et al., 2015) developed a sophisticated hardware setup—an immersive audiovisual interface between linked fMRI scanners—to make online eye signal exchange possible, and this paradigm allowed switching roles (sender and receiver of eye gaze) between participants. They reported significant neural coupling between the interacting dyads' right temporoparietal junction (TPJ), a key region for social interaction. These novel paradigms give rise to real-time exchange of eye gaze and may be extended to future exploration of joint action/attention. Although mutual exchange of eye gaze is only one facet of social interaction and such eye contact may be less flexible inside the fMRI scanner, this is certainly a significant step for interactive social neuroscience with fMRI. Hyperscanning fMRI allowed for the collection of data during real-time social interaction, but not during offline situations: data in the latter circumstance cannot be obtained using single-brain fMRI recording.

Indeed, two-person fMRI studies are difficult to perform, as two fMRI scanners are seldom available in one institute using the same LAN, and each participant is required to lie motionlessly in the scanner while being able to interact with another participant. Using a computer interface has the potential to alleviate this issue, but brings about additional problems, such as time lags and ecological validity (King-Casas et al., 2005). In addition, different characteristics of different fMRI instruments at different sites could induce a considerable inter-device variance (Montague et al., 2002). Complex calibration is required, but is not sufficient. Recent attempts using dual-coil setups in a single fMRI scanner with two participants lying side-by-side (Lee, 2015; Lee, Dai, & Dix, 2010; Lee, Dai, & Jones, 2012) or face-to-face (Hari, Henriksson, Malinen, & Parkkonen, 2015) will likely help to resolve the above-mentioned problems. However, due to low temporal resolution and strict limitation on the natural movements of participants, it is nearly impossible for fMRI to record brain activities during social interactions as ecologically as in daily life (Koike, Tanabe, & Sadato, 2015).

MEG Hyperscanning

MEG hyperscanning studies emerged recently to investigate brain-to-brain interactions with high temporal resolution and reasonable spatial resolution. The first MEG hyperscanning study was performed by Baess et al. (2012). They presented a novel method to realize a distant MEG-to-MEG link with accurate synchronization: two participants at separate laboratories 5 km apart communicated with each other in real time via an audio connection with negligible delay and jitter. Recently, the same group updated their MEG hyperscanning apparatus by including a video connection between the dyads and replacing the landline-based connection with an Internet link. The improved equipment enabled audiovisual interaction with minimal delay (~130 ms, one-way) and no impediments to smooth, natural communication regardless of large geographical distances between dyads (Zhdanov et al., 2015).

Hirata et al. (2014) developed a dual audiovisual presentation system that allowed for real-time face-to-face interaction—permitting the two parties to see each other's facial expressions—between a mother and her child through a mirror system during MEG hyperscanning. This system was the first MEG hyperscanning system to be administered in a single shielded room; and it can be generalized to the simultaneous recordings of inter-brain activities between adult participants. The same group extended their study by investigating neuromagnetic couplings between children with ASD (48–94 months old) and their mothers during task-free face-to-face spontaneous non-linguistic interactions using this MEG hyperscanning system (Hasegawa et al., 2016). They found that the degree of MEG mu suppression in the right precentral area of both the mothers and children was correlated with the mothers' social ability, as well as specific traits of the children with ASD. Moreover, they demonstrated a significant correlation between the strength of mu suppression in the mothers and their children. Irrespective of its size, MEG hyperscanning is capable of providing high-resolution spatiotemporal profiles of neural activities during fast-paced social interactions. In addition, the MEG device is child-friendly and has potential for future studies that aim to track inter-brain couplings between mothers and their children.

EEG Hyperscanning

Following the first dual EEG study (Duane & Behrendt, 1965), the technique was largely abandoned for several decades due to EEG's insufficient spatial resolution at the time. However, the concept of EEG hyperscanning underwent a resurgence about a decade ago as a result of dramatic technological progress. Recently, EEG hyperscanning studies have prospered due to EEG's distinguished temporal resolution, relatively low cost, high portability, and significantly shorter time lags between systems. These merits have made EEG hyperscanning popular in social interaction studies, particularly for those involving moment-to-moment interpersonal coordination in a natural environment.

Turn-based interaction. To our knowledge, after the attempt of Duane and Behrendt (1965), the first significant EEG hyperscanning studies were launched by F. Babiloni and Astolfi's group, adopting a four-player (two teams of two players) Italian card game similar to the international game of Bridge (Astolfi, Toppi, et al., 2010; F. Babiloni, Cincotti, et al., 2007; F. Babiloni et al., 2006). These studies evaluated inter-brain communication by computing inter-brain functional connectivity between selected regions of interest from interacting brains. By comparing the patterns from different pairs of brains (team colleague or not), Astolfi, Toppi, et al. (2010) reported that only players from the same team exhibited a significant functional link, and this functional connectivity was predictive of successful card choosing. Furthermore, the same group employed a variety of interesting games, such as Prisoner's Dilemma (Astolfi et al., 2009, 2011; Astolfi, Cincotti, et al., 2010b; F. Babiloni, Astolfi, et al., 2007; De Vico Fallani et al., 2010) and Chicken's Game (Astolfi, Cincotti, et al., 2010a), to probe cerebral processes related to decision-making in the game theory context. By applying advanced graph theory measurements to the inter-brain connectivity, De Vico Fallani et al. (2010) provided evidence for the possibility of predicting the outcome of the joint decisions of the dyads on the basis of the EEG hyperscanning data, and the prediction accuracy was greater than 90%. They also suggested that inter-brain hyperconnectivity may be an indicator that can predict the strategies used by the two brains in social interaction.

Kawasaki, Yamada, Ushiku, Miyauchi, and Yamaguchi (2013) used EEG hyperscanning to study brain rhythm synchronization between two persons engaged in an alternating verbal task in which they were required to list letters of the alphabet in sequence. Twenty dyads performed the task before and after they completed an individual training session wherein the partner is a robot-like computer. The authors reported significant enhancement in inter-person neural and verbal synchronization as a result of the training, and claimed that such augmentation may reflect the emergence of empathy for the partner's speech rhythms.

Compared to the experimental paradigms used in the fMRI studies reviewed above, these EEG hyperscanning studies have situated multiple persons in more natural interactions without fixed roles (sender and receiver), and the interactions have taken place in real-world settings rather than through a hardware interface. These studies allowed for the investigation of neural bases underlying inter-brain communication in the order of milliseconds due to EEG's fine temporal resolution; however, the interpersonal behavioral coupling did not occur on the millisecond scale, but in a turn-based manner (Konvalinka & Roepstorff, 2012).

Ongoing mutual interaction. In addition to the above-mentioned turn-based face-to-face interactions, EEG hyperscanning has also been widely applied in studies of dynamic ongoing interpersonal coordination, such as finger/hand movement synchronization (Dumas, Nadel, Soussignan, Martinerie, & Garnero, 2010; Naeem, Prasad, Watson, & Kelso, 2012; Tognoli, Lagarde, DeGuzman, & Kelso, 2007), simultaneous music performance (C. Babiloni et al., 2011, 2012; Lindenberger, Li, Gruber, & Müller, 2009; Müller, Sänger, & Lindenberger, 2013; Sänger, Müller, & Lindenberger, 2012, 2013), and verbal communication.

Tognoli et al. (2007) proposed the first research of such kind. In this study, two participants were asked to produce continuous, rhythmic finger movements, which can be either of their own style and pace or synchronized with their partner's finger actions, with or without vision of each other's hand. Dumas et al. (2010) proposed a similar experiment in which two participants were visually paired via a dual video system while producing hand gestures. Later, the same group from the Tognoli et al. (2007) study published a successive report of finger movement synchronization

(Naeem et al., 2012). Whilst different methods were used to evaluate the relationship between the two brains' responses, these studies reached a consensus in suggesting that interpersonal synchronized behavior modulates neural activity in the right centroparietal region (Dumas et al., 2010; Naeem et al., 2012; Tognoli et al., 2007), most likely within the human mirror neuron system (Tognoli et al., 2007), and the observed inter-brain synchronization may be the result of several aspects of ongoing mutual interactions, such as anticipation of the partner's actions and turn-taking (Dumas et al., 2010).

Performing in musical ensembles, another kind of behavioral coordination, provides an interesting environment for studying social interaction. Lindenberger and colleagues (2009) performed a series of experiments to examine inter-brain neural effects when dyads of guitarists played a short melody cooperatively. Inter-brain oscillatory couplings were found prior to and during the coordinated actions for music production, which could be attributed to the similarities in sensorimotor feedback. More marked between-brain couplings were induced during periods that necessitated high demands on performance coordination (Sänger et al., 2012). In addition, musical roles (leader, follower, or listener) were found to modulate the inter-brain synchronization (Müller et al., 2013; Sänger et al., 2013). C. Babiloni and coworkers (2011, 2012) expanded this area by revealing brain signatures for emotional empathy during professional quartet music production. Although these studies recorded multi-subject EEG signals simultaneously, they did not investigate the possible synchronization between brains, but rather adopted a source imaging approach to locate the responsible brain region and calculated the correlation between this region's activity and the empathy trait measured by a psychometric test.

Interactions in an ecological setting. In recent years, great progress has been made in breaking the routine of hyperscanning social brains within a laboratory environment. Exploring social neuroscience during situations as naturalistically as possible in real-world settings is the current trend. Given its relatively low cost and high portability, EEG hyperscanning is flourishing in various social experiments with ecological settings. For instance, Toppi et al. (2016) performed a unique EEG hyperscanning study involving two pilots jointly executing a simulated flight during which the coordinated interaction between the two brains was a matter of life and death. They demonstrated that the pattern of inter-brain connectivity, primarily linking the frontal and parietal regions, was representative of the level of cooperation between the pilots during different stages of the flight. Specifically, during the take-off and landing phases, denser functional links between the two brains were related to the higher demand in cooperation.

Recently, Dikker et al. (2017) extended hyperscanning experiments beyond the laboratory, and validated the feasibility of investigating the neural signatures of a large group of interacting persons in ecologically natural settings over a long period. They used portable EEG units to simultaneously record neural signals from a class of 12 high school students during activities in their regular biology class for an entire semester (i.e., 11 sessions). The students were asked to rate four types of teaching styles based on how much they enjoyed them. These ratings were used to evaluate class engagement. Brainwave coherence between multiple individuals at various levels (i.e., the whole class, student–group, and student–student synchrony) was calculated to quantify neural synchronization. Their findings are not only informative, but also practical: (a) when students were highly engaged during the class, their brains exhibited enhanced synchronization; (b) such synchronization was not simply modulated by stimulus property, but was also influenced by individual differences in various aspects (e.g., teaching-style preference and social traits, such as empathy and group affinity); and (c) the students who had eye contact with each other before class exhibited increased student–student synchrony during the subsequent classroom activity. Although this study did not provide much information regarding the precise brain regions responsible for the observed neural synchronization, it demonstrated the potential of using portable inexpensive EEG headsets to reliably associate behavior and brain in an ecological setting, and therefore should inspire many future studies on social neuroscience (Bhattacharya, 2017).

As reviewed above, EEG research has established fundamentals of interactive social neuroscience. EEG, in particular portable EEG, is a suitable method for performing hyperscanning under social situations in ecological settings, as the participants can interact with each other with fewer restrictions on body movement. However, eye movements and muscle artifacts easily arise. The most evident shortcoming of EEG is its limited spatial resolution. Scalp EEG is not able to measure neuronal currents deep within the brain. Whilst the progress in mathematical techniques has allowed researchers to estimate the source of EEG signal, precise location is nearly impossible to achieve (Hari, Himberg, Nummenmaa, Hamalainen, & Parkkonen, 2013; Koike et al., 2015). The issue is aggravated when there are multiple sources, or if the source lies in deep brain structures (Grech et al., 2008). The majority of brain rhythms originate from multiple sources, the dominance of which varies rapidly, in the order of merely hundreds of milliseconds. Even for those most prominent brain rhythms, their sources are difficult to discriminate (Hari et al., 2015). Therefore, EEG does not appear to be a good candidate to accurately determine the spatial profile of the inter-brain links involved in social interactions (Koike et al., 2015).

fNIRS Hyperscanning

Coordinated action. fNIRS hyperscanning is a novel trend in current social neuroscience. The present review summarizes such studies (Table 1) by categorizing interaction types and pinpointing on some noteworthy study. For detailed methodology for each experiment, please refer to Table 1. The first fNIRS hyperscanning study was recently published (Funane et al., 2011). The authors used two portable 22-channeled fNIRS instruments to simultaneously record the hemodynamic responses in the prefrontal cortex (PFC) of six dyads whilst they were engaged in a cooperative button-press task with feedback and without feedback (control condition). Two participants sat face-to-face across a table, and pressed a button after counting to 10 s in their own mind following an auditory cue. The authors detected enhanced spatiotemporal covariance of oxygenated hemoglobin (oxy-Hb) in the PFC of the two brains when the dyads' performance on the cooperative task was improved (i.e., a shorter interval between their respective button presses). This finding suggests that people's inter-brain synchronization is associated with their performance during cooperative action.

Cui, Bryant, and Reiss (2012) promptly took the relay baton of fNIRS hyperscanning by using a similar temporally synchronized motor task performed by 11 pairs of participants. Specifically, two participants, sitting side-by-side, were asked to press a button as soon as possible following the appearance of a visual cue. Two types of tasks (cooperative and competitive) were adopted. In the cooperative task, the participants were instructed to make the button-press as synchronously as possible, with the aim to reach a time difference shorter than a pre-defined threshold. In the competitive task, they had to press a button before their competitor did to gain a point. In both tasks, the outcome of each trial was visually fed back to the participants. The inter-brain coupling was quantified by wavelet transformation coherence (WTC), a measure of the cross-correlation between two hemodynamic waveforms as a function of time and frequency. The authors found that the coherence between the hemodynamic responses from the two participants' right superior frontal cortices increased during cooperation but not during competition, which could not be simply explained by the resemblances in action, as the button press was more temporally synchronized in the competitive condition. In addition, for

Table 1 List of the analyzed fNIRS hyperscanning studies

Reference (year)	Interaction type	Task description	fNIRS setup & probe setting	Participants	Analysis method	Results
Funane et al. (2011)	Face-to-face, cooperative	Button press minimizing time difference	Portable 22 CH R&L-PFC	6 dyads	Covariance, CC	PFC: Cov. ↑ during cooperation Correlation between the degree of IBS and task performance.
Cui, Bryant, and Reiss (2012)	Side-by-side, cooperative/ competitive	Button press minimizing time difference	22 CH R&L-PFC	11 dyads	WTC	R-SFC: IBS ↑ during cooperation but not competition. Correlation between the degree of IBS and task performance in cooperation only.
Dommer, Jager, Scholkmann, Wolf, and Holper (2012)	Side-by-side, cooperative, turn-based	Dual *n*-back Single *n*-back	Wireless 4 CH L-PFC	4 dyads 7 singles	WTC, BA	L-PFC: IBS ↑ during cooperation
Holper, Scholkmann, and Wolf (2012)	Face-to-face Imitation	Finger-tapping Imitation	Wireless 4 CH L-PMC	8 dyads	WTC, GC	L-PMC: IBS ↑ during imitation. The brain signal of the model G-caused that of the imitator to a greater extent as compared to vice versa.
Holper et al. (2013)	Face-to-face, turn-based	Teacher–student dialog interaction	Wireless 4 CH L-PFC	17 dyads	BA, CC	L-PFC: IBS ↑ in successful teaching. Activity: successfully taught students < unsuccessfully taught students
Duan et al. (2013)	Side-by-side, competitive	Neural feedback (competition game)	22 CH, L-SMA	1 dyad	CC	L-SMA: correlation ↓ when one participant was winning the game as compared to a draw situation.
Jiang et al. (2012)	Face-to-face/ back-to-back, turn-based	Verbal communication	20 CH L-FTPC, 3 CH L-DLPFC	10 dyads	WTC	L-IFC: IBS ↑ during face-to-face but not back-to-back conversation.

Table 1 Continued

Reference (year)	Interaction type	Task description	fNIRS setup & probe setting	Participants	Analysis method	Results
						The degree of IBS reliably predicted the occurrence of non-verbal interactive behaviors.
Jiang et al. (2015)	Face-to-face, turn-based	Three-person leaderless group discussion	10 CH L-IFC, L-TPJ	11 triads	WTC, GC	IBS in L-TPJ: leader–follower > follower–follower. Leadership can be successfully predicted basing on the IBS and communication behaviors shortly after the conversation onset.
Osaka et al. (2015)	Face-to-face/ face-to-wall, cooperative	Singing/humming together	34 CH R&L FTPC	15 dyads singing/ 14 dyads humming	WTC	L-IFC: IBS ↑ in the cooperative singing/ humming condition irrespective of face-to-face or face-to-wall; R-IFC: IBS ↑ for humming only.
Liu et al. (2016)	Face-to-face cooperative/ obstructive turn-based	Jenga game with verbal communication	19 CH R-PFC, R-STS	8 dyads	WTC	BA8: IBS ↑ during both cooperative and obstructive interactions; BA9: IBS ↑ during cooperative interactions only
Nozawa, Sasaki, Sakaki, Yokoyama, and Kawashima (2016)	Face-to-face cooperative turn-based	Natural verbal game	Wireless 2 CH FP	12 quadriads	WTC	FP: IBS ↑ during cooperation
Hirsch, Zhang, Noah, & Ono (2017)	Online interactive/ offline non-interactive	Eye contact	42 CH, both hemisphere	19 dyads	WTC	IBS: Interactive (eye-to-eye) > non-interactive (eye-to-picture) in multiple areas in the left hemisphere (superior temporal, middle temporal,

Table 1 Continued

Reference (year)	Interaction type	Task description	fNIRS setup & probe setting	Participants	Analysis method	Results
						supramarginal gyri, pre- and supplementary motor cortices).
Cheng, Li, and Hu (2015)	Side-by-side, cooperative/ competitive	Button press minimizing time difference	22 CH PFC	45 dyads	WTC	Frontal: IBS ↑ in opposite-sex dyads, but not in same-sex dyads. In opposite-sex dyads only, significant correlation between IBS changes and degree of cooperation.
Baker et al. (2016)	Face-to-face (divided by two PC displays), cooperative	Button press minimizing time difference	19 CH R-PFC, R-TC	111 dyads	WTC	R-TC: IBS ↑ in female–female dyads, R-IFC: IBS ↑ in male–male dyads, For same-sex only, IBS was correlated with task performance.
Pan, Cheng, Zhang, Li and Hu (2017)	Side-by-side (divided by a partition), cooperative	Button press minimizing time difference	22 CH R-frontoparietal	49 mixed-sex dyads (Lovers, friends, strangers)	WTC, GC	R-SFC: IBS ↑ in lover dyads, which also significantly correlated with their task performance. Stronger directional synchrony from females to males than vice versa.

Note. CH = channel; L = left; R = right; IBS = inter-brain synchrony; PFC = prefrontal cortex; SFC = superior frontal cortices; PMC = premotor cortex; SMA = somatosensory area; FTPC = frontal temporal and parietal cortices; DLPFC = dorsolateral prefrontal cortex; IFC = inferior frontal cortex; TPJ = temporal–parietal junction; STS = superior temporal sulcus; FP = frontopolar; TC = temporal cortex; WTC = wavelet transform coherence; GC = Granger causality; BA = block average; CC = correlation coefficient.

the cooperative task only, the coherence increment was associated with improved performance. Based on this evidence, the authors concluded that brain-to-brain coherence may be a proxy for humans' cooperative behavior. Interestingly, this study also performed individual time series analysis but failed to reveal any task-specific patterns of the hemodynamic response. This striking contrast underlines the necessity of both recording and analyzing multi-subjects' brain signals, which may provide additional information for the study of social neuroscience (F. Babiloni & Astolfi, 2014).

As pioneers of wireless fNIRS hyperscanning, Dommer, Jager, Scholkmann, Wolf, and Holper (2012) developed an unconstrained (no disturbing cables) hyperscanning setting in which two four-channeled wireless fNIRS devices were used to simultaneously record hemodynamic responses in the left PFC of participants during either cooperative or independent performance of an *n*-back task. Signal processing was focused on the changes in total hemoglobin (total-Hb) concentration (total-Hb = oxy-Hb + deoxygenated-Hb [deoxy-Hb]). Traditional block-averaged (total-Hb) revealed that the hemodynamic response was larger for paired players than for single players. WTC analysis revealed that inter-brain coherence increased in the left PFC during joint task performance. This increase was observed in both the heart rate frequency and the low-frequency oscillations (which underpin joint behaviors).

Using the same wireless fNIRS setup as Dommer et al. (2012), the same research group attempted to identify the origin of between-brain neural synchronization as participants engaged in a paced finger-tapping imitation task (Holper, Scholkmann, & Wolf, 2012). In the imitation task, one participant (the model) was asked to tap right-hand fingers rhythmically (either self-paced or auditory stimulus-paced) on a keyboard, and the order of fingers used was freestyle; the other participant (imitator) was required to imitate the model's finger tapping. In the control task, the two participants performed the finger-tapping task alone but with the same pacing mode pattern (self-paced or auditory stimulus-paced). WTC analysis of total Hb revealed increased between-brain coherence in the left premotor cortices during the imitation task, and the coherence was more remarkable when the imitation was self-paced compared to stimulus-paced. In addition, Granger causality (GC) analysis revealed that GC in the imitation task was larger than in the control task, and the hemodynamic responses of the imitator adapted to that of the model. This study is noteworthy for its use of GC to identify the original source of neural synchronization.

Real-world social interaction. Prior to the previously reviewed EEG hyperscanning study during multi-person classroom activities (Dikker et al., 2017), Holper et al. (2013) conducted the first hyperscanning experiment of teacher and student interaction using wireless fNIRS. Block-averaged hemodynamic responses revealed that students who obtained successful knowledge transfer exhibited less activity in the left PFC region than those who did not acquire the knowledge. Correlation coefficients between teacher and student demonstrated significant inter-brain coupling in the left PFC region when the teaching was successful. This study has paved the way for subsequent exploration of brain-to-brain connectivity involved in realistic complex educational interactions.

In order to investigate the relationship between multi-person neural synchronization and social behaviors, Duan et al. (2013) built an online *cross-brain neurofeedback* experimental platform using fNIRS and validated it with a two-person neurofeedback experiment. After successful neural feedback training, two participants were asked to actively imagine physically participating in a competitive tug-of-war game. They were instructed to refer to the visual feedback information and use any learnt mental strategy (such as kinesthetic motor imagery) during the fighting rounds to defeat their opponent. A rope with a ribbon in the middle was displayed on the screen. The position of the ribbon was determined by the difference between the amplitudes of the two participants' brain signals (average oxy-Hb changes) in the left sensorimotor area. The online data analysis confirmed that the participants were able to mentally shift the ribbon. Interestingly, the offline data analysis revealed that the correlation of the oxy-Hb changes decreased when one participant was winning the game as compared to a draw situation. Although only one dyad was hyperscanned in this preliminary study and further validation is needed, it is the first study to extend the application of the hyperscanning technique to a brain–computer interface.

Jiang et al. (2012) corroborated the unique quality of face-to-face communication using fNIRS hyperscanning whilst participant pairs were involved in four types of real-time conversation tasks controlling two conditions (i.e., face-to-face vs. back-to-back, monologue vs. dialogue). WTC analysis revealed that significant inter-brain activity occurred only in the face-to-face dialogue condition over the left IFG. Importantly, this study combined brain activity with videotaped behavior data and disclosed that the degree of IFG coherence reliably predicted the occurrence of non-verbal interactive behaviors, such as body gestures and turn taking.

The same group extended their fNIRS hyperscanning research to further study the neural basis of leader emergence, an essential feature of human society, during realistic three-person verbal communication (Jiang et al., 2015). WTC analysis showed that interpersonal neural synchronization (INS) of leader–follower was significantly stronger than that of follower–follower in the left TPJ. In addition, combining the INS results with behavioral video data provided further information in that the quality, but not the frequency, of the leader's communication contributed to the increased INS. Notably, GC analysis revealed that leadership can be successfully predicted based on the INS and communication behaviors shortly (~30 s) after the onset of the conversation. Based on this evidence, the authors concluded that leaders emerge by synchronizing their neural activity with that of followers through their diplomatic communication skills and competence to achieve a unanimous group decision.

Another recent study (Osaka et al., 2015) examined whether the neural synchronization mechanism functions differently when two participants are engaged in another type of verbal/vocal interaction—cooperative singing/humming—a type of semi-verbal interaction. The participant dyads performed the singing/humming tasks either face-to-face (FtF) or face-to-wall (FtW) in a cooperative manner (sing/hum a song together). WTC results revealed that the inter-brain coherence in the left IFG increased significantly in the cooperative singing/humming condition, compared to the singing/humming alone condition, irrespective of FtF or FtW, whilst the right IFG showed an increased inter-brain coherence for humming only. These findings suggest that the neural synchronization in the participants' right IFGs may result from non-verbal coordination, such as humming (no lyrics, vocal), whereas the between-brain couplings in the left IFG may be due to verbal coordination.

Liu et al. (2016) designed an fNIRS hyperscanning experiment in a naturalistic, interactive setting using a non-computerized Jenga game. Four conditions were used for each dyad: two patterns of interactive game (cooperative and obstructive), during which oral communication was permitted; one independent game; and one dialog-only condition. WTC analysis revealed that, compared to independent game and dialog-only conditions, inter-brain coherence was observed in the posterior region of the right middle and superior frontal gyri (particularly BA8) during both cooperative and obstructive interactions, suggesting BA8's role in common goal-oriented social decision-making when two persons interact. Interpersonal neural synchrony in the dorsomedial PFC (BA9) was observed during cooperative interactions only, indicating that BA9 might be involved in cases when theory-of-mind is necessary during interaction. This study made efforts to precisely determine the spatial profile of inter-brain synchronization induced by natural social interaction. Approaches such as registering to a standard

MRI brain template and using a structural node-based spatial registration method were adopted for intra-dyad and inter-dyad analyses, respectively.

Researchers have made further attempts to improve the precision of fNIRS hyperscanning. For instance, Nozawa, Sasaki, Sakaki, Yokoyama, and Kawashima (2016) carried out a wireless fNIRS hyperscanning experiment wherein four-person groups were engaged in a cooperative verbal word chain game, and provided a technical basis for future hyperscanning studies by introducing innovative methods of data recording and analysis. The wireless fNIRS device used one light source and two light detectors, forming two channels, to monitor both the cerebral hemodynamic response and the systemic blood-flow signal in the frontopolar region. The authors performed sophisticated data preprocessing, such as removal of artifacts due to superficial blood-flow and body movements. WTC analysis validated increased inter-brain synchrony in the frontopolar region during the communicative session compared to the non-communicative session. Their preprocessing approach substantially improved the sensitivity to capture communication-induced inter-brain synchrony, while, as the authors stated, caution should be taken to avoid excessive removal of signals of neural origin.

Recently, Hirsch, Zhang, Noah, and Ono (2017) utilized more detailed and sophisticated data-interpretation methods to investigate the functional specificity (intra-brain) and functional synchrony (inter-brain) of online eye contact, a primary element of real-world interaction, using fNIRS hyperscanning. The authors pioneered a novel level of global sampling of fNIRS by covering the majority of the brain region, with the exception of the occipital area of each dyad. Moreover, a novel dual eye-tracking system with monitoring cameras embedded into eyeglass frames for each participant was used during fNIRS recording and synchronized to the fNIRS signals. Participants were asked to either make eye-to-eye contact with their partners (online interaction) or gaze at the eyes of a face on the screen (eye-to-picture, offline interaction). Multidimensional analyses focused on the deoxy-Hb and revealed that, relative to eye-to-picture gaze, eye-to-eye contact led to increased activity in a left frontal cluster of regions (including pars opercularis, pre- and supplementary motor cortices, and the subcentral area) in the individual's brain, which is also functionally connected to other regions, such as the left superior temporal gyrus and primary somatosensory cortex. In addition, compared to eye-to-picture gaze, eye-to-eye contact elicited increased partner-specific between-brain coherence in the left superior temporal, middle temporal, supramarginal gyri, as well as pre- and supplementary motor cortices. As both intra- and inter-brain neural correlates of eye-to-eye contact are associated with previously established language systems, the authors suggest integrated face-to-language processing during online eye contact.

Effects of sex and relationship of dyads. Cheng, Li, and Hu (2015) and Baker et al. (2016) examined how the sex composition of an interacting dyad influences the behavior and brain activity during cooperative interaction. Both studies adopted the computer-based button-press task, yet obtained different results. Cheng et al. reported that only opposite-sex dyads exhibited cooperation-induced inter-brain synchrony in the frontal regions, and the degree of inter-brain synchrony was significantly correlated with the degree of cooperation. However, Baker et al. found that cooperative interaction led to inter-brain synchrony in the right temporal cortex of female–female dyads and in the right inferior PFC of male–male dyads, but not in the opposite-sex dyads. An additional finding of this study was that the inter-brain synchrony was positively correlated with task performance (degree of cooperation) for same-sex dyads only. As the two studies focused on different brain regions, it is plausible that both same-sex and opposite-sex dyads would exhibit increased inter-brain synchrony due to cooperative behaviors, nonetheless, in different brain regions. Future studies using whole-brain measurement may elucidate this sex effect on interpersonal neural synchronization.

Furthermore, Pan, Cheng, Zhang, Li, and Hu (2017) investigated the interacting partners' relationship effect on cooperation-induced interpersonal neural synchronization using the cooperative button-press task (Cui et al., 2012). They recruited mixed-sex dyads of lovers, friends, and strangers. In addition to improved task performance in lovers compared to friends and stranger dyads, WTC analysis revealed that lovers also exhibited increased inter-brain synchrony in the right superior frontal cortex, which significantly correlated with their degree of cooperation. GC analysis revealed stronger directional synchronization from females to males than vice versa, indicating a leading role for females in romantic relationships during cooperative interaction.

Summary of fNIRS hyperscanning. All the above-reviewed fNIRS hyperscanning studies have endeavored, by utilizing either innovative paradigms or novel data analysis methods (or both), to elucidate the neural processes underlying real-world interaction that are difficult to investigate using fMRI hyperscanning. These studies, in general, demonstrated that cooperative interaction enhances synchronized cerebral activities and detected the engaged brain regions. They have provided additional insights into EEG hyperscanning by disclosing the functional specificities of various natural social interactions. For instance, enhanced interpersonal neural synchronization was often found in the right hemisphere, primarily the right PFC, during cooperative behaviors with coordinated goals, whereas verbal-based communication typically induced inter-brain coherence in the left hemisphere, primarily the left PFC and TPJ. Additionally, based on fMRI and fNIRS literature, either the right or left IFG appears to be a critical area for interactive human activities. Unfortunately, most of the fNIRS studies did not fully utilize the advantageous spatial resolution and have provided limited information regarding the brain region of interest. Consequently, at this point, we would not attempt to determine precise brain areas and networks of interactive social science. Given fNIRS's moderate spatial resolution, only a few recent studies—for example, Hirsch et al. (2017) and Liu et al. (2016)—have attempted to precisely discriminate brain areas involved in realistic person-to-person interactions. Furthermore, fNIRS studies with a few channels should also be careful with this issue, and such studies should first determine the significant brain regions for attaching the probe. As has been found from fMRI and multi-channel fNIRS studies, some brain regions are crucially engaged in a certain cognitive processing of interaction. Determination of the target brain area and channel localization should be based on these studies. Future studies should take advantage of fNIRS's precision in localizing brain functions by employing spatial estimation methods (e.g., virtual registration; Tsuzuki et al., 2007) and develop more advanced approaches for data acquisition and interpretation to further extend the potential of fNIRS in social cognitive research.

Neuroimaging Social Interactions of Young Populations

Infants' Brain Responses to Live Social Stimuli

While we have already discussed the significance of live stimuli, neuronal evidence supporting the impact of live stimuli has been reported by studies using various measurement modalities, such as fNIRS (Shimada & Hiraki, 2006), EEG (Jones, Venema, Lowy, Earl, & Webb, 2015), and MEG (Jarvelainen, Schurmann, Avikainen, & Hari, 2001). An fNIRS study of infants, for instance, compared live and non-live stimuli of human action and observed a stronger response to the live stimuli. This is not an interactive paradigm, thus the larger activation to the live stimuli may relate to factor (a) and (d) (Figure 2), as stated in the first section. To the best of our knowledge, hyperscanning of the infant brain has rarely been performed; we have therefore focused on single recording of fNIRS studies with live interactive stimuli.

Four fNIRS studies have examined the social cognitive brain activity of infants using live social stimuli. Although these studies did not employ hyperscanning methods, the majority used interactive paradigms. Pioneering work was reported in a study of fNIRS measurement of the prefrontal area during live joint attention episodes by Naoi, Kobayashi, Hara, Yamamoto, and Kojima (2008; also reported in a book chapter: Minagawa-Kawai, Naoi, & Kojima, 2009). Joint attention is a crucial milestone for development of infants' social and communicative abilities, and is defined as a shared attention of two individuals for one object, which reflects ability to understand another's intention. Naoi et al. (2008) performed live episodes of responding to joint attention (RJA) and initiating joint attention (IJA) to measure frontal hemodynamic activity with the event-related paradigm. Mothers held their infants (15 9-month-olds, age range: 7–12 months) with whom one experimenter interacted for RJA and IJA episodes. The results showed strong responses in the right lateral PFC and medial PFC areas to RJA, in contrast to strong selective activation in the dorsomedial PFC during IJA episodes. These results are consistent with fMRI studies with adults reporting engagement of the dorsomedial PFC for IJA (Mundy, 2003). This study was successful in capturing the cerebral response to interactive live stimuli, and suggested that infants' early cerebral substrates of intention develop at around 9 months. A recent study by Urakawa, Takamoto, Ishikawa, Ono, and Nishijo (2015) also focused on the prefrontal area, and measured the response to live peek-a-boo stimuli by comparing conditions of direct and averted gaze. The results of 7-month-old infants revealed a significant role of the dorsomedial PFC during live mutual gaze consistent with Naoi et al. (2008).

Two fNIRS studies examined activation in the frontal and temporal areas during social interaction. Although one of the standard methods to examine intention is joint attention, Lloyd-Fox, Szeplaki-Kollod, Yin, and Csibra (2015) used a unique method to investigate cerebral correlates of identifying communicative intention in 6-month-old infants. Two infants simultaneously participated in the experiment to interact with one experimenter. The conditional difference from the participating infant's view was whether the experimenter intended to communicate with him or the other infant. The experimenter would sing or speak with gestures to either one of the infants for each condition by differentiating direct eye gaze. They found stronger activations for the self condition in multiple regions of temporal areas. This study is noteworthy in its attempt to employ a naturalistic context; however, in such an ecological experiment, it was difficult to control various factors (i.e., speech, gestures, contingency) to determine the correlates of brain activation. Hakuno and Minagawa (2016) attempted to limit such factors with the use of a suitable baseline task. The study intended to observe brain responses to mutual gaze and contingency during structured play between an infant and an experimenter. The experimenter reacted to the infant's behavior in terms of eye gaze and contingent responsiveness for each condition. The results of 6–8-month-olds showed large responses in the TPJ and posterior superior temporal gyrus on the right side to the contingent condition. Although the TPJ's role in processing contingency is well known, this could be the earliest evidence of the TPJ's function. Importantly, such cerebral response to contingency in a social context may have been obtained due to the impact of interactive live stimuli.

Hyperscanning Mother–Infant Interaction

What makes it difficult? Interaction with a parent primarily fosters the fundamentals of social skills in human infants and children. Particularly, mother–infant bonding early in life has been shown to play a critical role for social cognitive abilities, including emotion regulation and social responsiveness (Feldman, 2015). Indeed, rich social stimuli interactively provided by a parent are linked to optimal behavioral and cognitive development (Cabrera, Fagan, Wight, & Schadler, 2011; Lugo-Gil & Tamis-LeMonda, 2008), unlike parental insensitivity, which resulted in increased risk of childhood psychopathology

(Murray, Halligan, & Cooper, 2010). Yet, less is known about the neurobiological basis underlying the parent–infant interaction, due to the methodological difficulty. The advent of the fNIRS system has provided an optimal solution, as it enables live measurement of the mother–infant interaction with reasonable spatial resolution. However, there are several significant difficulties in performing mother–infant hyperscanning, as reported by Minagawa-Kawai, Naoi, and Kojima (2009). One of the predicaments was the presence of artifacts in recordings due to facial movements: Mother–infant communicative interactions are always conveyed via facial gestures, including forehead and oral movements. These kinds of movements critically interfere with fNIRS signals. Among 10 mother–infant dyads tested, several mothers showed unusually large signals (Figure 3). The task in the block design included a baseline condition, wherein a mother showed a neutral face to an infant, and a target condition wherein, a mother positively interacted with an infant with a smile. The signal in Figure 3 appeared task-specific; however, deoxy-Hb as well as oxy-Hb exhibited an unusual rapid increase. This type of signal does not originate from the cerebral cortex, but from change of probe distance and/or probe separation from the skin due to facial movement. Systemic blood change due to induction of emotion may have partially contaminated the signals. Another difficulty involved fNIRS probe caps; even if infants (aged 8–12 months) accepted a probe cap attached to their foreheads, they occasionally disliked the NIRS caps on their mothers. These difficulties with hyperscanning of mother–infant interactions could not be overcome (Minagawa-Kawai, Naoi, & Kojima, 2009). This attempt yielded results similar to a rather conventional fNIRS study using prerecorded social visual stimuli of mother and infant, providing neuronal evidence of mother–infant attachment (Minagawa-Kawai, Naoi, & Kojima, 2009).

The above-mentioned issue regarding motion-related artifacts and systemic effects remains valid for hyperscanning fNIRS studies, regardless of the population type. However, as reviewed in the previous section, researchers have tried to avoid the issue by using suitable tasks for adult study. Even with child populations, a recent study by Reindl, Gerloff, Scharke, and Konrad (2016) successfully performed fNIRS hyperscanning under the setting of computer game play. Higher synchronized activations between a parent and child (aged 5–9 years) were observed in the left dorsolateral PFC area during the cooperation task relative to the competing task. This task, which does not always associate with facial movement, is an adaptive task to assess interaction between children and adults.

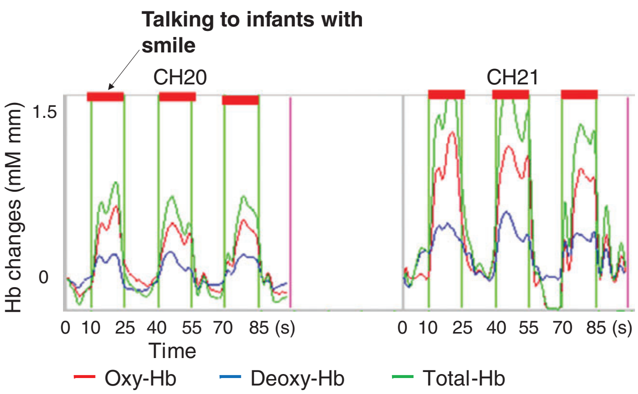

Figure 3 Hemoglobin changes predominantly elicited by motion artifacts during mother–infant interaction experiment.

However, this is not feasible for infant populations and populations with disabilities.

Synchronized brain activity between mothers and infants: Preliminary results and technical issues. It is known that human behaviors in nature tend to synchronize with others' movement, a phenomenon known as entrainment. This spontaneous synchronization involves various movements, such as walking, tapping, postural sway, and eye-blink (Okazaki et al., 2015; Shockley, Richardson, & Dale, 2009; Zivotofsky, Gruendlinger, & Hausdorff, 2012), which occur either explicitly or implicitly. Although the detailed neuronal basis underlying synchronization remains unclear, this motion-forming behavior may relate to the human mirroring system and/or self-organizing system, serving as a fundamental basis for human empathy (Koban, Ramamoorthy, & Konvalinka, 2017; Koehne, Hatri, Cacioppo, & Dziobek, 2016). It would appear that entrainment is characteristically observed in the most fundamental form of human dyad, mother and infant, as revealed by behavioral studies (Feldman, 2007, 2017). The degree of synchrony predicts infants' social development, such as self-control and empathy (Feldman, Greenbaum, & Yirmiya, 1999). Coherent physiological signals have also been observed for mother and infant. Specifically, cardiorespiratory activity was demonstrated to be synchronized between mother–infant dyads while infants lay on the mother's body (Van Puyvelde et al., 2015). Such synchronization is thought to be triggered by subtle perceptual cues, including eye gaze, subtle facial movement, and breathing, which may be processed implicitly.

Based on the findings reviewed above, it is now evident that examining mother–infant interaction without positive and spontaneous communicative signals is possible and meaningful. This allows for mother–infant hyperscanning free from several artifacts to be performed. Consequently, Minagawa (2016) carried out mother–infant hyperscanning during which mothers held their infants (holding condition) to compare to the control separation condition wherein an experimenter held the infants and the mothers were at rest. Infants were in an active sleep condition in both sessions. Each session lasted more than 5 min. Bilateral temporal area and frontal areas were measured using 44 channels for both the mother and the 3–4-month-old infants. Of the 20 participating dyads, the final data set included data from eight dyads, providing 4 min of clean data without artifacts. After preprocessing the data with the hemodynamic modality separation method (Yamada, Umeyama, & Matsuda, 2012) and wavelet-minimum description length, the mother and infant data were combined for each dyad (88 channels) to generate a time series of the data separated by condition. Independent component analysis–second-order blind identification (ICA-SOBI; Belouchrani, Abed-Meraim, Cardoso, & Moulines, 1997) was applied to the combined dyads' data in order to extract shared components across 88 channels. For components obtained from ICA-SOBI, we examined the difference of the components' amplitude between two conditions.

Figure 4 depicts preliminary results for holding versus control. Two components exhibited significantly larger amplitudes for the holding condition than for the control ($p < .05$, Wilcoxon-signed rank test). Figure 5 plots the time course of the component's amplitude and Figure 4 indicates where the component originated from and its amplitude of contribution to that component. The largest synchronization for the holding condition was observed in the mid-channel of the lowest channel line, which is assumed to be near the anterior orbitofrontal cortex (OFC) for both mother and infant. Namely, activation of the anterior left OFC was more strongly synchronized when mothers held their infants. As the OFC is known to be a significant cerebral area engaged in maternal attachment (Minagawa-Kawai, Matsuoka, et al., 2009; Schore, 2000), the results may further support its role. Other than that channel, large synchronizations were observed near the right PFC for mothers, while those for infants were in the right temporal and parietal areas, including TPJ. Unlike the correlation analysis or wavelet-coherence method generally used for fNIRS hyperscanning, ICA-SOBI allowed us to assess several components shared across different channels.

Although this is a preliminary study with limited participants, the results demonstrate that fNIRS has the ability to assess two-person synchronization, even in infants, with relatively good spatial resolution. As previously mentioned, synchronization relates to the self-organizing system and human empathy. Thus, fNIRS measurement of Hb synchronization in infants could be a powerful methodology for the developmental study of social neuroscience. In fact, using this method, hyperscanning between parents and infants at risk for ASD has been successfully performed at our laboratory. However, regarding the hyperscanning discussed above, several issues remain unresolved. One such issue is the analysis method. For the analysis, ICA-SOBI was used to extract hemodynamic activities shared between mother and infant; however, the hemodynamic time course differs between adult and infant (Minagawa-Kawai et al., 2011), most likely due to different rates of synaptogenesis and angiogenesis in the young developing brain. Thus, in discussing the synchrony, we require a novel analysis method that can detect synchrony with different frequencies. Further, the present method allowed for the extraction of shared components during a certain period of time (4 min in this experiment); such a time window was not sensitive

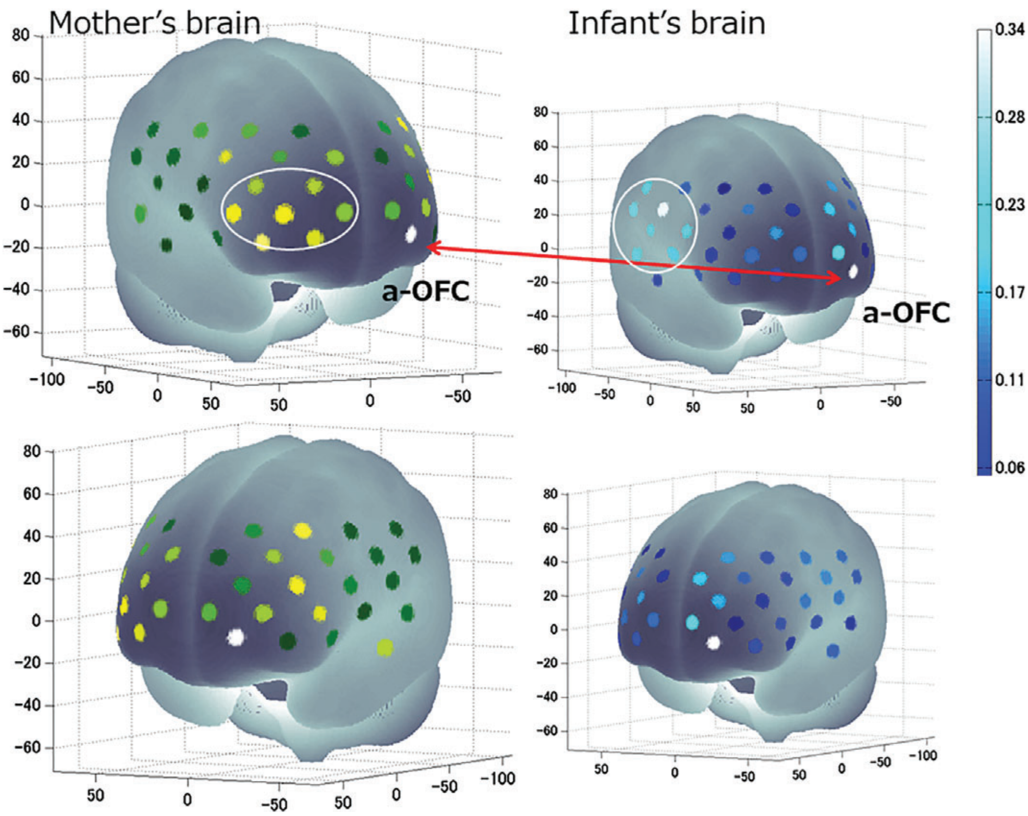

Figure 4 Brain synchronization when the mother held her infant. Amplitude of contribution to a synchronized component that is larger for the holding condition than the separate condition is plotted for mother and infant brains. Top panels indicate a view from the right side and bottom panels from the left side.

enough to detect a dynamic interplay between the mother and infant, which occurs over a relatively short period of time. As the aim of this experiment was to ascertain long-term synchronization, future studies should explore the dynamic aspect of mother–infant interaction further.

Mechanisms, Future Directions, and Conclusions

Mechanisms of Brain-to-Brain Coupling

Although hyperscanning of social brains is a burgeoning field, it has yielded limited insights into the mechanism of inter-brain coupling: the focus of many investigations that have used hyperscanning. However, on the basis of the studies reviewed previously, we would like to introduce a hypothetical mechanism for interactive brain systems, particularly focusing on synchronized neural activities.

The action–perception loop (Hari & Kujala, 2009) of the human brain appears to be one of the significant mechanisms that underlie synchronization; this loop works within the brain but also between different brains (Konvalinka & Roepstorff, 2012). Specifically, the behavior of individual A is tightly linked to the brain activities of individual B by eliciting B's mirror neuron system (MNS) activations and inducing automatic mimicry. On receiving B's contingent behavioral signals, A's brain is similarly affected; this results in causing a similar, contingent action. By exchanging such behavioral signals implicitly or explicitly, the inter-stimulus (action) interval between A and B would gradually decrease. As a result, their neural activities as well as behaviors would become in sync. This process was partly verified by a series of fMRI studies. Firstly, Sasaki, Kochiyama, Sugiura, Tanabe, and Sadato (2012) showed that the middle temporal gyrus (MTG) and IFG, which are known to be a fundamental neuroanatomy of MNS, are engaged in the automatic mimicry. In particular, connectivity between MTG and IFG was revealed to play a significant role in sending information of action execution and action perception. In fact, later fMRI hyperscanning studies indicated that IFG and MTG are the brain areas involved in the inter-brain coupling by consistently demonstrating synchronization of the right IFG of two persons during a joint attention task (Koike et al., 2015, 2016; Saito et al., 2010; Tanabe et al., 2012). The IFG synchronization appeared to be induced by behavioral synchronization of eye blinks, because amplitude of the IFG synchronization positively correlated with that of behavioral synchronization. Furthermore, intra-brain connectivity between MTG and IFG increased after a joint attention task and its increment correlated with the amplitude of the IFG synchronization within the dyad (Koike et al., 2016; Sadato, 2016). They further revealed that associative learning contributes to the construction of such synchronization networks (see the section on fMRI

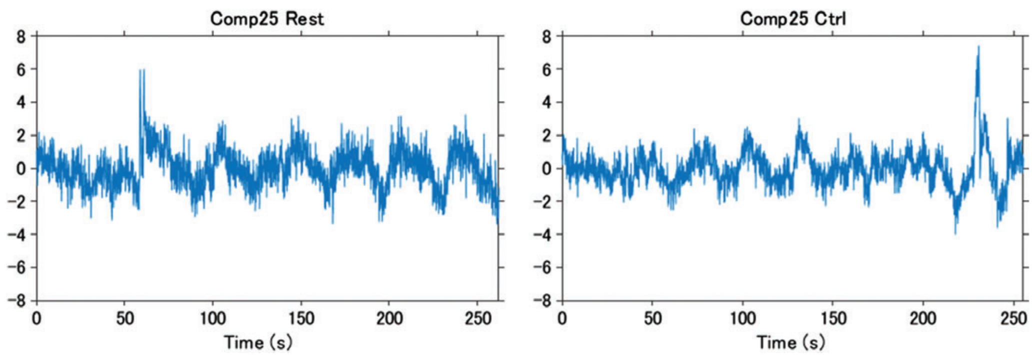

Figure 5 Time course of component amplitude for the mother–infant condition (left) and stranger–infant condition (right). These components are derived from all of the channels. This is an example of one dyad.

Hyperscanning, above, for more details). In summation, the IFG and MTG—as components of the MNS network—play crucial roles in inter-brain coupling during interaction (Figure 6).

Though its relation to the MNS network remains unclear, the mentalization network (MENT; Frith & Frith, 2006) is also proposed to be involved in inter-brain coupling (Schilbach et al., 2013) (Figure 6). Experiments on the interactive social paradigm have shown that activation of the MENT does not necessarily require emotional processing or explicit assessment of mental state (Schilbach et al., 2010), namely, MENT activates in response to eye gaze or presence of intention. This phenomenon may be referred to as *presence of mind*, as indicated by (d) in Figure 2. Results of infant fNIRS research on the live-interactive paradigm agree with this view. Naoi et al. (2008) and Urakawa et al. (2015) demonstrated strong activities of the dorsomedial PFC during the mutual gaze of joint attention tasks that did not accompany explicit emotional processing. Our fNIRS study supplies additional evidence supporting the dorsomedial PFC as a processor of sense of human mind: Using a live interactive paradigm, Hakuno (2018) measured responses of frontal and temporal areas of 6–7-month-old infants to human contingent stimuli (e.g., smile of the experimenter) in comparison to the responses of the aforementioned areas to non-human contingent stimuli (LED light). The study found that the dorsomedial PFC area evinced strong activation, as well as connections to the TPJ area, exclusively in response to human contingent stimuli. The effect was observed regardless of the valence of stimuli (positive and negative). Although these infant studies are not hyperscanning experiments and therefore lacking in sufficient evidence, some adult fNIRS hyperscanning reported synchronization of the dorsomedial PFC (Liu et al., 2016) and frontal pole areas that may recruit the medial PFC (Nozawa et al., 2016) only during cooperative tasks.

The TPJ is also a part of the MENT (Adolphs, 2009; Frith & Frith, 2006), and seems to provide an essential contribution to brain coupling: It distinguishes the signals addressed to self or others, and processes intentions and purposes of social signals to send to the MPFC (Gallese, Keysers, & Rizzolatti, 2004; Van Overwalle, 2009). A series of fNIRS studies using the live interactive paradigm (Hakuno, 2018; Hakuno & Minagawa, 2016) consistently showed the TPJ's role in processing contingency. Furthermore, an fMRI study (Bilek et al., 2015) and an fNIRS study (Jiang et al., 2015) reported inter-brain synchrony of TPJ during social interaction. Contingency is an important factor for interactive behavior as indicated by (b) in Figure 2.

As the network of reward processing is associated with the MENT, we assumed that it is also engaged in brain coupling. Social interaction itself is generally a rewarding process by which we can share feelings and experiences with others (Tomasello, 2009). Our preliminary study on mother–infant hyperscanning supported this interpretation by revealing inter-brain coupling of the OFC areas. Reward processing is critically related to associative

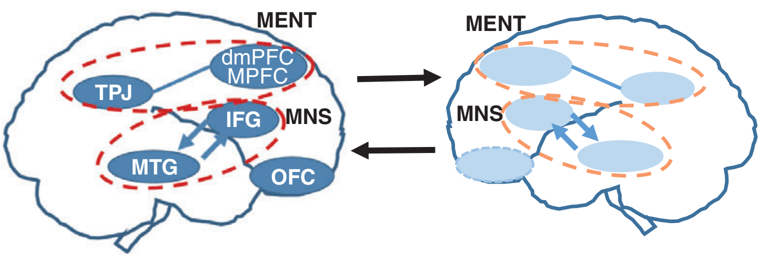

Figure 6 Brain areas that engaged in inter-brain coupling. MNS, MENT, and additional reward networks are cerebral substrates operating within the two-in-one brain system.

learning, which shapes the MNS network (Koike et al., 2016).

As evidenced by several studies, regardless of their measurement modality (Koike et al., 2016; Pan et al., 2017), inter-brain coupling is more easily observed between a familiar dyad than an unfamiliar dyad. Accordingly, more effective synchronization could be assumed between family members or colleagues in a professional performance, such as dance and music. Although such a synchronization network among familiar members could be regarded as an automatic process modulated partly in a top-down fashion, it could have been organized as a result of a bottom-up type of associative learning reported by Koike et al. (2016). Inter-brain coupling observed between a mother and her infant could present an example of this type of synchronization. Such a pre-established network could facilitate future human interactions. In this sense, inter-brain coupling would not always be the result of behavioral signal exchange, but that of a pre-organized network that can drive brain activity to enhance interaction. Other than such behavior-induced brain coupling, another type of top-down modulation may exist (Roepstorff & Frith, 2004) that may not accompany action perception.

To finalize this section regarding brain-coupling mechanisms, we will mention a temporal issue concerning the examination on the interactive brain. As previously reviewed, synchronization mediated by the action–perception loop emerges from exchanges of action signals within finite time windows. Thus, in many cases, the short time frame for each action cluster may inform the analysis window, particularly to analyze the causality of brain synchronization. However, once inter-brain activities are tuned and synchronized, long analysis time windows may better capture the synchronized components between two brains than observing dynamic changes.

Concluding Remarks

As described in this review, by following hyperscanning studies by EEG or fMRI, researches with fNIRS have played a dominant role in developing a new field of neurobiology: interactive social neuroscience. Although infant fNIRS hyperscanning studies with interactive paradigms have yet to be perfected, the studies reviewed above have demonstrated the potential of fNIRS to reveal the development of social cognitive abilities. This will eventually contribute to the disclosure of the ontogeny and phylogeny of the human interactive social brain.

Based on the evidence regarding adult interaction, it seems that this line of fNIRS research may diverge into two directions, one being mobile recordings for practical use. As reviewed in the second section, an fNIRS system with several channels has successfully observed social cognitive activities. With the technical advance of fNIRS instrumentation, we may be able to obtain the system and use probes with a more comfortable setting. This type of system could be utilized in various practical settings, such as education and marketing. Big data obtained by this modality would contribute to machine learning data for artificial intelligence.

The other direction is rather mainstream: basic research in social neuroscience. At present, the main interest of most fNIRS and EEG hyperscanning studies is determining the condition under which brain areas are in sync. This type of study would expand our knowledge and may yield an aforementioned practical use. However, as has been examined chiefly by fMRI studies, fNIRS studies should focus more on the basic mechanisms of interactive brains. As summarized in this review, MNS and MENT networks are two dominant mechanisms that contribute to inter-brain coupling. On the other hand, detailed mechanisms remain to be uncovered. Fortunately, fNIRS can measure most of these networks; fNIRS studies should therefore make the most of their advantage for live interactive experiments to clarify the two-in-one brain system. Defining the relationship between the MNS and MENT is one of the crucial issues in need of further investigation. Importantly, these networks will be uniquely revealed by hyperscanning with the interactive paradigm. Future studies should also investigate these interactive processes by showing causality, although there have already been some successful attempts at this. As stated in the introduction, bidirectional social interaction may involve feedforward and feedback processes between agents. There may be some global interactive social rule that depends on the social context and may crucially affect the MNS and MENT. Identifying the cerebral substrates underlying such processes, which may be dependent on the agent's personality and social background, would provide essential information for future research. To this end, simultaneous recording of behavioral and physiological data to correlate with fNIRS data will be beneficial. In addition, employing fMRI separately from fNIRS would be a reasonable option due to the higher spatial resolution and improved assessment of deep brain areas, including the reward network. Exploitation of fNIRS hyperscanning by more social neuroscientists in the fields of fMRI, EEG, or MEG would empower interactive social neuroscience in the future.

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【概要 1-１】fNIRS ハイパースキャンニングを用いた２者間の社会的相互作用の脳機能研究

Neural synchronization of social signals during naturalistic interaction: fNIRS study employing general linear model (GLM) and behavioral classification

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Introduction

Investigating a single human mind is insufficient to fully understand the neural mechanisms underlying human social behaviors, as the human social brain does not just observe social stimuli, but instead interacts in social encounters. Second-person neuroscience, or interactive social neuroscience, considers the dynamic interplay of multiple brains, and has become a burgeoning field of interest (Konvalinka and Roepstorff, 2012; McDonald and Purdue, 2018; Minagawa et al., 2018; Schilbach et al., 2013; Redcay et al., 2018). To date, hyperscanning technique has been actively used to study the neural correlates of multiple individuals engaged in social interactive situations. In such studies, the measurement modality determines what (and to what level) can be examined. Namely, electroencephalography (EEG) and functional near-infrared spectroscopy (fNIRS), which do not rigidly restrict participants' movement, are relatively good at imaging naturalistic human interactions, unlike functional magnetic resonance imaging (fMRI) and magnetoencephalography (MEG), which instead provide spatially detailed neural information (Minagawa et al., 2018). Due to its high flexibility and desirable spatial and moderate temporal resolution, fNIRS hyperscanning takes its place in the field of naturalistic imaging.

Early fNIRS hyperscanning studies adopted highly experimentally controlled tasks, which may not be sufficiently naturalistic, such as simultaneous motor action (Cui et al., 2012; Funane et al., 2011), motor imitation (Holper et al., 2012), and coordinated speech rhythm (Kawasaki et al., 2013). In these tasks, two participants were required to act synchronously, and thus the observed brain synchronization can be interpreted as being related to simultaneous motor movement. More recent studies have employed natural or free settings, such as non-structured verbal communication (Jiang et al., 2012; Jiang et al., 2015), eye-to-eye contact (Hirsch et al., 2017), turn-taking games (e.g., Liu et al., 2016), and group creativity (Xue et al., 2018). Target behaviors for these experiments were unscheduled, and thus, behavioral coding of the target behavior was necessary in most cases to calculate its correlations with brain synchronization.

These studies raise a dilemma: as tasks are made more natural, more time-consuming coding work is necessary. This is not an insignificant problem. Usually, two trained coders code these social behaviors, and subsequently, inter-coder reliability is tested at the time-point level for consistency, and the final correlation analysis between neural synchronization and behavior is performed using the highly consonant part of the coded behavior (e.g., Dai et al., 2018; Jiang et al., 2012). Such analysis is acceptable for short-term social interactions but difficult for longer ones.

Human interactive behaviors may not necessarily be short, and naturalistic behaviors should be captured free from such time restrictions.

The present study attempted to address this problem by proposing a new approach for naturalistic imaging with fNIRS. This methodological consideration was the first aim of the present study. More concretely, we employed a recent technique of image engineering, sometimes called “computer vision”, for automated behavior estimation from the video recording. Then, to combine the neuroimaging data, namely, the brain coherence index (i.e., wavelet transformed coherence, WTC) across two brains, with such automatically extracted behavior, a general linear model (GLM) was applied. With this method, we can estimate which social signal correlates with which type of brain synchronization, in addition to the ordinarily performed task-condition-based analysis.

The second objective of this study was to uncover brain synchronization mechanisms related to human cooperative behavior under naturalistic social conditions. As stated above, hyperscanning studies with fNIRS have typically assigned groups of participants to tasks that vary in their degree of naturalness. Such tasks generally have in common that they have relatively fixed goals that are known in advance. For instance, participants had to press a button at the same timing as much as possible (e.g., Cui et al., 2012; Funane et al., 2011) or complete a Jenga game together (Liu et al., 2016). For such tasks, as long as one’s non-verbal and/or verbal behavior does not deviate significantly from the task instruction, one does not need to mentalize his/her partner’s thinking moment by moment. However, human beings are social creatures able to cope with this dynamic interplay of thinking. Cooperative behaviors play an important role in daily communication, which is full of complex cases such as situations where the ultimate goal of communication is highly variable, depending on the ever-changing behavior and mental state of the communicating partners. Such situations require the communicating parties to continuously mentalize the intention of their partners and adjust their own behaviors accordingly and constantly.

To capture this dynamic aspect of social interaction under naturalistic situations, the present study designed a joint computer game with considerable freedom in terms of verbal/nonverbal communication but a high level of required mentalization of the partners. In addition, this computer-based task enabled us to record participants’ gaming behavior digitally. Specifically, two players were asked to design the interior of a room that satisfies either both parties or just oneself, without limitations on time or communication. Two conditions—cooperative and independent—were compared to reveal neural coordination across two brains during cooperation. Furthermore, from global neural signals for cooperation, we tried to extract specific signals corresponding to specific social behaviors (e.g., face-to-face). The facial orientation of a participant, which may be roughly comparable in presence or absence of eye-contact, contains active social cues to his/her partner (Emery, 2000; Ethofer et al., 2011; Hirsch et al., 2017; Koike et al., 2019; Myllyneva and Hietanen, 2015; Saito et al., 2010; Schilbach, 2015). Accordingly, the present study used face orientation of the dyads as GLM regressors to isolate the correlated neural synchronization between specific brain regions. Previous hyperscanning studies have demonstrated across individual neural synchronization induced by interactive tasks involving social behaviors like mutual gaze and cooperation in the mentalizing network (MENT) covering the dorsomedial/medial prefrontal cortex (dMPFC/MPFC) (e.g., Abe et al., 2019; Liu et al., 2016) and the temporo-parietal junction (TPJ) (e.g., Abe et al., 2019; Bilek et al., 2015; Hirsch et al., 2017; Jiang et al., 2015; Tang et al., 2016; Xue et al., 2018), as well as in the mirror neuron system (MNS) (Koike et al., 2019) encompassing the inferior frontal gyrus (IFG) (e.g., Jiang et al., 2012; Koike et al., 2016; Saito et al., 2010; Tanabe et al., 2012) and the middle temporal gyrus (MTG) (e.g., Hirsch et al., 2017). Such brain regions or networks are expected to relate to face-to-face behaviors.

The present study proposed a new analysis approach without manual behavioral coding to extract the neural correlates of targeted social signals (here, face-to-face). With this approach, we sought to uncover behavior-specific brain synchronization among various social interactive behaviors involved in a task with collaborative creation without time constraints, which requires dynamic interplay of mentalization processes across two brains.

Methods

Participants

Seventy-eight college students (54 females, age range: 18–32 years, mean ± standard deviation (SD) = 19.8 ± 2.0 years) participated in the experiment. This resulted in 39 same-sex dyads (27 female dyads). Five participants were left-handed. All participants had normal visual, hearing, and language abilities. None of them reported any neurological or psychiatric disorders. After instruction from the experimenters, written informed consent was obtained from all participants. The experiment protocol was approved by the ethical board of Keio University, Japan.

Task and Procedure

We designed a turn-based interior design browser game that ran on a server. Two client computers with a touch-panel display (Lenovo Yoga 900, 13.3 inch) were connected to the server with remote desktop software (TeamViewer 11) by LAN cables, so that the game could be played in turn by the two participants of a dyad through the two client computers. Operation of the game on one client computer was almost simultaneously projected on the screen of the other client computer, with a delay less than the NIRS sampling period (100 ms).

The two participants of a dyad sat face-to-face and manipulated their own touch panel (Fig. 1a, b). For the entire experiment, each dyad completed two sessions of cooperative game and two sessions of independent game, respectively. The order of the four sessions was counterbalanced among dyads. Before fNIRS recording, each dyad practiced until they fully understood the procedure and rules of the game under the instruction of experimenters. They were also informed that each room that they designed would be rated by three referees to motivate them.

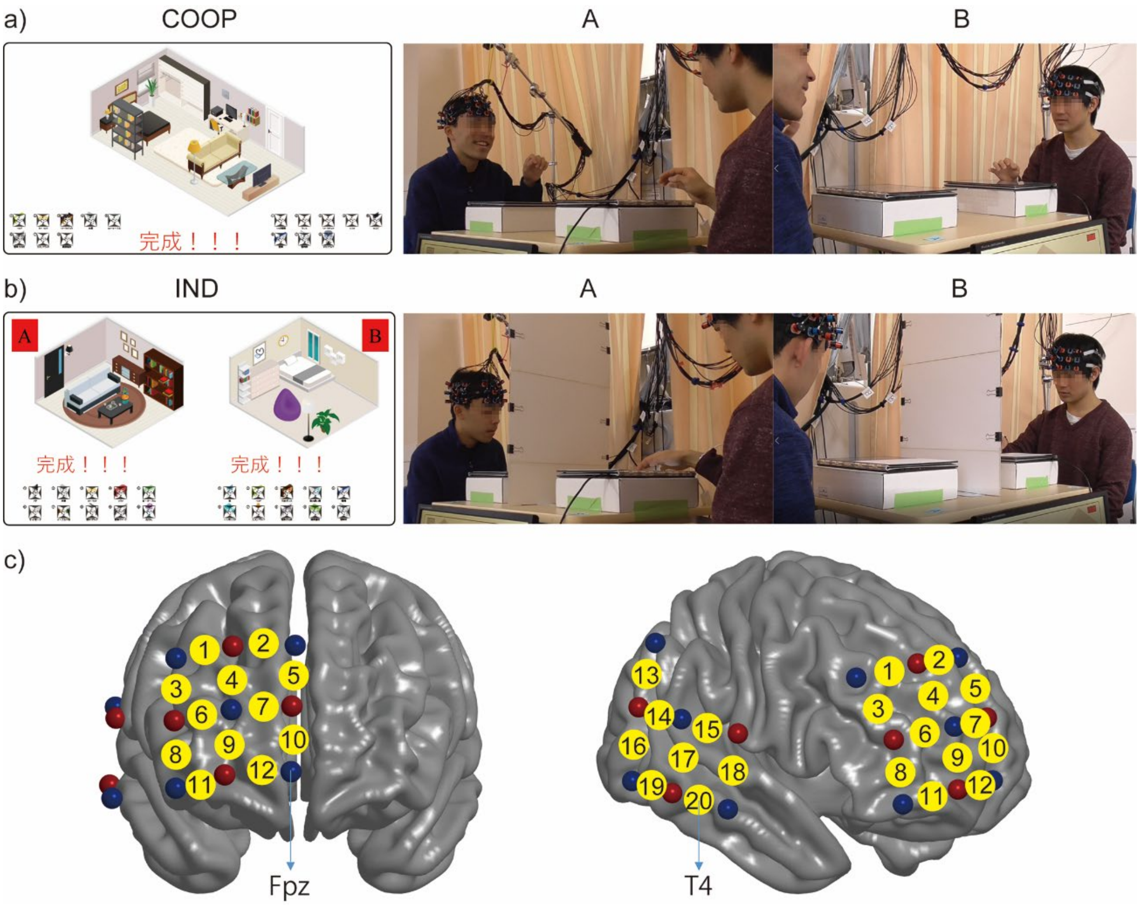

Fig. 1 Experimental design. a) and b) Experimental images for the cooperative (COOP) and independent (IND) task. Left side: completed interior design for a sample dyad. Right side: video recorded for a sample dyad. A: participant A, B: participant B. c) Probe set and channel layout (20 in total) on the PFC and temporal region of the right hemisphere. Red dots: emitters; blue dots: detectors; yellow dots: channels.

In the cooperative (COOP) condition (Fig. 1a), the participants of a dyad were asked to furnish a room that satisfies not only themselves but also their partner, in a turn-based manner. Therefore, they were encouraged to communicate verbally/nonverbally as much as necessary to form a consensus in furnishing a room. For each turn, four candidates of a specific piece of furniture or interior (e.g. bed and lamp) were presented, and the on-duty participant was asked to choose one from the four and place it in a position that suits the room well (Supplementary Fig. 1). In one turn, only the on-duty participant was allowed to manipulate the game. The whole landscape of the to-be-designed room was presented on the screen of each participant. Thus, they shared the same view of the on-going game, including the interior manipulation by their partners. The selection and placement of a furniture/interior could be modified (press the "cancel" button) as much as necessary until a consensus was reached (press the "OK" button) (Fig. 2). After the "OK" button was pressed, no modification was allowed and the next turn for the other person started. There were 16 types of furniture/interior (16 turns) in total and the sequence of their appearance in one session was fixed. The dyad had to complete the design of the present interior to proceed to the next interior. When the design of all 16 types of furniture/interior were completed, "Mission accomplished" (in Japanese) was presented on the screen to the dyad. Each session of COOP took about 11.5 minutes (SD = 9.6).

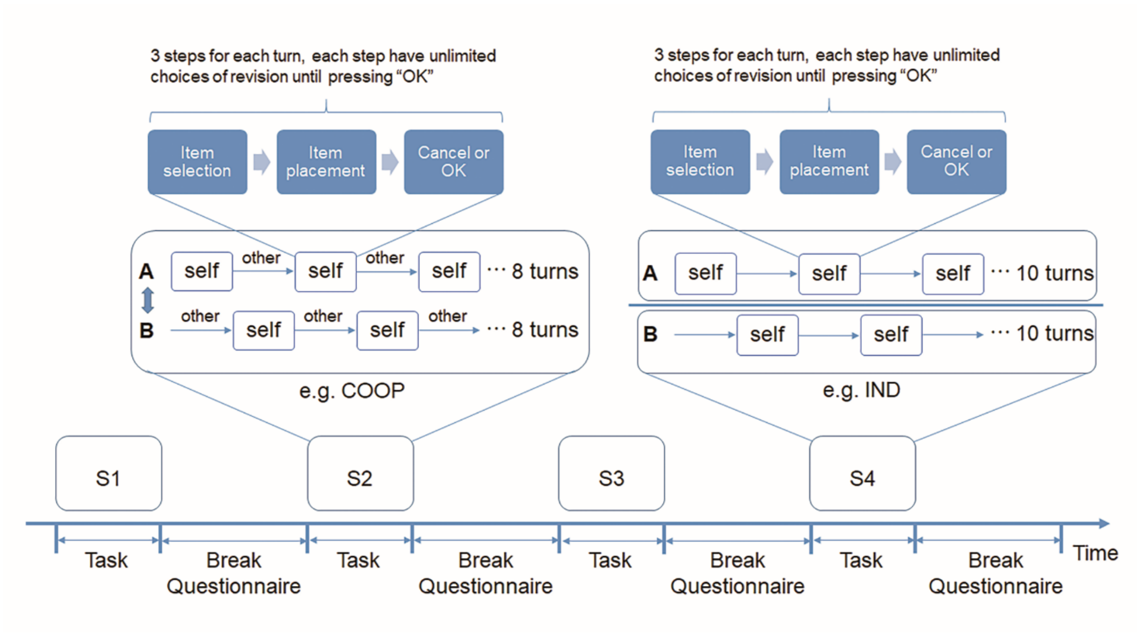

Fig. 2 Experimental paradigm for the turn-based computer game. S1–S4: four counterbalanced sessions including two cooperative (COOP, e.g. S2) and two independent (IND, e.g. S4) ones. Task and break: no time limit. A simple questionnaire was answered by each participant during the break.

In the independent (IND) condition (Fig. 1b), each participant of a dyad was asked to furnish a room all by her/himself. A partition board was physically placed between the two participants of a dyad, so that they could not see each other (right panel of Fig. 1b). No communication was allowed during IND. General rules and procedures of the game were identical to those in the COOP condition, except that the total number of interiors was 10 for each participant's room, and they were never able to see their partner's room. To control the waiting time to be similar to that in the COOP condition, each participant was supposed to engage in the task one by one. Namely, each participant had to wait for his/her own turn until the partner finished, which was indicated on the screen. Each session of IND took about 9.6 minutes (SD = 4.1).

Two video cameras (Full HD, 29.97 fps) were used to videotape the whole procedure of the experiment in order to record both verbal and nonverbal behaviors (e.g., face orientation) of the participants. Each camera focused solely on one participant of a dyad. In order to synchronize the video recording with the fNIRS signal, both cameras also recorded the on-going procedure of the game through one large display showing an identical screen to the monitor. This large display was positioned by the side of the dyad so that it was out of participants' sight (Fig. 1a, b, lower part of right panel).

fNIRS data acquisition

An optical topography system (OT-R40, a version for research of ETG4000, Hitachi Medical Company, Japan) was used to collect imaging data from the two participants of each dyad simultaneously. The absorption of near-infrared light at two wavelengths (695 and 830 nm) was recorded at a sampling rate of 10 Hz.

Two sets of identical customized probe arrays consisting of two separate probe pads were used for each dyad. For each set, one 3 × 3 probe pad was placed on the right prefrontal region (five emitters and four detectors, 30-mm probe distance, forming 12 measurement channels (CH)). The lowest probe line was placed along the Fp1–Fp2 line, with the lowest right-edged probe positioned on Fpz, according to the international 10-20 system; consequently, CH5 and CH10 were aligned along the sagittal reference curve (Fig. 1c). The other 3 × 3 probe pad (partially used, four emitters and three detectors, 30-mm probe distance, forming 8 eight measurement channels, Fig. 1c) was placed on the right temporal region. The lowest probe line was placed along the horizontal reference curve, with CH20 positioned on T4. The virtual registration method (Singh et al., 2005; Tsuzuki et al., 2007) was utilized to estimate the brain area covered by each fNIRS channel according to either the Automatic Anatomical Labeling (AAL) or the Brodmann area (Chris Rorden's MRIcro) (Rorden and Brett, 2000). These probes targeted to measure the PFC and the TPJ regions in the right hemisphere, which had shown to be robustly involved in social interactions (see Introduction section). All probes were adjusted carefully to ensure consistency of the positions on head across participants by measuring each participant's head size (e.g., nasion–inion length) to apply the international 10-20 system.

Questionnaires

Participants filled in the Autism Spectrum Quotient (AQ) before the experiment. After each fNIRS task session, they also filled in a task questionnaire (inquiring degree of satisfaction, cooperativeness, concentration, etc.). No discussion was allowed during the questionnaire session. Other than these, the Temperament and Character Inventory (TCI) was assigned before the experiment, and a familiarity questionnaire was performed twice at pre- and post-experiment. In addition, electrocardiogram and skin conductance response were recorded during the experiment. However, these were not analyzed in the present study because they were for other research purpose.

fNIRS data analysis

Changes in oxygenated hemoglobin (oxy-Hb) and deoxygenated hemoglobin (deoxy-Hb) concentrations were calculated in each channel using the modified Beer–Lambert law. The present study focused on the changes in oxy-Hb, the most sensitive indicator of changes in regional cerebral blood flow in fNIRS (Hoshi, 2007). For preprocessing, the hemodynamic modality separation method (Yamada et al., 2012) was applied to the oxy-Hb and deoxy-Hb data to remove systemic related artifacts. Then, WTC (Grinsted et al., 2004) was calculated to evaluate the cross-correlation between the two fNIRS time series generated by the dyads as a function of both time and frequency. This was applied to assess the synchronized hemodynamic signals between two persons as has been generally used in previous fNIRS hyperscanning studies (e.g., Cui et al., 2012). Specifically, for each channel, WTC was applied to the time series of oxy-Hb from the two participants of a dyad (to generate 2D coherence maps). As each participant of a dyad was measured at 20 channels, there were 20 identical channel pairs and 190 different channel pairs (here, e.g., CH1–CH20 and CH20–CH1 were considered as one different channel pair for a dyad), totaling 210 channel pairs, for each dyad. For each identical channel pair, one WTC value was obtained, while for each different channel pair, two WTC values were obtained (e.g., WTC between CH1 of participant A and CH20 of participant B, and WTC between CH20 of participant A and CH1 of participant B). In addition, there were 91 frequency bands at 1/3 octave interval from 0.0093 Hz to 4.7746 Hz for each channel pair. We calculated the mean value of the WTC time series for each channel pair at each frequency band, resulting in 210 × 91 = 19,110 channel-channel-frequency (ch-ch-fr) combinations of mean WTC for each dyad.

To investigate between-brain synchronization (BBS), we compared the mean WTC between the COOP and IND conditions. A two-tailed sign test was applied to each ch-ch-fr combination with a correction of multiple comparisons by false discovery rate (FDR). For the FDR correction, the linear step-up procedure was used (Benjamini and Hochberg, 1995). Those ch-ch-fr combinations with $p < 0.001$ (FDR-corrected) were considered statistically significant. Note that for the FDR p-value calculation, we treated the p-values from identical channel pairs and different channel pairs identically, though they were obtained from different sample sizes (i.e., 39 for each identical channel pair, and 78 for each different channel pair).

Meanwhile, the WTC within each participant (within-brain synchronization, WBS)—that is, the functional connectivity within a brain—was also calculated for each ch-ch-fr combination. There were 190 different channel pairs for each of the frequency bands, yielding $190 \times 91 = 17{,}290$ ch-ch-fr combinations in total. The same statistical method and criterion as in BBS was used.

Behavioral data analysis

As a pivotal social signal in participants' behaviors, we focused on the face orientations of dyads to model in this study. OpenFace 2.1.0 (Baltrusaitis et al., 2018), an open-source toolbox for Matlab (Mathworks Inc.), was used to estimate the face orientations of dyads in the two sessions of the COOP condition. OpenFace 2.1.0 can automatically detect facial landmarks for every frame and track the face orientation from video sequences (Fig. 3, left panel). Face orientation was estimated as rotation in world coordinates with the camera serving as the origin, and was represented as pitch, yaw, and roll form in radians.

We extracted face orientation data using automatic tracking in OpenFace 2.1.0. Periods with confidence values of landmark detection smaller than 0.8 were considered unreliable periods. The unreliable periods and the 30 frames (about 1 second) pre- and post- unreliable periods were excluded from the face orientation data.

As the display of each participant's touch panel was placed on a desk, the participant had to raise his/her face to look at the partner. We confirmed from the video that the participants raised their faces when they actively communicated to their partner and tried to observe their partner's state. In addition, we expected that the pitch angle, rather than the yaw and roll angle, would directly represent the posture of one's face to one's partner. Therefore, we exclusively focused on the pitch angle of the face orientation.

The pitch angle was transformed into a z-score to ignore the difference between the heights of dyad faces, and this was considered as the parameter for evaluating face-up events. For the criterion of classifying a face-up state in each dyad, we used 2 SD of the z-scored pitch angle as the threshold (Fig. 3, right panel; Supplementary Fig. 2, upper panel). This strict classification threshold would pick up about 2.3% of the video sequence as face-up states, and we expected that such a strict threshold would reliably extract face-up events, which can be considered as obvious social behavior, roughly corresponding to mutual gaze.

Face-up events were labeled in the two COOP sessions (Supplementary Fig. 2, lower panel) to utilize in the following GLM analysis. This labeling procedure extracted the temporal information of 1) when both participants raised their face at the same time ("both-up" events) and 2) when only one participant raised his/her face up ("self-up" and "other-up" events). Periods with consecutive events of one of these three types were regarded as face-up epochs and served as three regressors in the following GLM analysis.

Assessment of WTC correlates of social behaviors (WTC-GLM)

The GLM is a general model of multivariate linear regression. To investigate which type of social behavior was associated with synchronization between which brain areas, relationships between WTC and interactive behaviors (here, face-up events) were examined using GLM. WTCs that showed significantly larger values ($p < 0.001$) in COOP than in IND were used as dependent variables. Further, WTC from one representative frequency band was selected for each channel pair of interest, as WTCs from adjacent frequency bands were highly correlated. More specifically, the frequency band that showed the smallest *p*-value was selected. When two or more frequency bands had the same minimal *p*-value, the middle band was selected. For GLM analysis, the time courses of the above-mentioned three types of face-up events, in addition to constant serving as regressors, were linked to the time course of the WTC at each representative ch-ch-fr of interest selected by the above criteria. First, we adjusted the time courses of WTC (Y) and the behavioral regressors (X). Specifically, the time courses of the behavioral regressors were down-sampled to 10 Hz to correspond to that of the WTC. In addition, the time course of WTC was adjusted for the delay-of-peak effect (4 seconds). As the WTC is a temporal-spectral correlation between two fNIRS signals, not hemodynamic data, we modeled the active epochs in the regressors using box-car shapes. Second, we estimated the coefficient β to minimize the error ε, which was the difference between the WTC (Y) and the product of β and the regressors X, for each ch-ch-fr of interest (see the following equation).

$$Y = \beta X + \varepsilon$$

Y: WTC matrix

X: Design matrix ("both-up", "self-up", "other-up", and constant; four regressors)

Third, the β for "both-up" (identical for the two participants in a dyad) and "either-up" ("self-up" of participant A is identical to "other-up" of participant B in a dyad, and vice versa, so they were combined as "either-up" for each dyad) regressors in each ch-ch-fr of interest (COOP > IND) were tested against zero, respectively, using a one-sample *t*-test (FDR-corrected). Finally, the βs for "both-up" and "either-up" regressors were compared using paired two-sample *t*-tests (FDR-corrected).

Among the 39 dyads, only those with valid epochs that satisfied the following two criteria simultaneously were used in the GLM analysis: both participants of a dyad had 1) reliable face orientation data when the pitch angle of each participant's face orientation was above 2 SD of his/her own data (Fig.3); and 2) usable fNIRS data for WTC calculation. Consequently, 22 dyads satisfied the first criterion and 15 dyads satisfied both criteria and were used in GLM analysis.

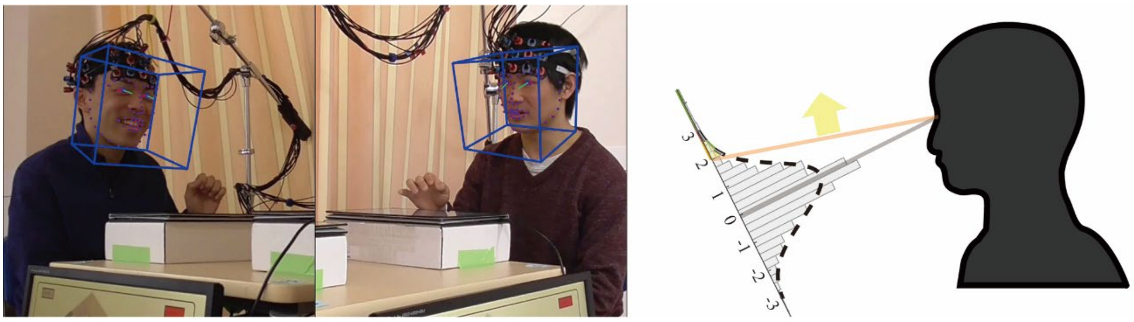

Fig. 3 Automated detection of face-up events using OpenFace 2.1.0. Left: illustration of the face landmarks (represented using dots) and face orientations (blue cubes) of a sample dyad. Right: illustration of the threshold (2 SD) used for the detection of face-up events. The axis represents the *z*-score of the pitch angle.

Correlation between WTC and questionnaire scores

To investigate the relationship between the activity of each ch-ch-fr of interest that showed a significant difference in the WTC-GLM analysis and subjective factors for social communication, we performed a series of correlation analyses. Specifically, the averaged WTC during the two COOP sessions for a particular ch-ch-fr that showed a significant difference between “both-up” and “either-up” in the β of WTC-GLM analysis was selected as the dependent variable. Then, AQ and task questionnaire scores were calculated and normalized. Finally, a series of Spearman correlation tests were performed between the WTC of each ch-ch-fr of interest and the scores of the AQ inventory and task questionnaires.

Results

Between-brain synchronization (BBS)

For the BBS, a significant difference ($p < 0.001$, FDR-corrected) between COOP and IND was found in 658 ch-ch-fr combinations, among which 633 showed significantly stronger WTC in COOP than in IND (COOP > IND). The remaining 25 showed significantly stronger WTC in IND than in COOP (COOP < IND). This indicates greater BBS for COOP, and this effect was relatively concentrated in frequencies around 0.2–0.3 Hz. In contrast, the significant frequency bands were more scattered (0.15–1.04 Hz) for COOP < IND (Supplementary Table 1, Supplementary Fig. 4). For a given channel pair, the frequency band with the smallest *p*-value was selected as the representative ch-ch-fr combination. Consequently, 135 representative ch-ch-fr combinations were selected, among which 129 showed significantly stronger BBS in COOP than in IND (two were from identical channel pairs and the remaining 127 were from different channel pairs).

For illustration, the positions and connections of the top 15 significant channel pairs with greater BBS in COOP than in IND are shown in Fig. 4（red lines). This suggests that most BBS occurred between the temporal region of one participant and the PFC of the other. Specifically, BBS primarily occurred between CH14 (right superior temporal gyrus (STG) 97.5%, 5 connections) in the posterior temporal region covering the TPJ in one participant and some channels in the PFC (e.g., CH11 (right frontopolar (FP) 62.2%, right inferior prefrontal gyrus 20%), and CH6 (right dorsolateral prefrontal cortex (DLPFC) 78.9%, right FP 21.1%), 3 connections, respectively) of the partner. On the other hand, there were much fewer BBS either between the PFCs or between the temporal regions of the dyads. Although Fig. 4 only shows the top 15 significant channel pairs, many other channel pairs in COOP yielded strong WTC (see the top 30 significant ($p < 0.05$, FDR-corrected) BBS ch-ch-fr combinations in Supplementary Table 1). Other than the top 30 significant pairs, there were additional significant BBS ($p < 0.001$, FDR-corrected), including those between the TPJ region (CH14, CH16 (right middle temporal gyrus (MTG) 34.9%, right angular gyrus (AG) 33.7%, right STG 18.1%)) and the MPFC region (CH7 (right superior frontal cortex (SFC) 73.5%, right superior MPFC 26.5%), CH10 (left superior MPFC 57.6%, right superior MPFC 42.4%), based on AAL).

By comparison, there were much fewer significant ch-ch-fr combinations for COOP < IND (Supplementary Table 1). The top 15 significant channel pairs (Supplementary Fig. 3, magenta lines) indicate weaker synchronization than in COOP > IND. In addition, these BBS were not only between temporal and PFC regions, but also between the PFCs of both parties, showing different spatial characteristics from those in COOP > IND.

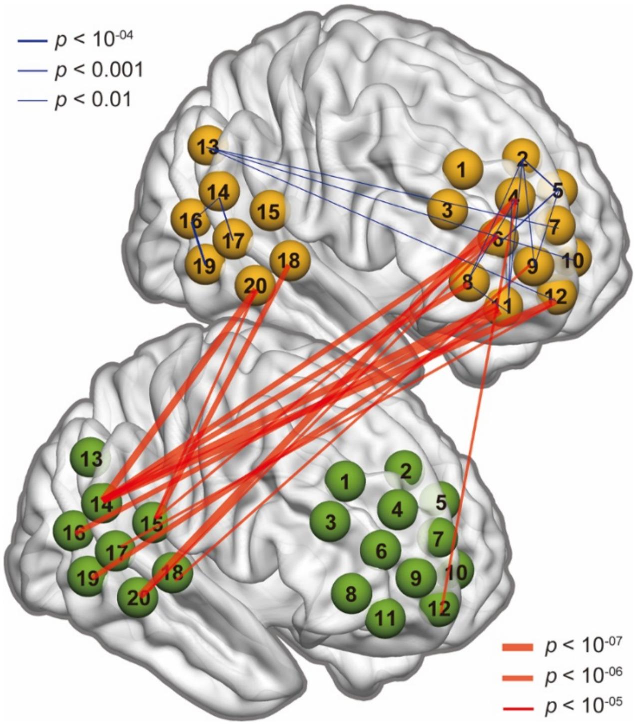

Fig. 4 Top 15 significant (COOP > IND) between-brain synchronization (BBS) (red lines) and within-brain synchronization (WBS) (blue lines). The width of the lines reflects the *p*-value (the smaller the *p*-value, the thicker the line). BBS primarily occurred between the right TPJ (rTPJ) and PFC regions. By comparison, WBS was weaker. In addition, WBS was not only between rTPJ and PFC but also between some PFC regions.

Within-brain synchronization (WBS)

WBS showed significant differences ($p < 0.001$, FDR-corrected) between COOP and IND in 25 ch-ch-fr combinations, among which 12 showed significantly stronger WTC for COOP > IND, while the remaining 13 showed significantly stronger WTC for COOP < IND. A representative selection of ch-ch-fr combinations using the same method as in BBS left 10 representative ch-ch-fr combinations, among which four showed significantly stronger WBS for COOP > IND (see Supplementary Table 2 for a comparison with the results of BBS).

The positions and connections of the top 15 significant WBS channel pairs for COOP > IND (Fig. 4, blue lines) show that WBS (blue lines, thinner) was not as strong as BBS (red lines, thicker). Here, similar to BBS, connections between the TPJ area (CH13: right AG 93%, right supramarginal gyrus (SMG) 7%) and the PFC area were also observed. Specifically, CH13 showed connectivity with three MPFC channels (CH7 and CH10) and anterior orbitofrontal channel (CH12 (right superior orbitofrontal 82.7%, right superior frontal 13.5%)) along the midline. In addition, unlike BBS, WBS occurred mostly within PFC (e.g., CH2 (right DLPFC 100%), CH5 (right FP 53.3%, right DLPFC 46.7%), and some other PFC channels).

By comparison, WBS for COOP < IND (Supplementary Fig. 3, cyan lines) did not show TPJ and PFC connectivity. Most WBS occurred between channels within PFC, and between the lower temporal region (e.g., CH19, CH20) and some PFC channels.

WTC-GLM

The above results for BBS and WBS revealed significantly stronger synchronization in COOP than in IND for many channel pairs (129 pairs for BBS and four for WBS). To elucidate which of these channel pairs' synchronization was related to specific social behaviors in COOP, we applied GLM using "both-up" and "either-up" as regressors to those significant BBS and WBS results. Because the GLM analysis was applied to those dyads' data who had both apparent face-up behaviors and effective WTC (see Methods for criteria), the final dataset for the GLM analysis came from 15 dyads.

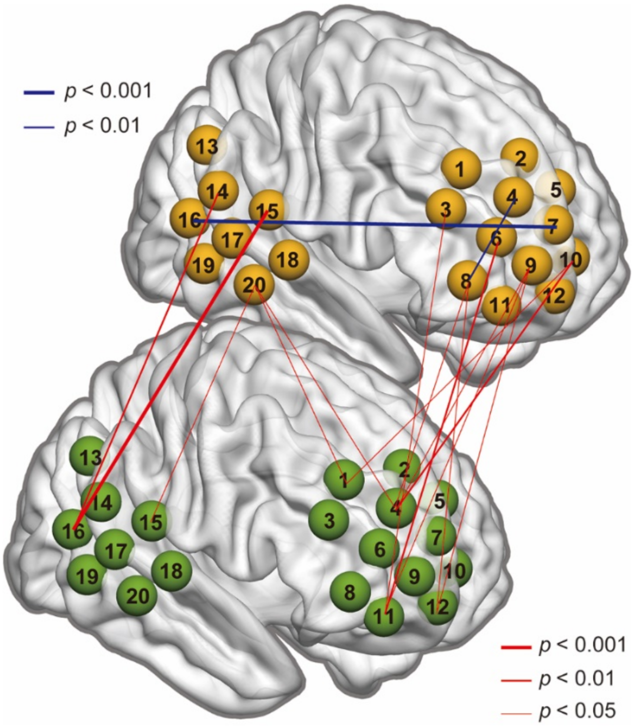

Fig. 5 WTC-GLM analysis. The results of one-sample *t*-tests on the beta values for the "both-up" regressor ($p < 0.05$, FDR-corrected). Red lines: BBS, 14 significant connections; Blue lines: WBS, two significant connections.

The results of the GLM analysis ($p < 0.05$, FDR-corrected) revealed 16 significant ch-ch-fr combinations (two for WBS and 14 for BBS), primarily between PFC regions of the dyads (Fig. 5), for the "both-up" regressor. There were no significant ch-ch-fr combinations for the "either-up" regressor. Further, comparisons of the GLM results between the "both-up" and "either-up" regressors revealed significant differences in three ch-ch-fr combinations (Fig. 6a; $p < 0.05$, FDR-corrected). Two were between-brain channel pairs and one was within-brain channel pair. The "both-up" regressor was associated with BBS between PFC regions (CH4 (right DLPFC 90%) and CH10 at 0.278 Hz, $t = 4.62$, $p = 0.007$), whereas the "either-up" regressor was associated with BBS between the temporal and TPJ regions (CH15 (right SMG 53.5%, right STG 41.7%) and CH16 at 0.226 Hz, $t = -4.47$, $p = 0.007$), as well as WBS between the MPFC and TPJ regions (CH7 and CH16 at 0.260Hz, $t = -5.38$, $p = 0.0017$).

Discussion

Cooperative interaction is an evolutionarily preserved human social behavior. However, understanding of its fundamental neurobiology remains inadequate. In this study, we used fNIRS hyperscanning to investigate the neural correlates of cooperative interaction during a naturalistic turn-based computer game with changeable goals depending on the mutual cooperative behaviors of dyads. In order to extract particular neuronal synchronization due to specific social-communicative signal among various behaviors, we developed a novel analysis approach. Specifically, we utilized an automatic behavioral detection technique to mark epochs with targeted social behaviors, that is, when the participants of a dyad raised their faces (face-up), and then examined the relationship between face-up behaviors and neuronal synchronization using GLM. Routine WTC analysis revealed that the neural synchronization of two brains show distinct patterns in different situations: as compared to the IND condition, the COOP condition induced greater BBS between the TPJ and PFC (e.g., DLPFC and MPFC) of the dyads, as well as some WBS between the MPFC and TPJ region of a single participant. The GLM analysis using face-up behaviors as the regressors unraveled possible functions of the large degree of BBS. For instance, one specific BBS (COOP > IND) originating from the PFC regions (DLPFC and FP) between two brains was more related to behavior when both members of a dyad raised their faces at the same time ("both-up") than when only one participant raised his/her face ("either-up").

Results of conventional WTC analysis

In the first step, conventional WTC analysis on the fNIRS data revealed that in comparison to individual play (IND), joint play (COOP) elicited significantly stronger neural synchronization (BBS) in many channel pairs between the PFC of one participant and the temporal region of the other participant at frequencies around 0.2–0.3 Hz (Fig. 4, Supplementary Table 1). The number of significant channel pairs for COOP > IND was very high (129 pairs in contrast to six pairs for IND > COOP), and the statistical results were very suggestive (*p*-value: 2.01E-08 ~ 1.62E-06 for top 15 pairs, FDR-corrected). These robust synchronizations indicate that human cooperation to pursue common goals induces various and strong inter-brain coupling. Intriguingly, such synchronization occurs more prominently between brains than within brain. That is, functional connectivity between two different brains is stronger than it is within one single brain, as though two brains function together like a single system. This phenomenon is consistent with the notion of "we-mode", where interacting agents share their minds in a collective mode (Gallotti and Frith, 2013). This mode has been described to highly facilitate the interaction by accelerating access to another's cognition (e.g., perspective taking, beliefs, and concepts) (Gallotti and Frith, 2013; Hasson and Frith, 2016). By utilizing such a system, participants might have achieved their shared goal, and the social dynamics in our natural task setting may have enabled us to capture a robust "two-in-one system" (Beer, 2000; Konvalinka and Roepstorff, 2012). However, comparison of BBS and WBS requires careful consideration, as the number of ch-ch-fr combinations and the number of data points for each ch-ch-fr differed between BBS and WBS, which might bias the statistical results.

What specific cognitive process does BBS during joint interaction reflect? The observed BBS primarily occurred between CH14 (chiefly corresponding to the right TPJ (rTPJ) region) and channels in the right PFC, representatively, CH6 (right DLPFC (rDLPFC)) and CH11 (right FP (rFP), right inferior prefrontal gyrus). Other than these representative channels, the rTPJ region also projected to the dMPFC and MPFC regions (Supplementary Table 1).

Among these BBS, a specific inter-brain substrate (rTPJ and rPFC) may underpin mutual cooperation by processing the exchanged neural information during coordination within a specific temporal range (0.2–0.3 Hz). The spatial localization of this cross-brain neural substrate approximately corresponds to the MENT (which mainly consists of TPJ and MPFC/dMPFC), as predicted from previous social neuroscience work (Adolphs, 2009; Decety and Lamm, 2007; Frith and Frith, 2006; Gallese et al., 2004; Van Overwalle, 2009). Indeed, a number of hyperscanning studies using interactive tasks with theory of mind demands have identified evidence for the recruitment of the brain regions including the PFC, FP, rDLPFC and rTPJ, largely the MENT (e.g., Abe et al., 2019; Baker et al., 2016; Cheng et al., 2015; Decety et al., 2004; Dommer et al., 2012; Dumas et al., 2010; Nozawa et al., 2016; Tang et al., 2016; Xue et al., 2018). In light of these prior work, it is reasonable to speculate that the observed BBS in the rPFC and rTPJ may be neural indicators for cooperation that requires reading others' intentions in dyads.

It should be noted that WBS also showed a smaller but clearer recruitment of the MENT, which connects the rTPJ and dMPFC/MPFC regions. As the MENT was proposed based on single-brain studies (Frith and Frith, 2006; Gallese et al., 2004), this network may better represent cerebral processing within an individual brain. On the other hand, because BBS showed more connections and stronger intensity than WBS did, the "two-in-one system" for social interaction may be a system beyond the MENT. Indeed, our task involved various social exchanges during the cooperation period, including perspective taking and understanding other's belief and concepts. Thus, disentangling BBS by taking each possible functional role into account is desirable.

Results of WTC-GLM analysis

As we adopted a highly naturalistic task allowing nearly unconstrained dyadic interaction, a variety of social behaviors accompanying cooperation would have been associated with the large number of synchronized channels (brain regions) obtained using conventional WTC analysis. To clarify specific relationships between certain kinds of social interactive behavior and certain types of neuronal coupling between brains, we applied GLM to the WTC results (WTC-GLM) for the first time in the field of hyperscanning studies.

The "face-up" behavior was chosen as the target social behavior in this study, which should approximately correspond to eye gaze, likely reflecting a person's thoughts or intentions (e.g., Hirsch et al., 2007). Concurrent "face-up" is likely to reflect mutual gaze, while one participant's "face-up" may correspond to a form of communicative intention. This includes talking to the partner as well as observing or guessing the partner's behavior and/or mental state. As the screen of the touch panel was positioned parallel to the desk, participants had to raise their heads to face the partner. We verified from the recorded videos that the participants raised their faces when they actively talked to and made an appeal to their partners. The video sequences were automatically marked with face-up epochs (i.e., "both-up", "self-up" and "other-up"). Then, these labels with temporal information were used as regressors in the GLM to examine the relationship between face-up behaviors and BBS and WBS during cooperative activity. It is necessary to note that the "self-up" and "other-up" regressors were combined as the "either-up" regressor (as mentioned in the section "Assessment of WTC correlates of social behaviors (WTC-GLM)"). This analysis narrowed down the results of conventional WTC and yielded only 16 channel pairs (14 BBS and two WBS) showing a significant relationship with the "both-up" regressor, while no significant findings for the "either-up" regressor (Fig. 5). Most of these channel pairs were from the PFC regions of the two brains. Then, comparison of the GLM results between the "both-up" and "either-up" regressors further extracted three channel pairs (two BBS and one WBS) showing a significant difference (Fig. 6). These results provide evidence for the putative relationship between certain social behaviors (i.e., face-to-face interaction) and neural synchronization of certain brain regions within a certain temporal range.

In particular, BBS between CH4 (rDLPFC) and CH10 (rFP) of the dyads was more related to the "both-up" regressor than the "either-up" regressor. One reason for this might be that when both members of a dyad raise their faces at the same time ("both-up"), they are better able to communicate explicitly and simultaneously judge each other's intentions and feelings via facial information as compared to when only one member raises his/her face ("either-up"). Previous studies have demonstrated that increased BBS is typically related to mutual understanding, which might be interpreted as an indicator of a cooperative state between group members (e.g., Cui et al., 2012; Dommer et al., 2012; Funane et al., 2011; Tang et al., 2016; Xue et al., 2018). Consistent with the present finding, recent hyperscanning studies have also reported involvement of the rDLPFC and FP in tasks demanding cooperative interaction (e.g., Nozawa et al., 2016; Xue et al., 2018).

In addition to the generally accepted functions of DLPFC such as attention and goal maintenance (e.g., Miller and Cohen, 2001), it has also been reported to play key roles in suppressing self-centered behavior and self-interested motivation (Baeken et al., 2010; Knoch et al., 2006), monitoring responses and inhibiting prepotent ideas (Mansouri et al., 2009; Miller and Cohen, 2001), as well as relationship commitment (Petrican and Schimmack, 2008). Considering the robust involvement of the DLPFC in these functions, it is reasonable to suppose that BBS between CH4 and CH10 (both cover the rDLPFC) of dyad members showing stronger relationship with the "both-up" regressor may reflect mutual endeavors to monitor their partners' responses by observing their facial information and adjust their own mind and behavior accordingly (make a concession) to design the room to satisfy themselves as well as their partner. Xue et al. (2018) found similar results in their creativity-demanding task, especially for dyads where both members were low in creativity—such dyads were more willing to cooperate with their partners.

In contrast, BBS between CH15 and CH16, corresponding to the rTPJ region of the dyads, was more related to the "either-up" regressor than it was to the "both-up" regressor. The TPJ is a broad region inclusive of SMG, AG, and posterior STG (pSTG), serving as a crucial part of the MENT (Adolphs, 2009; Frith and Frith, 2006), which is also proposed to be involved in inter-brain coupling (Schilbach et al., 2013). In the social neuroscience literature, the TPJ is thought to be central in representing mental states during theory of mind tasks (Ciaramidaro et al., 2007; Saxe and Powell, 2006). This region, and the pSTG in particular, processes goals and intentions of social signals by monitoring the visual properties of human biological motion and the background context (Deen and McCarthy, 2010; Grossmann et al., 2008; Jellema et al., 2000; Lloyd-Fox et al., 2009; Pelphrey, Morris, and McCarthy, 2005; Saxe et al., 2004; Wyk et al., 2009), and sends this information to the MPFC (Gallese et al., 2004; Van Overwalle, 2009), another fundamental part of the MENT thought to process sense of human mind (e.g., Urakawa et al., 2015). Moreover, regardless of measurement modality, several hyperscanning studies have reported increased BBS in TPJ between individuals while engaged in social interactive tasks (e.g., Abe et al., 2019; Bilek et al., 2015; Jiang et al., 2015; Xue et al., 2018). In light of the range of functions attributable to the TPJ, one possible explanation for the stronger relationship between BBS of TPJ and the "either-up" regressor might be as follows: as the information exchange of social signals and/or speech is largely limited to one direction for the "either-up" regressor, cooperating dyads may have tried very hard to conjecture the intention of their partners, triggering simultaneous activation of the TPJ.

This possibility also applies to the finding that WBS between CH7 and CH16 had a stronger relationship with the "either-up" regressor. Specifically, the brain regions underlying CH7 (MPFC) and CH16 (rTPJ) are approximately the MENT of one individual, which may show more robust functional connectivity when the facial and/or verbal information of one's partner is so restricted that more effort is required to infer the partner's intention. Such an explanation is further supported by another finding that the subjective evaluation of "goodness of cooperation" is positively correlated with the strength of WBS between CH7 and CH16. Namely, the stronger functional connectivity between the TPJ and MPFC (reflective of a more sensitive MENT) of one individual, the more one is satisfied with the cooperation and willing to cooperate with the partner, and therefore the harder one tried to surmise the intention of the partner when the information of the social signal from the partner is incomplete ("either-up").

Because we used such an interactive task with highly fluctuating goals set by both members of the dyads during the task, the hyperscanning of concomitant brain signals could capture the above-described dynamic interplay of brain regions involved in the MENT. To further elucidate this mechanism, causality analysis is necessary in future work.

Significance of the automatic estimation of social behaviors and new analysis approach

Research focusing on the real dynamic interactions among multiple humans using hyperscanning technique is an emerging field in social neuroscience and has provided many valuable insights to understanding the brain correlates of social cognition (Konvalinka and Roepstorff, 2012; Minagawa et al., 2018; Schilbach et al., 2013). Recently, the use of naturalistic stimuli under more ecologically valid situations is uncovering novel evidence for social neuroscience and advancing this field significantly. The use of naturalistic paradigms in neuroimaging may yield abundant information about human social behaviors, as well as brain functions associated with social cognition. On the one hand, such rich behavioral information can contribute to a more comprehensive understanding of the social brain. On the other hand, conventional methods used for examining the relationship between certain social brain function and social behavior, such as manual encoding of social signals from videotapes by multiple trained coders, will be limited as big data continues to emerge from social neuroscience in naturalistic settings. The trend towards big data underscores the importance of developing new analytical techniques that can more efficiently reveal brain–behavior relationships.

The present study sought to address this issue by utilizing automated computer vision techniques to extract metrics of human behavior during naturalistic social interaction. We focused on face-up events, thought to be the most direct representation of mutual social interaction between members of dyads in the cooperative task used here. As the display of a touch panel in front of each participant was placed parallel to the desk, where dyads were seated face-to-face, the pitch angle of the participant's face relative to the horizon of the touch panel should contain the most direct representation of social signal exchange. Though holding less social information than the pitch angle, the roll and yaw angles of the participant's head should also be considered in future analysis for precision. Beyond this face orientation information, other information like facial expression and verbal behavior are also fundamental social signals and hence should be considered in future quantitative analysis of social interaction. As the first attempt to apply this automatic method, the present study selected one type of salient human motion to extract, while we could apply this method to more detailed social behaviors in future studies. For such attempts, techniques that can effectively video-record these multidimensional social behaviors would be necessary to facilitate a more comprehensive understanding of the neural correlates of dynamic social interaction under ecologically valid conditions.

Regarding the results of face-up events, the occurrence rate of "both-up" and "either-up" events in the four types of behavior logs (item selection, item placement, ok, cancel) during COOP showed no significant difference (Kruskal–Wallis test, $p < 0.05$;). This result excluded the possibility that the specific neural synchronization related to the face-up regressor is biased toward a certain game behavior. Rather, the observed relationship between social behavior and neural synchronization is universal in the present naturalistic cooperation setting.

With respect to the *z*-scored standardization for the pitch angles of participants' faces, a threshold of 2 SD was used. We used such a stringent threshold in order to accurately assess the timing information for when a participant actually raised his/her face to his/her partner, and labeled only those timing that surpassed the threshold as face-up events. In addition, because the participants looked at their display most frequently to perform the task, the mean of the pitch angle (0) was set at the position of the display. However, the pitch data of many dyads did not fit the normal distribution well, possibly because Japanese participants did not look at their partner's face much even during

By analyzing both between- and within- brain synchronizations, our cooperation task that required flexible pursuit of a shared goal was found to induce robust BBS that could be characterized as functioning in a two-in-one system. Combined with the findings of previous studies, the present results partly reflect dynamic activation and interplay of the MENT of two brains during a goal-free cooperative task with naturalistic settings. Furthermore, the present study uncovered the underlying relationship between certain neural correlates and specific social behavior among numerous brain synchronizations by combining GLM analysis with automatic behavioral detection. This new analysis approach for fNIRS hyperscanning has achieved preliminary yet intriguing results. This approach, which could reveal neural correlates of naturalistic behavior, may provide considerable insight and avenues for future work in interactive social neuroscience.

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【概要１-1】fNIRS ハイパースキャンニングを用いた 2 者間の社会的相互作用の脳機能研究：母子関係

異なるダイナミクスを持つ母子間の fNIRS 信号同期解析

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１．研究の背景と目的

二者以上の脳活動を同時計測するハイパースキャニングにより、直接的な行動の同期がなくても脳活動において個体間で同期が生じることが明らかになってきた。fNIRS は低拘束で計測が比較的容易であり、小型化も可能であることから、日常的な空間におけるコミュニケーション等を対象としたハイパースキャニング研究に有望な計測手法である。これまで成人で計測されたデータに関して時間相関分析やウェーブレット・コヒーレンスによる分析手法などが提案され広く用いられてきたが[1]、母親と乳児間のような脳血流ダイナミクスの異なる二者間においては、これらの既存手法は適用前提が異なるため適切ではない。そこで本研究では異なるダイナミクスを持つ脳活動信号における同期現象を扱う手法の開発に取り組んだ。

２．方法

2-1.　非負値行列因子分解

非負値行列因子分解[2]は非負の要素で構成される行列を非負の基底行列と非負の重み係数の積の形に分解する手法であり、データマイニングのほか特に音情報処理の分野において音源分離のモデルとして用いられ発展してきた。例えば複数の音源を含む音波形のパワースペクトログラムは、各音源のもつ音源スペクトルが既知であれば加法性の成立を仮定することで分解可能となる。同様に fNIRS 信号に関しても、母子で同時計測した信号のスペクトログラムをひとつの行列として解釈すれば、同期する活動を基底として分解することが可能となる（図 1)。

fNIRS 計測データには ETG-7000（Hitachi Medical Corporation, Tokyo, Japan）で計測した、3～4 歳児の母子ペア 55 組分を用いた。授乳中（授乳条件)、抱っこ中（レスト条件)、第三者が乳児を抱っこ中（コントロール条件）の 3 つの条件において母子それぞれの前頭を中心とした 44 チャンネル（計 88 チャンネル）を同期計測した。各条件の長さは 3～5 分間とした。データは OxyHb および DeoxyHb 信号に変換したのち、母親のデータに対し血流動態分離法[7]で頭皮血流ノイズを除去し、さらに母子両方についてウェーブレット MDL[8]により低周波数のノイズを除去した。その上で Morlet のマザーウェーブレットを用いて、ObyHb 信号を 0.02- 0.5 Hz の範囲で 1/3 オクターブずつ計 15 分割したパワースペクトログラム

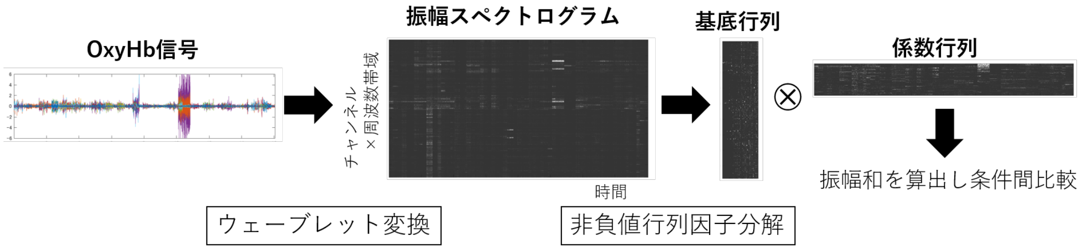

図１　非負値行列因子分解を用いた同期活動解析のフロー

OxyHb 信号に対してウェーブレット変換により振幅スペクトログラムを求め、非負値行列因子分解で基底及び係数行列を得たのち、それぞれの条件ごとに振幅和を算出する。
参加者間でパワーの平均値が揃うようにノーマライズしたパワースペクトログラムを全参加者ペア・条件分集めて結合したのち、非負値行列因子分解を適用した。非負値行列因子分解は fNIRS 信号の特性を考慮し、時間方向の連続性の制約[3]に加え周波数方向の連続性の制約も加えたアルゴリズムを採用した。最大基底数は 100 とし、得られた係数行列についてそれぞれの参加者ペアと条件について振幅平均値を算出し、ボンフェローニ補正した符号検定で条件間に差が認められる基底を求めた。
基底の由来は基底行列の値に表現されるが、元信号に占める実効的な大きさは係数行列の値にも依存するため、以下のような実効活動値$\mathcal{E}$で評価した。

$$\mathcal{E}_{\omega,\phi,k} = W_{\omega,\phi,k} \sum_{\tau} H_{k,\tau}$$

ただし、Wは基底行列、Hは係数行列、ωとϕとkとτはそれぞれ基底と周波数帯域と fNIRS チャンネルと時間のインデックスを表す。また空間的な情報は周波数方向の違いを無視して、以下に示す空間活動値$\mathcal{W}$で評価した。

$$\mathcal{W}_{\omega,k} = \sum_{\phi} \mathcal{E}_{\omega,\phi,k}$$

2-2.　ウェーブレット・コヒーレンスの拡張

ウェーブレット・コヒーレンスは時間周波数領域におけるコヒーレンスを計算するもので、血流応答を計測しているために高いサンプリングレートに対して脳活動の時定数が遅い fNIRS 信号のハイパースキャニングデータ解析において最も広く用いられている解析手法である（例：[4]）。我々は異なる帯域間でのコヒーレンスを計算するため、周波数軸方向におけるスムージング係数を低いほうの周波数帯域における係数を採用する形で拡張を試みた。テストデータとして Matlab(Mathwork 社)から提供されている Cui らの二者間タッピング相互作用実験[4]のサンプルデモデータを用い、拡張版ウェーブレット・コヒーレンスを算出した。

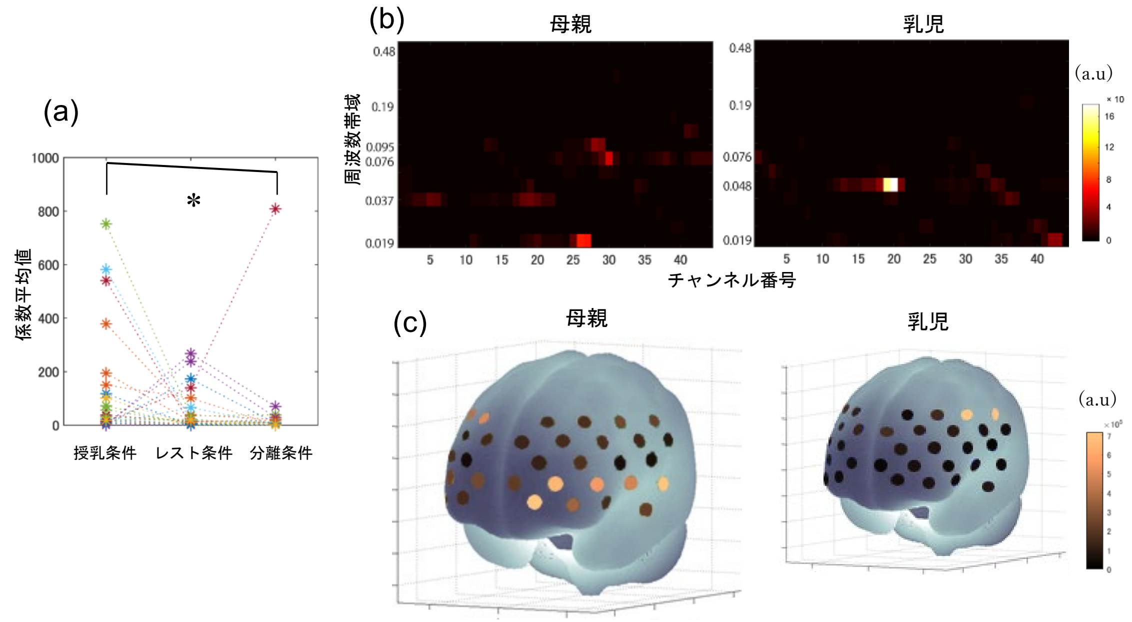

図 2　授乳条件において高い振幅平均値を示した基底の例

(a)振幅平均値の各条件におけるプロット。この基底では授乳条件と分離条件の間に有意差が認められた。(b)信号のチャンネルと周波数帯域における実効活動値。母親と乳児の異なる周波数帯域に由来する成分であることがわかる、(c)空間活動値を脳表にプロットした図。母の内側前頭前野と乳児の背外側前頭前野間に機能的結合があることを示す。

2-3.　位相相互情報量

相互情報量は 2 つの確率変数間の相互依存関係を定量化する情報量である。脳活動における情報量を計算するためには、まず脳活動を何らかの基準のもとで量子化して確率表現に置き換える必要がある。位相は活動の大きさと比べて値域が限定されるため量子化が容易であり、位相に着目した位相移動エントロピーが提案されている[5]。本研究では同期に着目するため、位相移動エントロピーと同様の形で確率分布を定義した相互情報量を用いた。前処理として信号をスペクトログラムに変換し、各周波数帯域について位相変動を求めた上で、それらの組み合わせについて相互情報量を求めた。

ウェーブレット・コヒーレンスとの関係を調べるため、シミュレーション用データとしてレスティング状態の全脳計測データを含む公開データベースである MULDS dataset (https://bicr-resource.atr.jp/mulds/)を用いた。全脳計測データは多数のチャンネルからなり、様々な強さと周波数の同期・非同期信号が含まれるため、他の同期計算手法との結果を直接比較できる。血流動態分離法[6]で頭皮血流ノイズを除去したのち、ウェーブレット MDL[7]により低周波数のノイズを除去して位相相互情報量とウェーブレット・コヒーレンス

ンスを算出し、得られた結果を比較した。

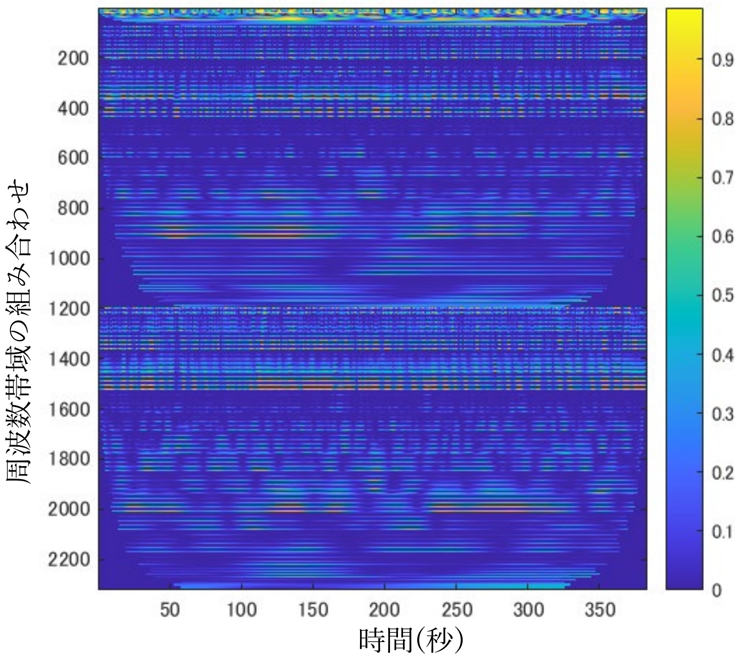

図3　拡張版ウェーブレット・コヒーレンスの計算例

横軸は時間、縦軸方向に周波数帯域の組み合わせを並べ、色彩でコヒーレンスの強度を表す。縦軸の上部は同じ周波数におけるコヒーレンス（通常のウェーブレット・コヒーレンスと同）である。なお低周波数領域で計算上生じる欠落部分（円錐状影響圏の外側）は青色で表示している。

3. 結果と考察

3-1.　非負値行列因子分解

得られた22個の基底について条件間で平均値の比較を行い、授乳条件において他条件と比べ有意に大きい値を示す基底を得た。例として図 2 に得られた基底と実効活動地及び空間活動値の一例を示す。実効活動値で基底の由来するチャンネルと周波数を評価したところ、異なる複数の周波数帯域に共通する同期成分が抽出されていることが確認できた（図2(b)）。これらの結果から母子間の脳活動において異なる周波数帯域間における同期現象の存在が示唆された。

非負値行列因子分解は元となる fNIRS 信号の振幅スペクトログラムを近似的に 2 つの正の値を持つ行列に分解する手法である。本研究では時間及び周波数両方向についてなめらかな基底が得られる効果を持つパラメータをトップダウンに設定して推定したが、fNIRS 信号

の特性に合致したパラメータ範囲を別途検証するか、ノンパラメトリックモデルとして推定する必要がある。また、推定された結果の妥当性について評価基準を設けることも重要である。例えば得られた基底の頑健性を、交差検定の形で評価することが考えられる。

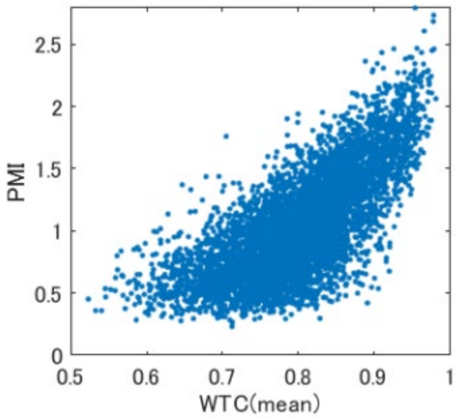

図 4　位相相互情報量とウェーブレット・コヒーレンスの関係

位相相互情報量（縦軸）とウェーブレット・コヒーレンスの平均値（横軸）の 0.02 Hz における散布図。両者は正の相関を示すが（r=0.73）、非線形な関係が伺える。

3-2.　ウェーブレット・コヒーレンスの拡張

タッピングデータに対し、拡張したウェーブレット・コヒーレンスを算出した例を図 3 に示す。デモデータは成人 2 人の計測データであるが、近接する周波数帯域間でコヒーレンスが強くなっている。

本手法は従来用いられてきた解析手法の拡張であるため、コヒーレンスの強さについての議論も先行研究に従って容易である。一方で周波数帯域の組み合わせが増えると指数関数的に計算コストが上がる難点があり、チャンネルの組み合わせも含めると膨大な計算を必要とする。そのため、あらかじめ計算対象とする周波数帯域の検討を別途行う方法が現実的である。

3-3.　位相相互情報量

位相相互情報量とウェーブレット・コヒーレンスを算出し、その相関関係を調べた。例として特に相関の高かった 0.02 Hz の周波数帯における散布図を図 4 に示す。ウェーブレット・コヒーレンスのような統計量と異なり、相互情報量は非線形な同期も評価できる利点が期待される。散布図の結果は両者が似た性質を有しつつも非線形な関係を示しており、情報量による同期の定量化によって、従来は見えていなかった同期関係を明らかにできる可能性を示唆している。

4．総合考察

本研究では母子間のような血流ダイナミクスが異なると予想される二者間における脳活動の同期現象を調べるための解析手法として、非負値行列因子分解、拡張版ウェーブレット・コヒーレンス、位相相互情報量の 3 つを検討した。3 つの手法それぞれのメリットとデメリットを表 1 に示す。

非負値行列因子分解は従来手法とは異なり、同期成分の時系列パターンを抽出することができる。一方で分解はモデルのパラメータやデータの質に依存することから、データ量やデータの欠損に対する頑健性について検証を進める必要がある。拡張版ウェーブレット・コヒーレンスは従来手法とも互換する簡易な拡張である。しかし分割帯域数やチャンネル数、データ数に応じて計算量が膨大になるため、探索的な使用は現実的でない。位相相互情報量は特に課題時間内の平均的な同期の評価において、非負値行列因子分解や拡張ウェーブレット・コヒーレンスと比べて計算コストが少なくて済む。ただし、同期の時系列変化を調べるためには確率を求めるための時間窓を別途指定する拡張が必要となる。

母子間相互作用を計測する目的に即したときに、特に考慮すべき課題の一つが欠損値への対処である。乳児の計測では成人の計測のような長時間に渡る拘束が現実的ではない。そのため、一部チャンネルや一時的なデータの欠損を許容せざる得ない状況も生じやすい。低周波帯域の活動評価には計算のために十分に長い連続するサンプルが必要であり、データの欠損頻度が低い周波数帯ほど増加することになる。非負値行列因子分解による分析では、解析対象とする周波数帯域において欠損のないサンプルがすべてのチャンネルにおいて揃っている状態が理想的であり、欠損部分を外した適用自体は可能であるものの、低周波領域における同期をうまく評価できない可能性がある。

また各種運動ノイズによる影響も改めて検討が必要である。特に非負値行列因子分解は母子それぞれのデータから求められたスペクトログラムを直接分解するため、同期量に変換する他の手法と比べるとノイズが結果に直接影響を与えやすいと考えられる。

各手法の性質を併せると、計算コストの面で有利な位相相互情報量によって母と乳児の脳活動の同期が起こる周波数帯域を絞り込んだうえで、拡張版ウェーブレット・コヒーレンスにより同期の大きさを検証する方法論が最も現実的である。位相に着目した情報量として他に位相移動エントロピー[5]が挙げられるが、移動エントロピーは情報の向きを含んだ指標であり、同期だけでなく因果関係まで含めた議論が可能になると期待できる。これまでの fNIRS のハイパースキャニング研究では、情報量に着目した分析はグレンジャー因果の解析を行った例[8]などがあるがほとんど行われていない状況である。今後は同期以上の相互作用を検証するために、情報の流れに着目した解析が重要になってくるであろう。

表１　提案手法のメリット・デメリット

提案手法	メリット	デメリット
非負値行列因子分解	■ 同期の大きさだけでなく、時系列パターンを抽出できる	■ 加法性の仮定は厳密には成り立たない ■ アーティファクトの影響を受けやすい ■ データの欠損に弱い
拡張版ウェーブレット・コヒーレンス	■ 先行研究との比較が容易	■ 計算コストが極めて高い
位相相互情報量	■ 計算コストが比較的低い	■ 時系列パターンを出すためには、拡張が必要

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(3) 研究概要報告書に述べた研究内容の詳細と補足資料

2． 感情情報処理の脳機能と生理指標

2-1. パーソナリティと感情情報処理の脳機能

2-2. 母子の感情刺激に対する脳反応

2-3. 高齢者の感情情報処理の脳機能と生理指標

2-4. 若年者，高齢者のコミュニケーションにおける視聴覚情報の役割

【概要 2-1】

前頭葉における情動反応とTCI気質・性格特性との関連

孫 怡（2016年戦略ＰＤ研究員）
木島信彦（戦略参加研究者）

１．研究の背景と目的

感情制御は、感情を喚起するような刺激に対して、意識的または無意識的に自己の感情について多様な認知処理を行うものである。感情制御は前頭葉の関わりが指摘されており、個人の性格特性に左右されやすいとの報告もある（Minagawa et al., 2009)。個人の性格特性と前頭葉の感情制御についてはこれまで主にBig5特性との関連から検討されているが、本研究では、Cloninger et al.（1994）により生物学神経基盤に基づき考案されたTCI気質・性格特性を用い、気質・性格特性と感情刺激に対する前頭葉の脳活動との関係を検討した。

２．方法

2-1.被験者

健康な大学生22名（10 Females,年齢 Mean=19.91, SD=1.54）

2-2.感情刺激図

OASIS(Open Affective Standardized Image Set)の中から、参加者と別の128名の大学生へのweb調査により快/不快/中立刺激写真を各30枚選定した。

2-3.TCI気質・性格特性

Temperament & Character Inventory気質・性格検査（TCI)は、Novelty Seeking (NS), Harm Avoidance (HA), Reward Dependence (RD), Persistence (PS), Self-Directedness (SD), Cooperativeness (CO), Self-Transcendence (ST)の７特性からなる。参加者は計140質問項目にどの程度合致するか自己特性を５段階評価で回答した。

2-4.実験デザイン

上述した感情刺激を呈示した際の前頭前野22chのヘモグロビン濃度変化量をfNIRS(ETG-4000、Hitachi Medical Co.)で計測した。

2-5. 解析手法

各刺激図に対する血流量変化量は、総平均Oxy-Hbピーク（刺激提示終了時点） 前後2.5秒（5秒間）のOxy-Hb変化量平均値から刺激呈示前5秒間のOxy-Hb変化量平均値の差分で求めた(activation-baseline)。これを快・不快・中立刺激それぞれで平均値を求めた後、〈快-中立〉及び〈不快-中立〉を各参加者の感情刺激による前頭葉活動の指標とした。さらに各被験者のTCI気質・性格特性とこの脳活動指標との相関を求めた。脳の部位はvirtual spatial registration 法を用いて推定した。

3. 結果

Oxy-Hb の変化量は、Activation 区間が baseline に比べ、ch18 以外すべてのｃｈにおいて有意差がみられた。Oxy-Hb が快刺激に対して若干減少し、不快刺激に対して大きく減少している傾向がみられた。また、気質・性格特性と感情刺激に対する脳反応に有意な相関がみられた。(図 1) 快刺激に対しては、OFC 付近、前頭極(ch1, ch2, ch3, ch4)においてNS3・PS1 および背外側前頭前野 (dl-PFC) (ch5, ch8, ch9)において PS・ST と脳活動指標に正の相関、NS4 は負の相関がみられた。(図 2) 不快刺激に対しては、左右の前頭極(ch1, ch4)と dl-PFC(ch5, ch9, ch10, ch13)において PS・ST と脳活動指標に正の相関がみられ、中央部 dm-PFC (ch16, ch20) において RD・CO・PS・SD と脳活動指標に負の相関、NS3 は正の相関がみられた。

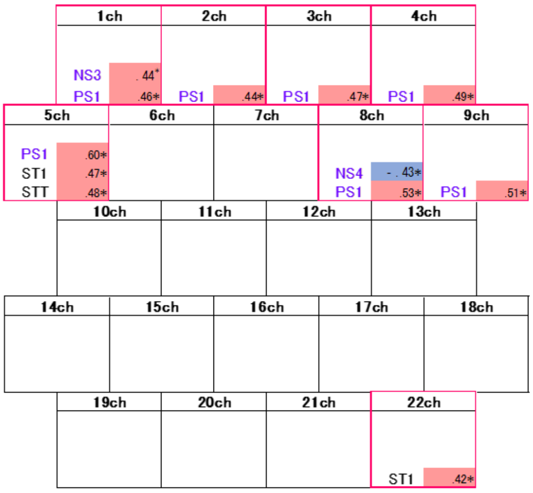

図 1 気質・性格と脳活動との相関（快刺激）

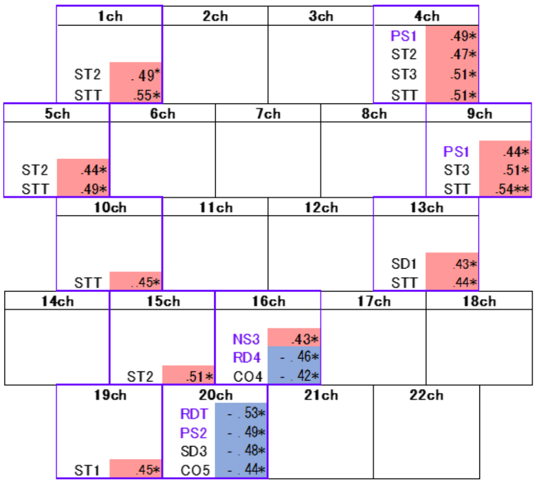

図 2 気質・性格と脳活動との相関（不快刺激）

４. 考察

はじめて TCI 気質・性格検査を使用し、それと感情刺激に対する前頭葉反応との関連がみられた。個人の気質・性格によって、感情刺激に対する反応が異なることが示唆された。OFC 付近および前頭極部位：PS が高いほど、快/不快刺激への反応が弱い; dl-PFC :NS4 が高いほど、快刺激への反応が強い ; dm-PFC: RD・CO が高いほど、NS3 は低いほど、不快刺激への反応が強い。

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前頭葉における情動反応とTCI気質・性格特性との関連

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1.慶應義塾大学戦略的研究基盤形成支援事業、2. 立命館大学グローバル・イノベーション研究機構
3. 慶應義塾大学文学部、 4. 慶應義塾大学商学部

【概要】
感情制御は、感情を喚起するような刺激に対して、意識的または無意識的に自己の感情について多様な認知処理を行うものである。感情制御は前頭葉の関わりが指摘されており（Quirk & Bear, 2006）、個人の性格特性に左右されやすいとの報告もある（Hariri et al., 2000; Minagawa et al., 2009）。個人の性格特性と前頭葉の感情制御についてはこれまで主にBig5特性との関連から検討されているが、本研究では、Cloninger（1997）により生物学神経基盤に基づき考案されたTCI気質・性格特性を用い、気質・性格特性と感情刺激に対する前頭葉の脳活動との関係を検討した。

【方法】

被験者：健康な大学生22名（10 Females,年齢 Mean=19.91, SD=1.54）

感情刺激図：OASIS(Open Affective Standardized Image Set)の中から、参加者と別の128名の大学生へのweb調査により快/不快/中立刺激写真を各30枚選定した。

TCI気質・性格特性：Novelty Seeking (NS), Harm Avoidance (HA), Reward Dependence (RD), Persistence (PS), Self Directedness (SD), Cooperativeness (CO), Self Transcendence (ST)の7特性からなり、参加者は計140質問項目にどの程度合致するか自己特性を5段階評価で回答した。

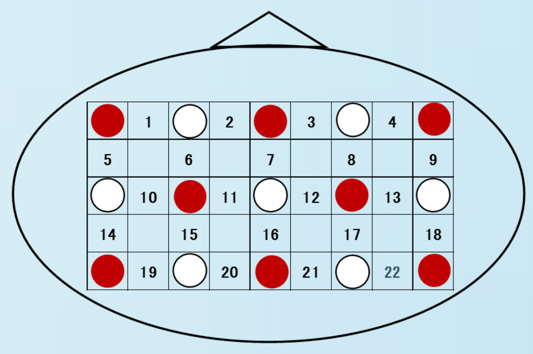
実験デザイン：上述した感情刺激を呈示した際の前頭前野22chのヘモグロビン濃度変化量をfNIRS(ETG-4000、Hitachi Medical Co.)で計測した。

解析手法：各刺激図に対する血流量変化量は、総平均Oxy-Hbピーク（刺激提示終了時点）前後2.5秒（5秒間）のOxy-Hb変化量平均値から刺激呈示前5秒間のOxy-Hb変化量平均値の差分で求めた(activation-baseline)。これを快・不快・中立刺激それぞれで平均値を求めた後、〈快 -中立〉及び〈不快 - 中立〉を各参加者の感情刺激による前頭葉活動の指標とした。さらに各被験者のTCI気質・性格特性とこの脳活動指標との相関を求めた。脳の部位はvirtual spatial registration法（Tsuzuki et al. 2007）を用いて推定した。


中立刺激


不快刺激


快刺激



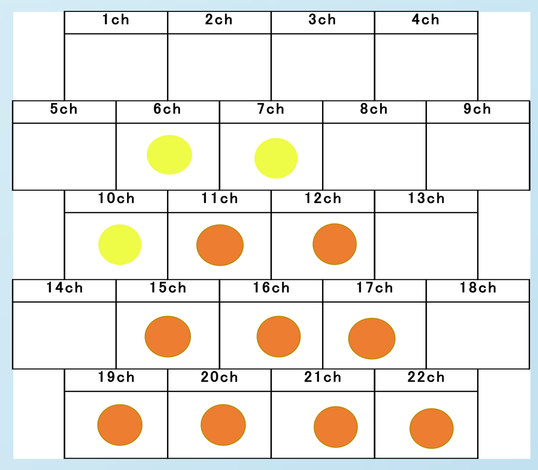


図1 不快刺激への反応強さ

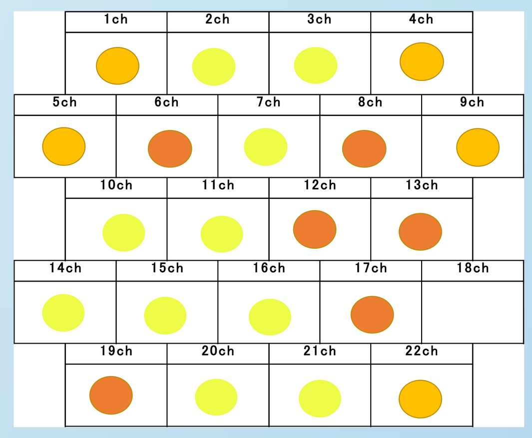
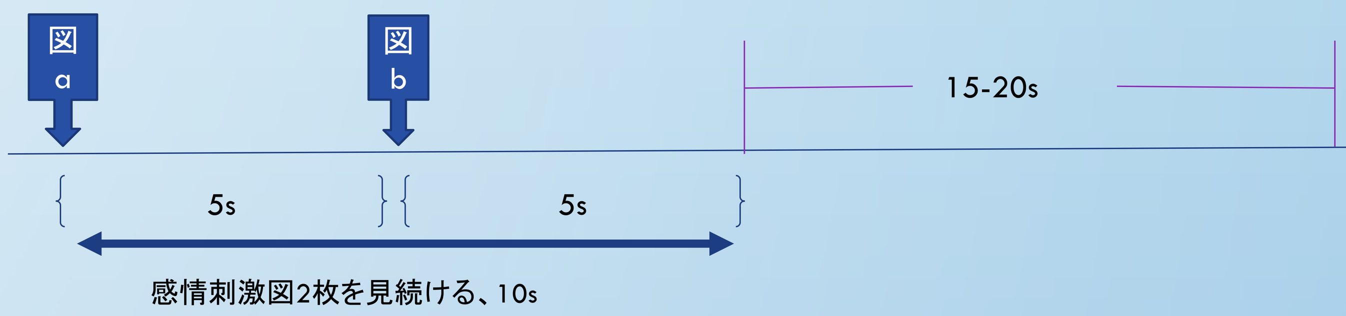
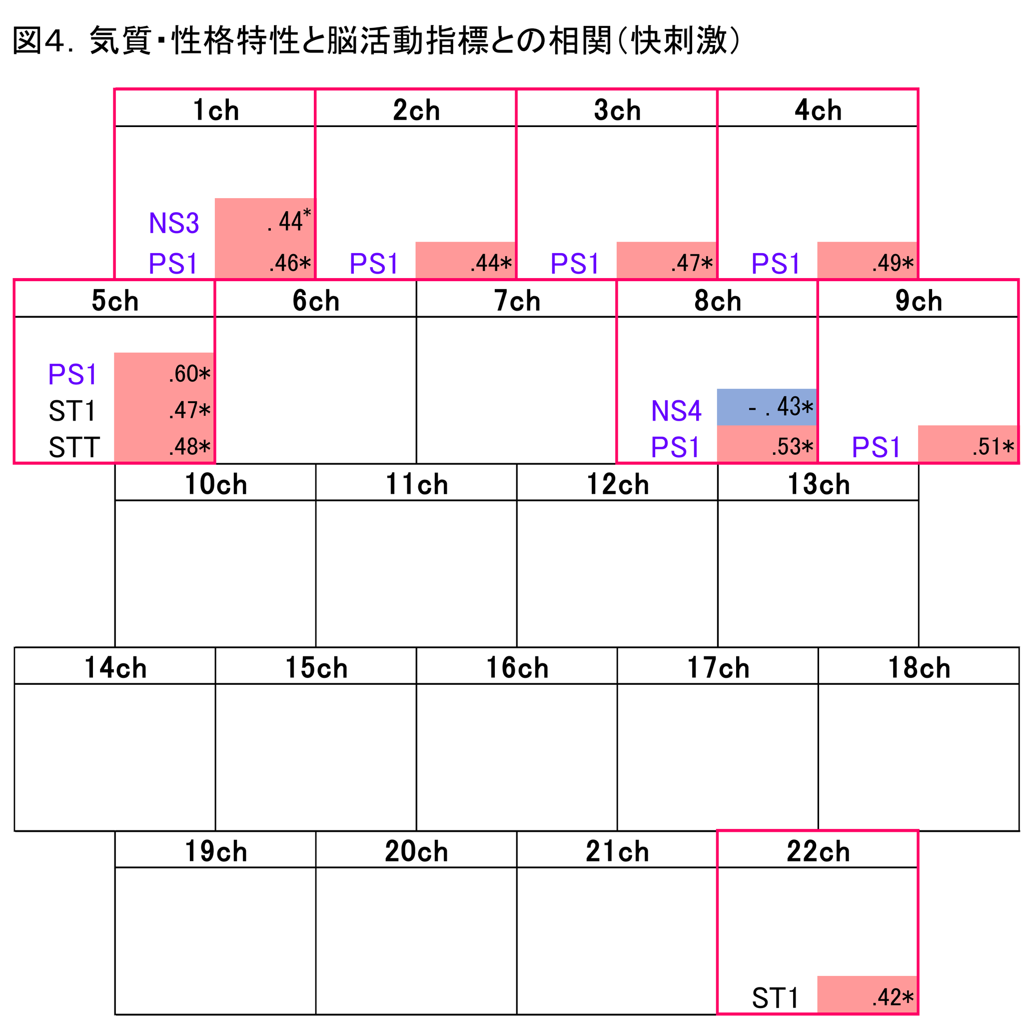


図2 快刺激への反応強さ





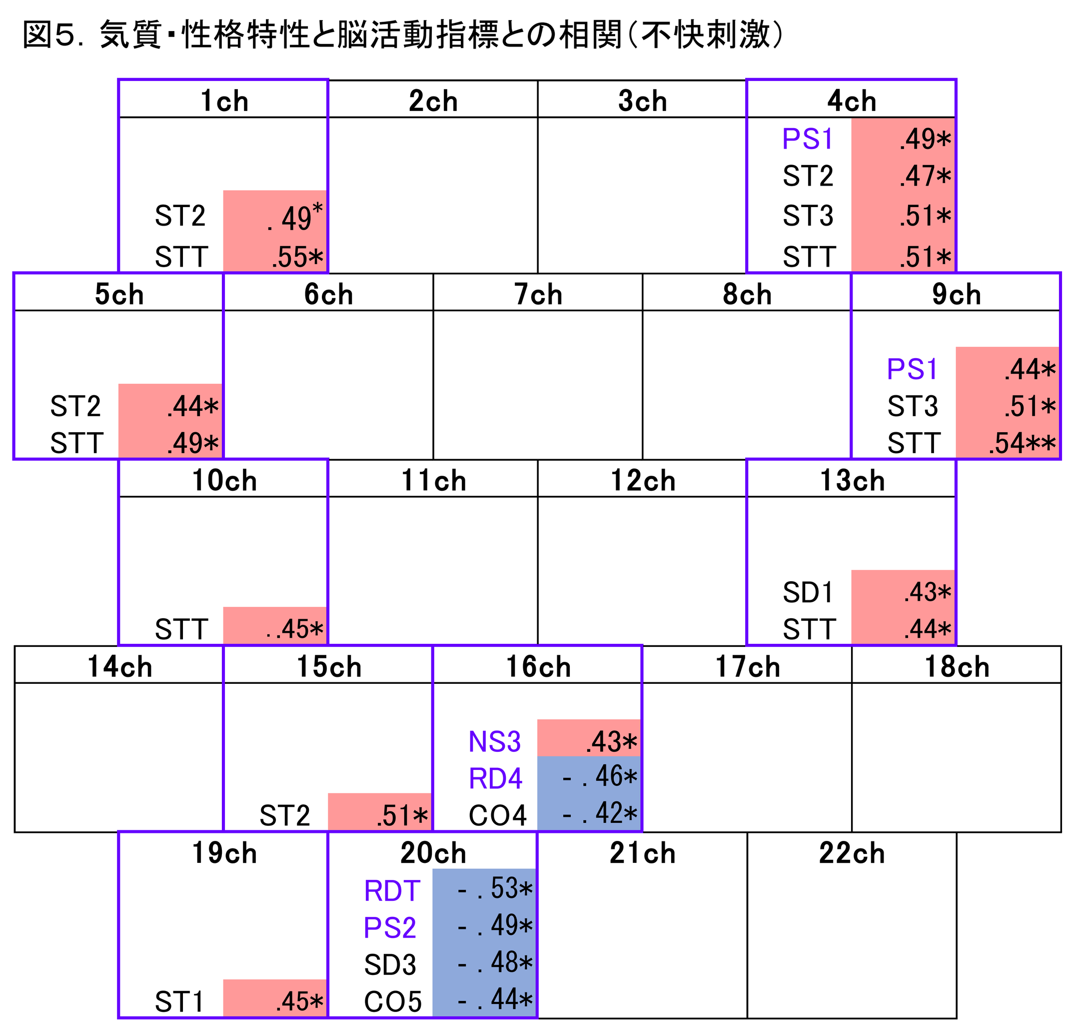
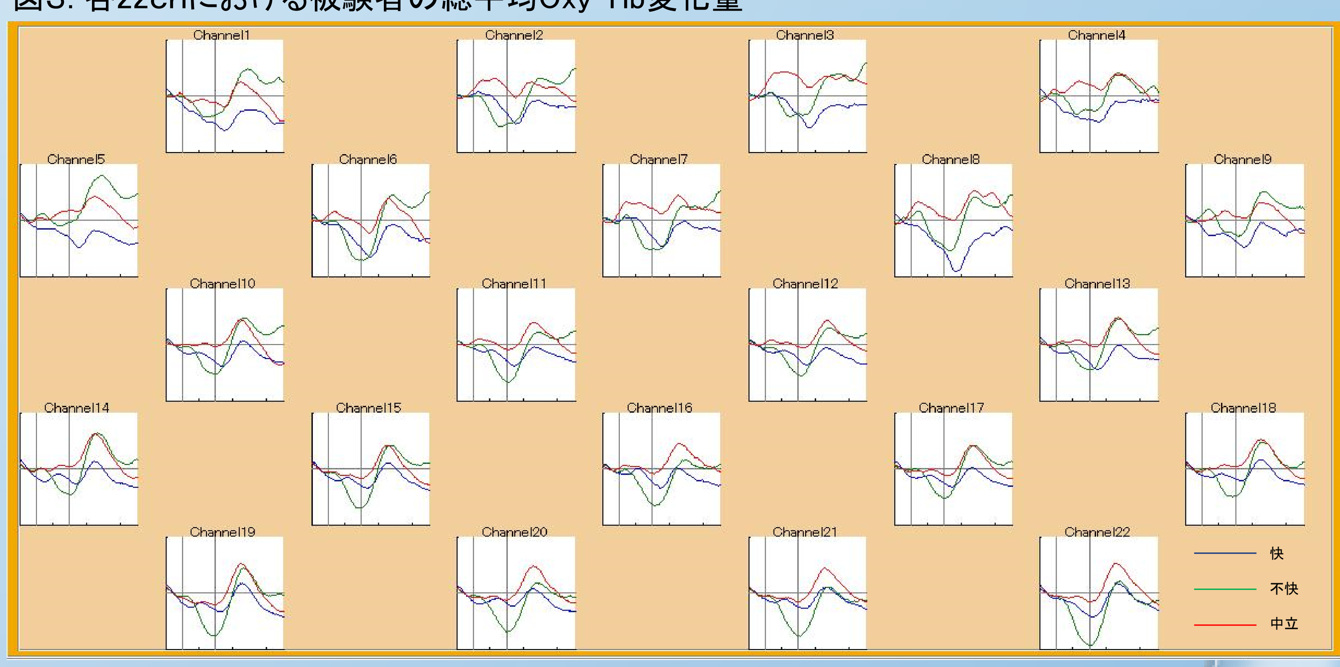
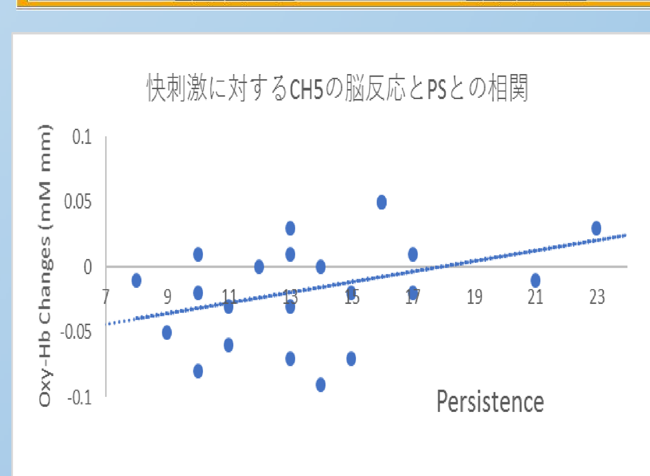
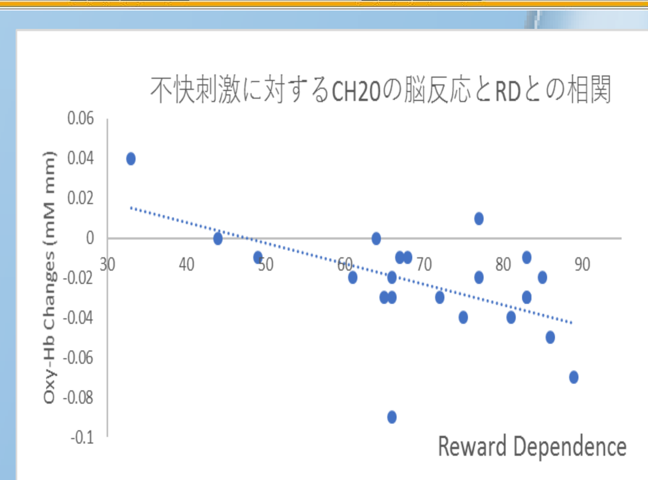


図3. 各22chにおける被験者の総平均Oxy-Hb変化量







【結果】

Oxy-Hbの変化量は、Activation区間がbaselineに比べ、ch18以外すべてのchにおいて有意差がみられた（図1、図2）。図3は、各感情刺激に対する各22chにおける被験者22名の総平均Oxy-Hb変化量である。Oxy-Hbが快刺激に対して若干減少し、不快刺激に対して大きく減少している傾向がみられた。また、気質・性格特性と感情刺激に対する脳反応に有意な相関がみられた。（図4）快刺激に対しては、OFC付近、前頭極(ch1,ch2,ch3,ch4)においてNS3・PS1および背外側前頭前野（dl-PFC）(ch5,ch8,ch9)においてPS・STと脳活動指標に正の相関、NS4は負の相関がみられた。（図5）不快刺激に対しては、左右の前頭極(ch1,ch4)とdl-PFC(ch5,ch9,ch10,ch13)においてPS・STと脳活動指標に正の相関がみられ、中央部dm-PFC（ch16,ch20）においてRD・CO・PS・SDと脳活動指標に負の相関、NS3は正の相関がみられた。

【考察】

はじめてTCI気質・性格検査を使用し、それと感情刺激に対する前頭葉反応との関連がみられた。個人の気質・性格によって、感情刺激に対する反応が異なることが示唆された。
OFC付近および前頭極部位：PSが高いほど、快/不快刺激への反応が弱い；
dl-PFC :NS4が高いほど、快刺激への反応が強い；
dm-PFC: RD・COが高いほど、NS3は低いほど、不快刺激への反応が強い。

NS1: Exploratory excitability
NS2: Impulsiveness
NS3: Extravagance
NS4: Disorderliness

HA1: Anticipatory worry
HA2: Fear of uncertainty
HA3: Shyness
HA4: Fatigability

RD1: Sentimentality
RD2: Openness to warm communication
RD3: Attachment
RD4: Dependence

PS1: Eagerness of effort
PS2: Work hardened
PS3: Ambitious
PS4: Perfectionist

SD1: Responsibility
SD2: Purposeful
SD3: Resourcefulness
SD4: Self-acceptance
SD5: Enlightened second nature

CO1: Social acceptance
CO2: Empathy
CO3: Helpfulness
CO4: Compassion
CO5: Pure-hearted conscience

ST1: Self-forgetful
ST2: Transpersonal identification
ST3: Spiritual acceptance

【概要 2-3】高齢者の感情情報処理の脳機能と生理指標

Age-related changes of emotion recognition and interoception

寺澤悠理（戦略参加研究者）
梅田聡（戦略参加研究者）

１．Introduction

Interoceptive accuracy varies across individuals and the accuracy is closely related to contents of emotional experience. Our previous research reported that individuals who are highly sensitive to their own interoception are sensitive to their own and others' emotions (Terasawa et al., 2014). Also, associations between interoception and psychiatric symptoms (anxiety, depression etc.) have been examined.　However, little is known about the effects of aging on the interoceptive accuracy and its impact on emotional experience.

In the present study, we examined aging effects on interoceptive accuracy and emotional sensitivity by the experimental task.

２．Methods

2-1. Participants

Older adults: 35 older adults (25 male) participated (mean 59.7 years ±6.1). Seventeen out of thirty five participants were involved in an fMRI study (9 males, mean 59.8 years ±6.2).
Younger adults: 30 undergraduate and graduate students (17 male and 13 female) participated (mean 21.4 years ±1.8) in this study.

2-2. MRI

3D T1 images (1mm × 1mm ×1mm) were acquired and visually inspected for Voxel Based Morphed (VBM) analysis with a 3T MRI machine (GE, SIGNA).

2-3. Tasks

Emotional sensitivity task (Fig. 1): We selected 5 types of facial expression, those were happy, sadness, disgust, anger and neutral. We made morphed continua photos between neutral and each facial expression: for instance happy-neutral, sadness-neutral, disgust-neutral and anger-neutral. Eight steps between neutral-100% and each emotion 100% were prepared. Each stimulus was presented in random order and participants judged whether they can feel any emotion from the stimulus or not, and chose most appropriate emotion when they judged the stimulus have emotional valence. There were 200 trials in total. Individual's threshold to feel the emotion from photos were obtained from their responses against the facial expression photos.

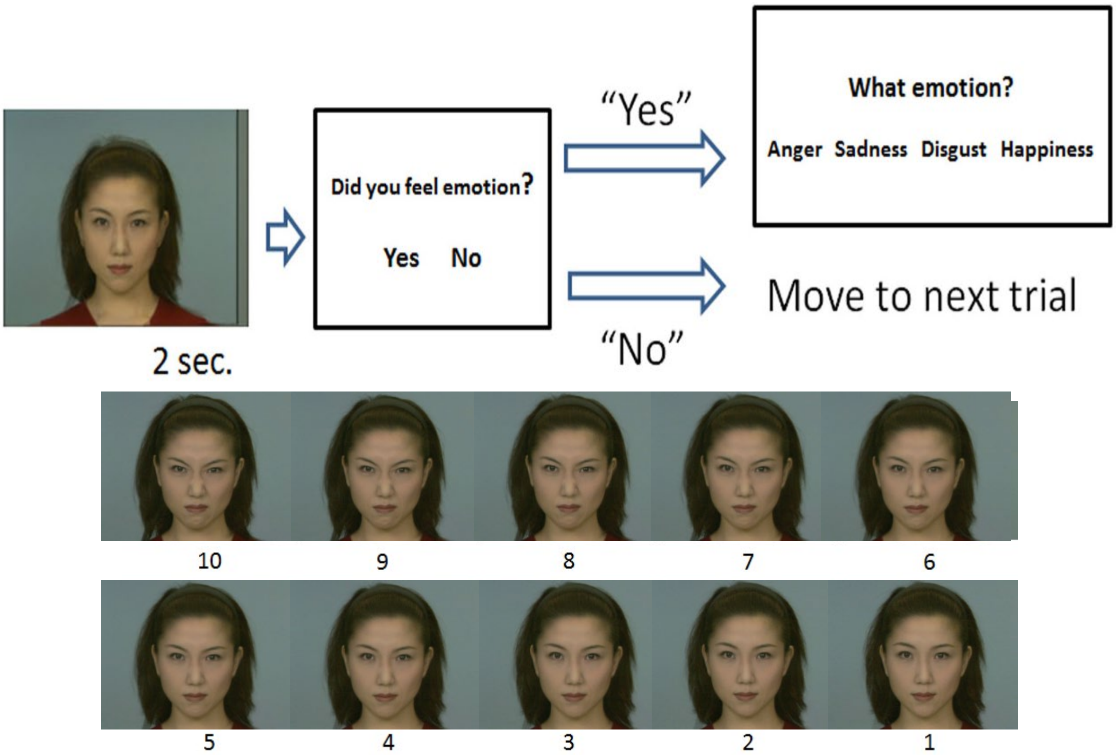


Fig. 1 Outline of a trial and examples of stimuli used in the task

Heartbeat Perception Task

(Schandry, 1981; Ehlers & Breuer. 1992): Participants were required to report number of heartbeats that they could feel over a period of time, such as 45 sec, 35sec and 25 sec. Actual heartbeats were measured by pulse oximeter. Interoceptive sensibility was evaluated by the levels of dissociation between reported and actual heartbeats (HDT error rate), which was calculated by following equation; (|actual heartbeats-reported heartbeats|)/ actual heartbeats.

Time Estimation Task

(Dunn et al., 2010): Participants were required to report number of seconds during a given period, such as 56 sec, 40 sec and 23 sec. The reported length was compared with the actual duration. Time estimation error rates were calculated in the manner similar to the heartbeat perception task.

3. Results

Emotional sensitivity task

We classified the stimuli that made participants feel an appropriate emotion at least three times out of five (i.e., at least 60% of the trials) as having sufficient value to identify the emotions. As Fig. 2 shows, the sensitivity to anger, disgust and sadness expressions were lower in the older group (Anger: F (1, 58)=8.82 p<.0.05, Disgust: $F(1, 47)=5.13$ $p<0.10$, Sadness: $F(1, 57)=14.58$ $p<0.05$). The effect of age was not found for the happy expression.

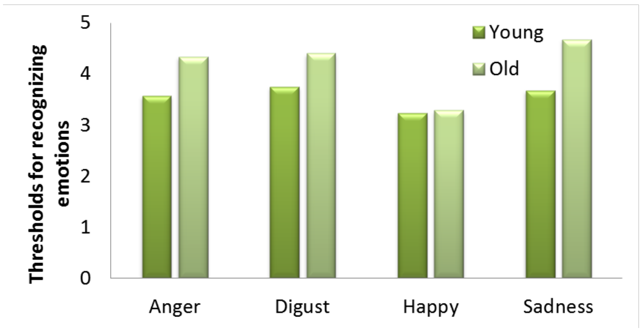


Fig. 2 Sensitivity to emotional expressions.

Heartbeat Perception Task

Mean error rate in the older group was significantly higher than the younger group ($F(1, 116)=53.859$ $p<.0001$, Fig. 3). The performance of the time estimation task was equivalent for both groups(mean error rates: young = 0.2±0.11, Old = 0.24±0.17).

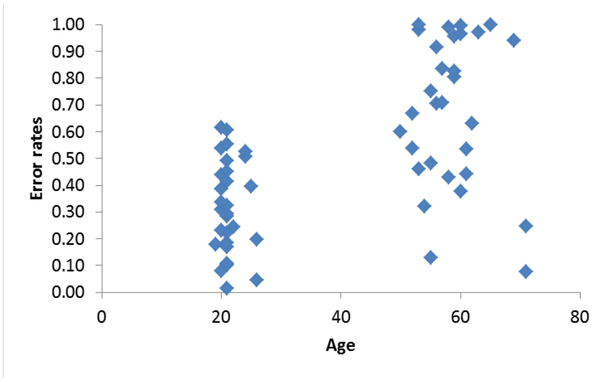


Fig. 3 Error rates in the heartbeat perception task.

Interoceptive accuracy and emotional sensitivity and insula cortex

Insula cortex is known as a common neural substrate for interoception and emotion (Terasawa et al., 2013). We set the insula cortex as the Region of Interest (ROI) and conducted Voxel Based Morphed analysis with T1 images by CAT 12 (SPM 12). Negative correlations between thresholds for Anger and gray matter volume of bilateral insula cortex were observed after controlling for age (Fig. 4).

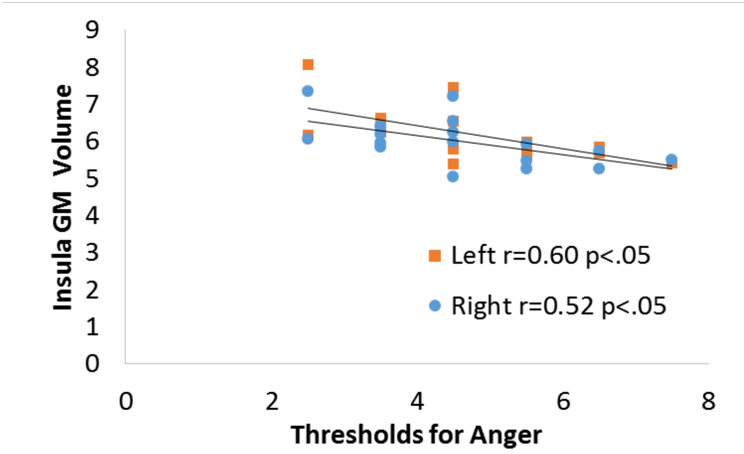


Fig. 4 Sensitivity to anger and insula GM volume

Interoceptive accuracy and emotional sensitivity

In our previous study (Terasawa et al., 2014) with the younger group, we reported that individuals who were sensitive to their own bodily sensations exhibited lower thresholds for emotions. However, the pattern was not observed in the older group, except for sadness. The opposite pattern was observed for anger and disgust. (Fig. 5)

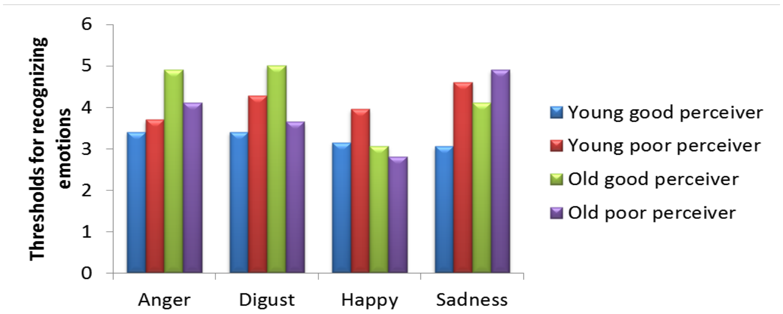


Fig. 5 Performance of heartbeat perception task and emotional sensitivity.

4. Discussion and conclusion

We found significant aging effects on interoceptive accuracy. Sensitivities to anger, disgust and sadness were lower in the older group. Contrary to the younger group, good perceiver of their interoception revealed lower sensitivity to anger and disgust in the older group. Declined interoceptive accuracy would underlie the changes of emotional sensitivity, but the detailed mechanism is still being discussed.

The insula cortex is one of the important neural substrates of interoception, and the region was found to show faster aging progression on cortical thickness. We suggest that the faster drop will cause the decreased interoceptive accuracy and changes in emotional experience, and found the negative correlation between thresholds for anger and GM volume of bilateral insula cortex. Further studies using neuroimaging techniques are needed to clarify the details.

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視覚情報が高齢者の雑音下の発話理解に与える影響：

脳波と行動指標による検討

関根和生（特任助教，ＰＤ研究員）

１．研究の背景と目的

日常のコミュニケーション環境には，多少の雑音が含まれている。我々はそうした雑音下で情報を伝達し理解している。これまでの研究によれば，発話に付随して生じる視覚情報，とりわけ唇の動きと身振りが，雑音下における発話理解を助けることがわかっている（Schubotz et al.，in prep)。しかし，これらの研究は，英語やオランダ語など， 日本語と比べ，音素(母音と子音)数の多い言語を対象に行われてきた。英語やオランダ語などの言語では，微細な口唇の動きが音韻を弁別するのに大きな影響を及ぼしていると考えられるが（Sekiyama & Tohkura, 1991)，日本語話者とっても口唇の動きが同程度影響を与えているかを検討する必要がある。また，発話理解に及ぼす視覚情報の影響が，成人や高齢者でどの程度異なっているかはわかっていない。聴力の低い高齢者は，聴覚情報処理の低下を補うため，視覚情報を成人よりも 多く利用する可能性がある。こうした 2 つの問題意識から，本研究では，成人と高齢者において，視覚情報 が雑音下の発話理解に与える効果を検討した。

本研究目的を遂行するため，視覚情報(口唇と身振り動きの有無)と聴覚情報(信号対雑音比（SNR）の程度)を制御したビデオ刺激を作成した。ビデオ提示中の研究参加者の脳波と行動指標を取得することによって，オンラインとオフラインの情報処理に関するデータを得ることができる。事象関連電位を計測した先行研究（Drijvers & Özyürek, 2017)に従い，視覚情報の聴覚情報に対する影響を N400 成分の振幅という脳指標によって判断した。また，課題の正答率を，騒音下における視覚情報の利用の行動指標として，計測した。現在，脳波データは分析中であるため，本報告書では，この行動指標の結果を報告する。

本研究は 2 つの意義がある。一つ目は理論的な意義であり， 文脈や年齢を考慮した発話理解過程のモデル化に役立つ情報を得ることができる。二つ目は実践的な意義 で，高齢者のコミュニケーションを支援するための，視聴覚情報の提示方法に関する基礎データを提供することである。

２．方法

2-1．調査参加者

若年成人 25 名（平均年齢 20 歳， SD= 3.3，女性 13 名）と高齢者 25 名(平均年齢 69 歳，SD=4.1。女性 12 名)が参加した。成人は大学の授業を通じて，また高齢者は人材派遣会社を通じて募集した。参加者はすべて健常で，視聴覚の障害や認知症は患ってはいなかった。

2-２． 実験刺激

視聴覚刺激を作成するため，はじめに身振りで表すことができる 220 の日本語の動詞を選択した。女性の役者がそれぞれの動詞を 2 つの異なるバージョンで発話する場面を録画した。一つのバージョンでは，動詞の行為を表す身振りを産出しながら動詞を発する条件で，もう一つのバージョンでは，身振りは産出せず，動詞のみを発話した。また，発話に雑音をくわえるため，上記の 2 つのバージョンの発話に，それぞれ SNR-12 と SNR-18 のマルチトーカーバブル（複数人の話者が同時に発話をしているガヤガヤ声のノイズ）を重ね合わせ，ノイズ発話を作成した。また，動画の方は，唇の影響を検討するため，口元をマスキングしたバージョンも作成した。以上のような加工・編集により，最終的に以下のような１１条件が作成された：

１．V 条件（発話はない， 口の動きのみが見える）
２．VG 条件（発話がない，口と身振りの動きのみが見える）
３．S-C 条件
４．SV-C 条件
５．SVG 条件
６．S-12 条件
７．SV-12 条件
８．SVG－12 条件
９．S-18 条件
１０．SV-18 条件
１２．SVG－18 条件，

S=発話，V＝口の動き，G＝身振り, C=ノイズのないクリアな発話，数字=SNR の度合

2-3． 手続き

調査はすべて大学の脳波実験室で個別に行われた。実験当日，研究参加者は，実験室に到着後，研究目的や測定機器の安全性に関する説明を受け，同意書に記入した。その後，聴力検査を行い，実験に取り組んだ。脳波計装着後，参加者はモニターの前に座った。モニターには，ある動詞を伝える役者のビデオが映し出され，役者がどのような動詞を言ったのか，モニター横のマイクに向かって話すように教示された。合計 220 試行呈示され，各条件が 11 回ずつ出現するように，条件と動詞の呈示順はランダマイズされた。1 ブロック 22 試行が呈示され，合計 5 ブロック行った。

3．結果と考察

各条件の正答率（20 試行中の正答した試行）を算出した。ここでは条件が等しくなるように， V 条件と VG 条件を除外し，残りの 9 条件の正答率を従属変数とし，混合計画の 3 要因の分散分析（年齢(成人，高齢者)＊ モダリティー（S, SV, SVG） ＊ ノイズ （ノイズなし，-12, -18)）を行った（図 1 ）。

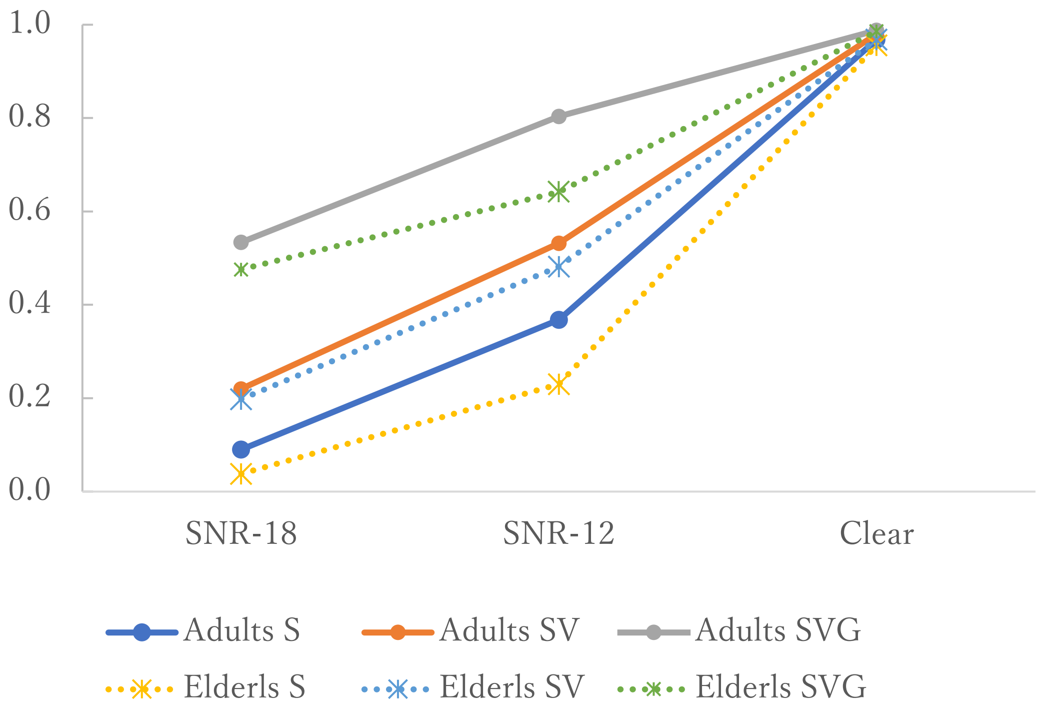

図 1　条件ごとの正答率

３要因の交互作用は有意ではなかったが，年齢の主効果，F（1，48）＝12.2，p <.001，ノイズの主効果, F（2，96）＝1773.3，p <.001，モダリティーの主効果，F（2，96）＝401.9，p <.001 がみられた。また，年齢とノイズ，F（2，96）＝10.2，p <.001，モダリティーとノイズ，F（4，192）＝97.4，p <.001，の交互作用が有意であり，年齢とモダリティーの交互作用が有意な傾向にあった，F（4，192）＝2.79，p <.07。以上のことから，以下の３点が明らかになった；１）成人は，高齢者よりも発話の理解がよいこと，２）両年齢群とも，発話にノイズがある場合，口の動きと身振りが発話の理解を促進すること，３）特に成人は，ノイズが中程度の場合，高齢者よりも身振りから情報を得ていること，が明らかにされた。このことから，雑音のある発話の場合，口の動きも身振りも両年齢の発話理解を助けるが，とくに成人では身振りが強く発話理解に影響を及ぼすことが明らかにされた。

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（3） 研究概要報告書に述べた研究内容の詳細と補足資料

３．　音声コミュニケーションにおける音韻，プロソディーの役割

３-1.　新生児の音韻，プロソディー刺激に対する脳反応

３-2.　音韻配列規則に関与する音韻知覚についての研究

３-3.　フレーズプロソディー知覚についての対照言語研究

３-4.　遠隔コミュニケーション事態における
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The cerebral hemodynamic response to phonetic changes of speech in preterm and term infants: The impact of postmenstrual age

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ABSTRACT

Higher brain dysfunction, such as language delay, is a major concern among preterm infants. Cerebral substrates of cognitive development in preterm infants remain elusive, partly because of limited methods. The present study focuses on hemodynamic response patterns for brain function by using near-infrared spectroscopy. Specifically, the study investigates gestational differences in the hemodynamic response pattern evoked in response to phonetic changes of speech and cerebral hemispheric specialization of the auditory area in preterm infants ($n = 60$) and term infants ($n = 20$). Eighty neonates born between 26 and 41 weeks of gestational age (GA) were tested from 33 to 41 weeks of postmenstrual age (PMA). We analyzed the hemodynamic response pattern to phonemic and prosodic contrasts for multiple channels on temporal regions and the laterality index of the auditory area. Preterm infants younger than 39 weeks of PMA showed significantly atypical hemodynamic patterns, with an inverted response shape. Partial correlation analysis of the typicality score of hemodynamic response revealed a significant positive correlation with PMA. The laterality index of preterm infants from 39 weeks of PMA demonstrated a tendency rightward dominance for prosodic changes similar to term infants. We provide new evidence that alterations in hemodynamic regulation and the functional system for phonemic and prosodic processing in preterm infants catch up by their projected due dates.

1. Introduction

Major disabilities in preterm infants are becoming less frequent as medical technologies advance. However, higher rates of brain dysfunction in such infants compared with term infants remain an issue (Mwaniki et al., 2012). Even if preterm infants do not present with major central nervous system disorders or other significant complications (e.g., grade 2 to 4 intraventricular hemorrhage, periventricular leukomalacia, bronchopulmonary dysplasia, BPD or necrotizing enterocolitis, NEC) at discharge from hospital, higher brain dysfunctions may appear during development (Luu et al., 2009; Aarnoudse-Moens et al., 2009). Such dysfunctions in the cognitive system can be examined by neuroimaging of the brain function and brain anatomy of infants. However, assessment of the hemodynamic response function to cognitive processing could also reveal some aspects of physiological traits of higher brain functions.

Higher brain dysfunction should be identified in the early stages of development to enable early intervention. However, methods for early detection among preterm infants have not yet been established (Mento and Bisiacchi, 2012). Development of such methods is hindered by the lack of research into the neuronal substrates associated with early speech perception in preterm infants, even though this is one of the most important higher brain functions (Mento and Bisiacchi, 2012; Tusor et al., 2014). Studying these processes in preterm infants will provide insights into early developmental milestones and the relationship between brain maturity and function.

EEG studies of term and preterm infants have provided evidence of the neuronal processes underlying early speech perception, with a particular focus on auditory-evoked potentials called mismatch negativity (MMN). For instance, prematurely born infants exhibited MMN to phonemic contrasts of /y/ and /i/, suggesting they had the ability to discriminate between them (Cheour-Luhtanen et al., 1996). However,

Abbreviations: BPD, bronchopulmonary dysplasia; NEC, necrotizing enterocolitis; MMN, mismatch negativity; PMA, postmenstrual age; fNIRS, functional near-infrared spectroscopy; Oxy, oxygenated; Deoxy, deoxygenated; HRF, hemodynamic response function; GA, gestational age; PNA, postnatal age; SOA, stimulus onset asynchrony; ROI, region of interest; BOLD, blood oxygenation level dependent; IQR, interquartile range

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preterm infants tend to show smaller MMN amplitude than do age-matched full-term infants in their first year of life (Alho et al., 1990). Likewise, recent EEG studies have reported that neural maturation, reflected by postmenstrual age (PMA), has a large impact on speech discrimination (Pena et al., 2010; Bisiacchi et al., 2009). EEG studies have also revealed the developmental course of language-specific phonemic processing, showing developmental changes to produce stronger MMN to native phonemic contrast (Cheour et al., 1998; Dehaene-Lambertz and Gliga, 2004). Moreover, the MMN index in 7.5-month-olds was shown to predict language development at 2 years old (Kuhl et al., 2008).

Although EEG studies have provided accumulating evidence on the functional neurodevelopment as reviewed above, functional near-infrared spectroscopy (fNIRS) is an emerging neuroimaging technique that can strengthen the role of EEG study in the understanding of brain development. This technique has better spatial resolution and so can increase our knowledge of the cerebral substrates for receptive language in preterm infants, particularly hemispheric specialization of specific brain regions. Although the temporal resolution of fNIRS is lower than that of EEG, fNIRS uses an infant-friendly headset without any paste or gel and is a more portable system, which has better temporal resolution (10 Hz) than fMRI. fNIRS measures neuronal activity reflected in changes in concentrations of oxygenated (oxy-) Hb and deoxygenated (deoxy-) Hb and it has been used to identify various neurocognitive developmental processes in infants (Minagawa-Kawai et al., 2011; Gervain et al., 2011; Minagawa-Kawai et al., 2008). Such findings have elucidated the cerebral responses of infants to two spoken language components: phonemes and prosody (Sato et al., 2003; Arimitsu et al., 2011). Phonemic structures (e.g., vowels and consonants) tend to be processed predominantly in the left temporal area, while prosody (e.g., intonations or rhythms) activates the right side more in both children and adults. This functional hemispheric specialization is called functional cerebral laterality of the auditory cortices and it facilitates efficient processing in the cerebral cortex (Minagawa-Kawai et al., 2011; Sato et al., 2003; Arimitsu et al., 2011).

Although language comprehension involves various processes, the perceptual analysis of phonemes and prosody is a crucial initial step for language acquisition in the first year of life. Indeed, perceptual analysis of phonemes deeply affects an infant's learning of their native language. Likewise, prosody is important, because it provides various cues, such as pitch changes, intensity, and rhythmic structures—all of which facilitate the infant's speech acquisition, as exemplified by infant-directed speech offering rich prosodic cues.

Apart from the investigations of cognitive functions stated above, fNIRS is also one of the significant tools to examine hemodynamic physiology in infants as well as in adults. Typical hemodynamic activity of the adult cerebral cortex is characterized by an increase in oxy-Hb and a slight decrease in deoxy-Hb. This is known as the hemodynamic response function (HRF) (Boynton et al., 1996; Friston et al., 2000). However, the development of the HRF pattern in the human brain remained unclear, and some fNIRS studies reported an inverted HRF pattern for young infants in response to perceptual stimuli, whereas some studies did not (Minagawa-Kawai et al., 2008; Sato et al., 2003; Arimitsu et al., 2011). This has been a controversial issue, and evidence of its presence in preterm infants is particularly sparse, partly because the fNIRS investigation of HRF is a relatively new subject. Notably, a recent fNIRS study reported developmental changes in phase differences of oxy- and deoxy-Hb in preterm infants (Watanabe et al., 2017). Although such developmental changes in neurovascular regulation are very intriguing, these results come only from resting-state measurements; HRF patterns during perceptual or cognitive processing should also be investigated.

Consequently, the present study attempts to determine developmental differences in the HRF in response to different functional speech stimuli in preterm and term infants at each PMA. For stimuli, we employed well-established instances of linguistic contrast (phonemic and prosodic contrasts) that are crucial for early language development, as mentioned above. In this study, we specifically examined two aspects of the brain response in neonates: (a) the hemodynamic response pattern of oxygenated (oxy)-Hb changes and (b) functional hemispheric specialization in the temporal cortices. We chiefly focused on PMA, also taking gestational age (GA), post-natal age (PNA), and birth weight into consideration, because HRF is closely related to the physiological development of neonates' vascular systems, which may continuously develop before and after birth. Furthermore, as stated above, the EEG literature on speech perception has reported a significant role of neural maturation corresponding to PMA.

Previous fNIRS studies have also reported increased functional hemispheric specialization during development in the first year of life, reporting developmental changes in laterality but with a normal HRF in every age group. However, no study so far has attempted to examine functional cerebral laterality and HRF regulations in preterm infants (Minagawa-Kawai et al., 2011). We therefore explore whether preterm infants show functional cerebral laterality similar to that reported in term infants.

2. Methods

2.1. Participants

The parents of participants were approached for consent and enrollment between 2010 and 2012. The study included 20 term and 60 preterm neonates, who were all from monolingual Japanese families. Participants were divided into four groups according to their PMA at time of examination. Demographic data for each group are shown in Table 1. An additional 16 neonates were excluded because of noise due to motion artifacts and/or loose probe attachments.

The GA was determined by an obstetrician using data including the last menstrual period, the first accurate ultrasound examination, and assistive reproductive technology. We excluded infants with chromosomal or congenital anomalies including congenital heart anomalies, grade 2 to 4 intraventricular hemorrhage, periventricular leukomalacia, moderate and severe BPD defined as per the National Institutes of Health criteria, NEC, deafness diagnosed by automated auditory brainstem response and those who were medically unstable (Jobe and Bancalari, 2001). Ductus arteriosus was clinically closed at the time of

Table 1
Characteristics of participating infants grouped by PMA at time of examination. IQR stands for interquartile range.

	Preterm infants			Term infants
Group of CGA at the examination	33–35 weeks (n = 27)	36–38 weeks (n = 17)	39–41 weeks (n = 16)	37–41 weeks (n = 20)
Male, n (%)	14 (51.9)	8 (47.1)	7 (43.8)	9 (45.0)
Age at the examination, days, median (IQR)	16 (12–27.5)	17 (9–29)	49 (43.75–56)	4 (3.75–6.25)
GA at birth, weeks, median (IQR)	32 (30 – 33)	33 (32–35)	32 (31–34)	38 (37–39)
Birth weight, g, median (IQR)	1668 (1313–1898)	1733 (1421–1834)	1614 (1453–1846)	2798 (2705–3029)
Apgar score at 1 min, median (IQR)	7 (5.5–8)	8 (6–8)	7 (4.75–8)	8 (8–9)
Apgar score at 5 min, median (IQR)	8 (7.5–9)	9 (8–9)	8 (8–9)	9 (9–9)
Weight at the examination, g, median (IQR)	1886 (1773–2046)	1940 (1850–2228)	3007 (2980–3302)	2735 (2638–2948)

examination in infants whose birth weight was > 1500 g. For infants whose birth weight was < 1500 g, the closure of ductus arteriosus was confirmed by echocardiography before the fNIRS measurement. This study was conducted at the Keio University Hospital (Tokyo, Japan). The institutional review boards of the hospital approved all protocols related to the study, and informed consent was obtained from the parents of all participating infants.

2.2. Stimuli and conditions

For stimulus words, we used three different forms of one Japanese verb /itta/, /itte/, and /itta?/. These sounds were synthesized from speech signals produced by a male adult as described elsewhere (Imaizumi et al., 1998). The two main experimental conditions were the phonemic contrast (/itta/ vs. /itte/), which differed in the final vowel, and the prosodic contrast (/itta/ and /itta?/), which differed in pitch contours. We employed a block design where the target block for these two conditions was alternately presented against an identical baseline block. Specifically, participants received a baseline block where the stimulus /itta/ was repeated with 1 s of stimulus onset asynchrony (SOA) for a total of 15 s. They then received another 15 s of the target block for either the phonemic or prosodic condition. Under the phonemic target block, /itta/ and /itte/ were presented in a pseudo-random order at 1 s of SOA. Similarly, the prosodic condition comprised a serial presentation of /itta/ and /itta?/ in a random order. The two blocks (baseline and target blocks) under each condition were alternated at least seven times per condition.

2.3. Procedure

The auditory-evoked responses in the bilateral temporal area and part of the frontal regions were recorded using fNIRS (ETG 4000, Hitachi Medical Corporation, Tokyo, Japan). A silicon pad with five incident and four detection probes, arranged in a 3 × 3 square lattice with a separation of 20 mm, was placed laterally on each side of the infant's head (Fig. 1a). Each pad comprising 12 channels was attached to the head so that the center detector probe at the bottom of the horizontal probe line corresponded with the T3 or T4 position in the international 10/20 system as described elsewhere (Boynton et al., 1996). Over these two probe pads, thin plastic plates were inserted for better attachment to the head; these pads and plates were held in place by elastic bands. Average infant head circumference was 30.8 cm (SD = 2.1) for the youngest group and 33.8 cm (SD = 0.8) for the oldest group, and this was statistically different ($P < 0.01$). Taking 4.0 cm of the probe pad into consideration, this creates a difference of 1.1% coverage of the measurement area for each temporal pad. Although this indicates a slightly larger measurement area for younger infants, this difference is negligible considering the spatial resolution of fNIRS. The infants were tested when asleep and received stimulation at amplitudes of approximately 67 dB via two speakers, which were positioned about 45 cm away from the participant.

2.4. Data analysis

First, we analyzed each channel separately to assess whether the oxy-Hb response increased or decreased with the shape of a typical HRF. We aimed to examine the general hemodynamic time course, so we analyzed all channels used. We focused on the oxy-Hb response because this general indicator was greater than the deoxy-Hb response (Minagawa-Kawai et al., 2007; Lloyd-Fox et al., 2010). Next, a region of interest (ROI) in the temporal auditory area was tested to examine functional hemispheric specialization (Fig. 1a). For spatial estimation of the channel location in the brain, we employed the virtual registration method to map fNIRS data onto the MNI standard brain space (Tsuzuki et al., 2007). Oxy- and deoxy-Hb concentrations were calculated from the absorption of 695 and 830 nm laser beams sampled at 10 Hz and smoothed with a 1-second moving average.

We used the same methods to those in our previous study for data preprocessing, including artifact rejection, data blocking, and detrending (Arimitsu et al., 2011). The time courses of Hb concentration changes in the analysis blocks were averaged more than four times for each of the stimulus conditions. To determine whether the obtained

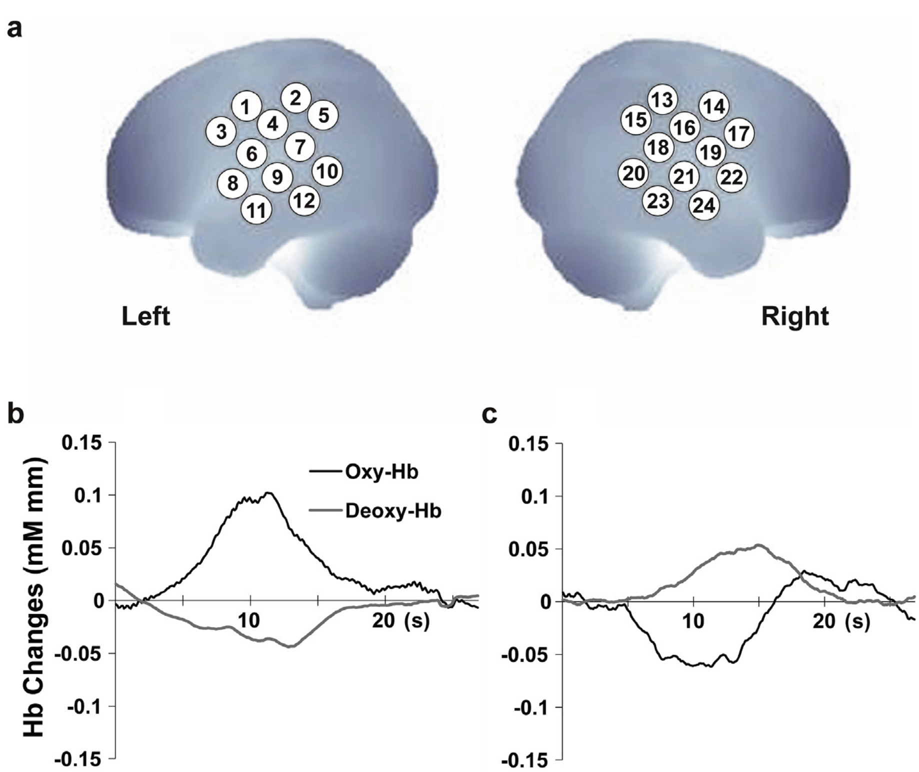

Fig. 1. HRF patterns in the temporal regions. (a) Location of 12 channels for each hemisphere. Each channel is represented by a number. Channels 1 to 12 are located on the left hemisphere (left) and channels 13 to 24 are located on the right hemisphere (right). (b, c) Representative examples of time courses of Hb changes. The typical HRF pattern is characterized by an increase in oxy-Hb and a slight decrease in deoxy-Hb (b), while the inverted pattern is characterized by a decrease in oxy-Hb (c).

time course of the Hb changes fits with the typical HRF pattern or an atypical reversed one, the correlation between the canonical HRF model (Boynton et al., 1996; Friston et al., 2000) and the oxy-Hb data was calculated for each channel for each infant. The canonical HRF model uses a Gaussian smoothing kernel which represents the typical HRF pattern and is regularly employed in fMRI analysis (Boynton et al., 1996; Friston et al., 2000). A positive correlation coefficient suggests an increased pattern similar to the typical HRF model, while a negative value represents a decreased pattern, indicating an atypical HRF pattern. These values are then transformed to Fisher's *Z*-score, which we denoted the HRF-typicality score. From these data, the average HRF-typicality score for 24 channels was obtained for the phonemic and prosodic conditions in each infant.

We categorized the participants into three types: (1) "typical" where the oxy-Hb change showed an increased pattern (positive HRF-typicality score) for both phonemic and prosodic conditions, (2) "intermediate" where oxy-Hb increased for only one condition, and (3) "atypical" where oxy-Hb decreased (negative HRF-typicality score) for both conditions (Fig. 1b and Supplemental Fig. S1). In addition to this categorical assessment, we performed ANOVAs to investigate the HRF-typicality scores. For this analysis, the dependent variables were the averaged HRF-typicality scores of phonemic and prosodic conditions. Finally, we performed regression analyses to examine the relationship between the HRF-typicality score and PMA, controlling for PNA at examination, birth weight and GA.

Next, to examine functional hemispheric specialization, we followed the same method for calculating the laterality index as described elsewhere (Sato et al., 2003; Arimitsu et al., 2011; Minagawa-Kawai et al., 2007; Sato et al., 2007). This involved first defining an ROI in the auditory area at channels 6, 8, 9, and 11 on the left hemisphere and channels 19, 21, 22, and 24 on the right (Fig. 1a). These channels were chosen because their locations likely incorporate the auditory areas, according to the virtual registration method (Tsuzuki et al., 2007). For each participant, we selected one channel that showed the maximum oxy-Hb response within the auditory area. We employed this method as it has been used in previous studies that have successfully elicited hemispheric lateralization (13, 16, 17, 22, 25,). We used the peak oxy-Hb value 5–15 s after stimulus onset for channel selection. For negative HRF-typicality scores, we took the negative peak. The laterality index was calculated using these values and the formula (L − R)/(L + R), where L and R are peak values on the left and right sides, respectively.

3. Results

3.1. Impact of PMA on development of HRF patterns

In response to speech stimulation, preterm infants showed variable patterns of auditory-evoked hemodynamic changes in the measured channels (Fig. 1a–c). Term infants generally demonstrated a HRF typically seen in adults, with an increase in oxy-Hb and a slight decrease in deoxy-Hb in the temporal area in response to speech stimulation (Minagawa-Kawai et al., 2007; Lloyd-Fox et al., 2010) (Fig. 1b). However, preterm infants demonstrated variable Hb patterns, with either a similar pattern to term infants (Fig. 1b; typical Hb pattern) or an inverted pattern with decreased oxy-Hb (Fig. 1c; atypical Hb pattern). Regardless of the direction of HRF, all the neonates showed consistent responses to the target stimuli compared with the baseline stimuli.

To objectively assess the typicality of HRF patterns, we calculated the fit between the data and the canonical HRF model. Then we created three categories using HRF-typicality scores from the average data of 24 channels. If the score was positive for both of stimuli conditions, it was grouped as "typical". If one of the scores was negative, it was categorized as "intermediate" (see Methods for more detail). Fig. 2a shows the proportions of HRF patterns for each PMA group. The proportion of infants with a "typical" HRF increased with PMA. Conversely, the proportion of infants with an "atypical" HRF decreased with PMA. A similar pattern was also observed in HRF-typicality scores depending on stimulus condition (Fig. 2b). Thus, positive HRF-typicality scores gradually increased as PMA increased.

To confirm this pattern, two-way ANOVAs were conducted on the HRF-typicality scores, with PMA as a between-subject factor and the stimuli (prosody and phoneme) as a within-subject factor. The results indicated a main effect of PMA [$F(3,76) = 3.86$, $P = 0.01$, $\eta^2 = 0.15$]. There was no significant effect of stimulus type [$F(1,76) = 0.50$, $P = 0.48$, $\eta^2 = 0.00$] and no significant interaction between PMA and stimulus type [$F(3,76) = 0.15$, $P = 0.92$, $\eta^2 = 0.00$]. Homogeneity of variance among different age groups was confirmed [$F(3,156) = 1.33$, $P = 0.26$] using Levene's test.

Because PMA had a significant effect on HRF-typicality scores, we further analyzed the differences between each PMA group using a post-hoc test (Ryan's method). Significant differences were observed between the term group and both the 33–35 weeks of PMA group ($t(76) = 3.59$, $P < 0.001$, $d = 0.82$) and the 36–38 weeks of PMA group ($t(76) = 2.37$, $P = 0.02$, $d = 0.57$). No significant differences were found between the term infants and the group of infants at 39–41 weeks of PMA. The results demonstrated that regardless of stimulus type, the HRF pattern for speech stimulation in preterm infants developed with PMA, becoming more similar to that in term infants from 39 weeks of PMA.

3.2. Correlation between PMA and HRF patterns

Having demonstrated the significant effect of PMA on HRF patterns, we evaluated the correlation between PMA and HRF-typicality scores. Simple correlation analysis demonstrated a significant relationship between PMA and HRF-typicality scores ($R = 0.304$, $P = 0.006$; Fig. 2c). To exclude possible effects on HRF-typicality scores of factors other than PMA, we conducted a partial correlation controlling for PNA at examination, birth weight and GA. PMA still showed a significant correlation with HRF-typicality scores after controlling for PNA at examination ($R = 0.32$, $P = 0.002$) and birth weight ($R = 0.206$, $P = 0.034$). The correlation was marginally significant after controlling for GA ($R = 0.175$, $P = 0.062$). This indicates that PMA can well explain typicality scores in the present dataset, but there is also a moderate influence of GA.

3.3. PMA and functional hemispheric specialization in speech perception

The laterality index was calculated for each PMA group. As observed in Fig. 3, term infants show a tendency to right-dominant responses to prosodic contrasts, as most of the laterality indices (LI) are below zero in contrast to the higher LI for the phonemic contrast. This tendency to a right-sided reduction is also seen in the oldest PMA group. Two-way ANOVAs comparing LI indices, with PMA and stimulus condition as independent variables, indicated a marginally significant interaction between PMA and the stimuli [$F(2,77) = 2.71$, $P = 0.050$, $\eta^2 = 0.01$]. A simple main effect test further revealed that this interaction was due to the group of term infants [$F(1,76) = 5.03$, $P = 0.027$] and those at 39–41 weeks of PMA [$F(1,76) = 3.95$, $P = 0.050$]. These two groups showed lower LI for the prosodic contrast. Namely, these groups showed lower LI in the prosodic contrast than in the phonemic contrast.

4. Discussion

Although the prognosis of preterm infants has improved, understanding of the effects of preterm birth on neurodevelopment of various language functions remains elusive despite their significance. In this study, we examined functional hemodynamic regulation using linguistic stimuli and demonstrated that the HRF pattern for phonemic and prosodic stimulation in preterm infants developed with PMA, becoming similar to that in term infants after 39 weeks of PMA. After

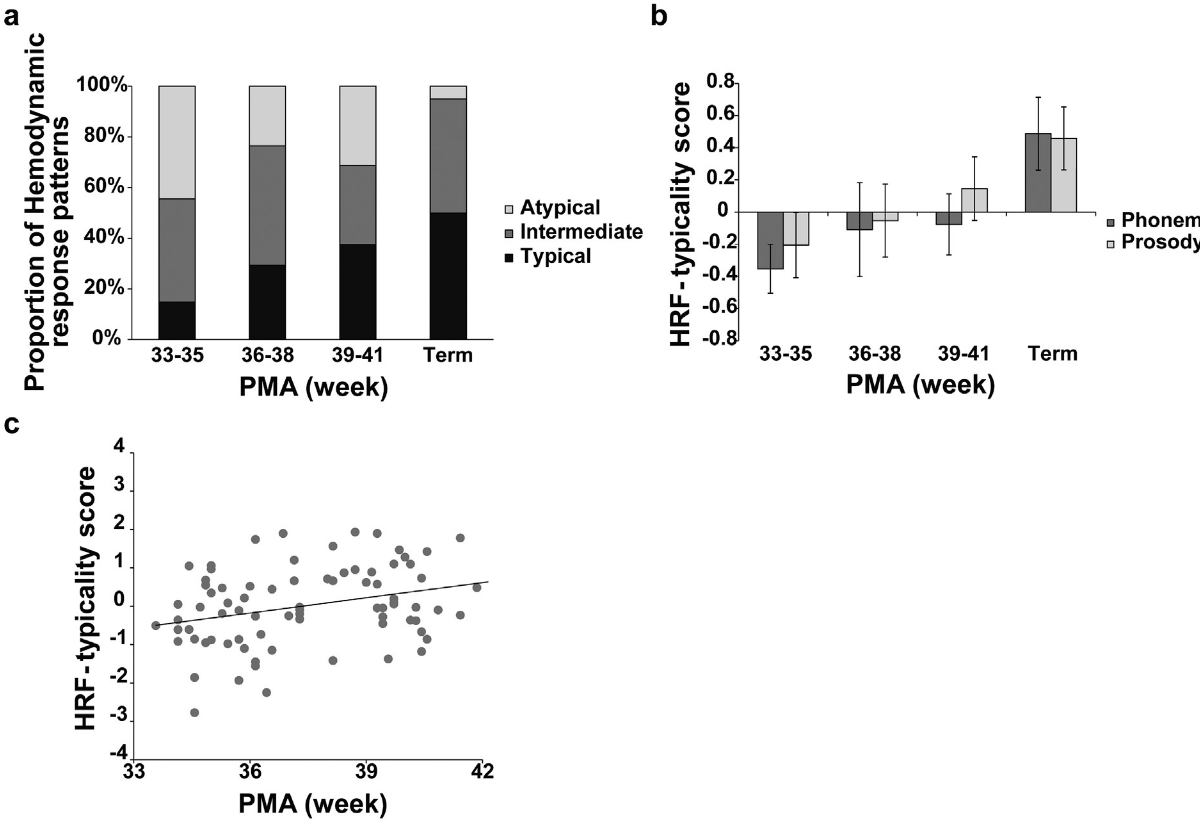

Fig. 2. The HRF pattern according to PMA. (a) The proportion of HRF patterns for each group. The three types of categories are: "typical" showing the normal HRF for two conditions, "intermediate" showing a normal HRF for one condition, and "atypical" showing an inverted HRF for two conditions. (b) HRF-typicality scores according to stimuli and PMA group. (c) Correlation between HRF-typicality scores and PMA ($R = 0.30$, $P = 0.006$).

39 weeks of PMA, the laterality index for prosody processing was lower than that for phoneme processing. In term infants, prosodic structure was processed predominantly in the right auditory area. Together, these results indicate that preterm infants begin to demonstrate right-dominant functional cerebral laterality for prosody after 39 weeks of PMA, such that they come to resemble term infants. The present study succeeded in using fNIRS to capture developmental differences in auditory-evoked neuronal activity represented by the HRF and functional hemispheric specialization of auditory areas that process speech contrasts. Consistent with previous studies showing a discriminative response to phonemic differences in preterm infants, even at 32 weeks of PMA, we also observed differences in the hemodynamic response to phonemic and prosodic differences (Cheour-Luhtanen et al., 1996; Mahmoudzadeh et al., 2013). Our results further suggest that in preterm infants both the cortical HRF and functional hemispheric specialization in temporal regions related to speech stimulation normalize to resemble term infants at 39 weeks of PMA. This was demonstrated in a relatively large sample of preterm and term infants. It is possible that these fNIRS markers represent a milestone of early language development.

In this study, before 36 weeks of PMA, approximately half of the infants showed an atypical HRF pattern for both phonemic and prosodic auditory stimulation. Only about 10% of infants showed a typical HRF pattern. Indeed, the average HRF-typicality score for term infants was significantly different from infants at 33–35 and 36–38 weeks of PMA. The average HRF-typicality score in preterm infants gradually increased in proportion to PMA, until 39 weeks of PMA, at which point they resembled term infants.

What neurophysiological processes does the atypical Hb response reflect in preterm infants? The physiological mechanisms underlying

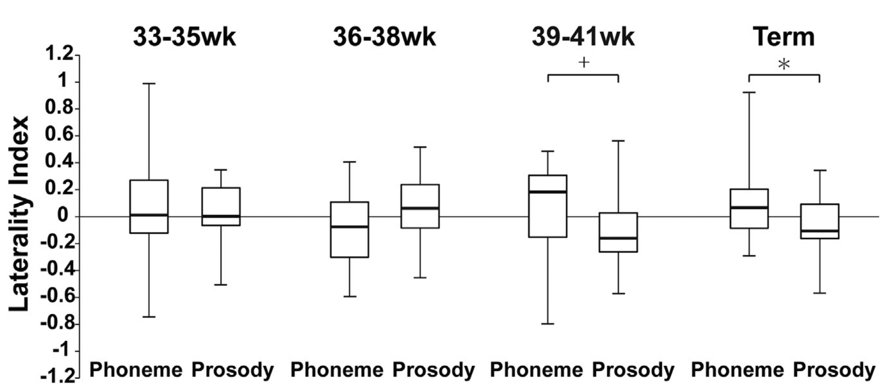

Fig. 3. Laterality indices for phonemic and prosodic conditions according to PMA group. A positive value means left-dominance, whereas a negative value means right-dominance. * = $P < 0.05$.

the reversed Hb response of preterm infants remain unclear. However, it could possibly be explained by immature neurovascular and/or metabolic systems in the cerebral cortex. Specifically, immature functioning of the synaptic structure with less myelination might result in inefficient energy use requiring more oxy-Hb (Kozberg et al., 2013). Furthermore, because of the immaturity of the arteriole vessels and capillaries, blood flow may not be sufficient in response to brain activity in preterm neonates. The resulting lack of oxygenation is reflected in the inverted HRF. While it is well-known that synaptic development rapidly occurs during the 6 months after birth, capillary formation starts between term to 3 months of age (Norman and O'Kusky, 1986; Huttenlocher, 1990). A recent fNIRS study examining phase synchrony of oxy-Hb and deoxy-Hb (Watanabe et al., 2017) further revealed rapid changes in neurovascular regulation from 34 PMA to term infants, which is relatively consistent with our results. We therefore speculate that brain maturity in terms of both synaptogenesis and angiogenesis in preterm and term neonates is a possible factor influencing the hemodynamic response pattern. In particular, maturity of the neurovasculature of the perisylvian area may specifically affect language processing.

Although we demonstrated clear developmental differences in the HRF in preterm infants, the HRF in infants has been a controversial and critical issue in the neuroimaging literature. In contrast to the oxy-Hb increase typically observed in adults, young infants sometimes show an inverted (i.e., decreased) pattern of oxy-Hb or a negative fMRI blood oxygenation level dependent (BOLD) response, as observed in our study (Csibra et al., 2004; Kusaka et al., 2004; Born et al., 1996). However, results have been inconsistent and other studies have reported typical Hb patterns even in neonates (Taga et al., 2003). This diversity may partly be explained by differences in the cognitive stimuli or task given to the infants and their state of wakefulness (Kusaka et al., 2004; Meek et al., 1998). A recent fNIRS study (Mahmoudzadeh et al., 2013) reported that preterm neonates approximately 31 weeks of PMA responded to phonemic differences. These results are in line with our own data showing preterm infants' sensitivity to phonemic differences. However, in contrast to our results, the authors observed a typical HRF for very premature infants. This discrepancy can be explained by differences in the task, specifically the perceptual component engaged by the task. Specifically, our task paradigm used speech stimulation even for the baseline time period, which differed from their study using silence (Mahmoudzadeh et al., 2013). Our paradigm made it possible to elucidate a pure phonetic component related to phonemic/prosodic differences by excluding sensory components that may be due to whether sound is present or not. Therefore, it appears that maturity of HRF-typicality may also be dependent on the level of neurocognitive processing. Our paradigm, using sounds at baseline, may have imposed a greater neuronal load than a silent baseline, thus requiring more neurovascular activity in the neonates.

Another crucial factor influencing Hb patterns is the targeted brain region. While an inverted pattern is frequently observed in the occipital area, this pattern has not often been reported in the temporal area (Arimitsu et al., 2011; Gervain et al., 2008). Different brain regions follow different developmental pathways, and it appears that development may be slower in the occipital cortex than in the temporal cortex (Lin et al., 2013). Such region-dependent development should be further explored in future studies. In this study, we presented the same auditory stimulation to infants and measured the same perisylvian area in infants at different PMAs. Using this paradigm, we observed that preterm infants tended to show an inverted HRF in the temporal area, and that a typical HRF developed gradually as PMA increased.

We employed phonemic and prosodic speech contrasts, which have been shown to elicit Hb changes in previous studies of functional cerebral laterality (Sato et al., 2003; Arimitsu et al., 2011). These studies suggest that functional hemispheric specialization in auditory areas emerges at term birth and 11 months of age for phonemic and prosodic contrasts, respectively. However, no study has examined this developmental process in preterm infants (Sato et al., 2003; Arimitsu et al., 2011). Our results indicate that rightward dominance appears at 39–41 weeks of PMA in preterm infants such that they resemble term infants. This is consistent with recent studies comparing speech perception in term and preterm infants (Pena et al., 2010; Pena et al., 2012). Earlier maturation of the right hemisphere in both term and preterm infants can partly be explained by the right-dominance of cerebral hemodynamic and oxygen metabolism. Specifically, the level of cerebral hemoglobin oxygenation, the blood volume, and the metabolic rate of oxygen are reported to be greater in the right hemisphere particularly in temporal and occipital areas (Lin et al., 2013).

The tendency to right-dominance for prosodic processing in preterm infants from 39 weeks of PMA suggests that they could process prosodic variation as efficiently as term infants. This also implies that preterm infants, at their projected due dates, possess adequate perceptual functioning to process infant-directed speech by their mother, which is characterized by rich prosodic information, such as intonation and amplitude. Because stimulation with infant-directed speech is important for language development, our results may also indicate that language function in preterm infants can develop as well as that in term infants by hearing infant-directed speech. This may support the efficacy of early intervention for language delay (Zimmerman et al., 2009; Caskey et al., 2011; Spittle et al., 2012). Preterm infants after 39 weeks of PMA have a similar cerebral response to speech as term infants. As such, they can at least absorb phonemic and prosodic components, which are crucial for language development, as well as term infants can. Thus, early intervention could further train their fundamental language ability to proceed to the next step. This study, which demonstrated mature auditory cerebral function in preterm infants at their projected due dates, is a significant first step in understanding the cerebral mechanisms underlying language development in preterm infants. Furthermore, stuttering children and children with autistic spectrum disorders are reported as showing different lateralization patterns to the stimuli used in this study (Sato et al., 2011; Minagawa-Kawai et al., 2009). LI and HRF-typicality examined in this study could be used to assess language delay at certain points in the developmental process. Future study should further explore this possibility.

Although fNIRS has provided neurocognitive evidence in studies of basic neuroscience, several technical issues remain to be resolved. One such issue is the influence of systemic blood flow on fNIRS signals as reported by several studies (Kohno et al., 2007; Takahashi et al., 2011). On the other hand, a recent fNIRS-fMRI coregistration study reported the efficacy of fNIRS during a working-memory task (Sato et al., 2013). The study revealed that fNIRS-Hb significantly correlated with fMRI-BOLD rather than with the skin-blood flow in the adult prefrontal cortex. Further, on measuring Hb changes in both deep and shallow tissue layers in infants (Funane et al., 2014), cerebral rather than extracerebral hemodynamics greatly contributed to fNIRS signals during speech listening and in the resting state. Nonetheless, the systemic signal should always be carefully considered for fNIRS study, as systemic effects may have different effects depending on the nature of the cognitive task. Beyond systemic effects, there remain some issues in the clinical use of this technique. The study of fNIRS is a young, emerging field and therefore the neural substrates of the HRF pattern and its relation to other measures of physiological development are still unclear. Furthermore, the HRF state may differ depending on the state of wakefulness. These issues make it difficult to assess individual brain state precisely. Therefore, accumulation of basic data with fNIRS is still required for its clinical use.

Interpretation of the results of this study is limited by variation in the intrauterine environment of our participants. Intrauterine environment, reflected by 'small for gestational age', is known to affect long term outcomes of infants. Although we demonstrated a significant correlation between PMA and HRF-typicality after excluding birth weight, we did not exclude infants who were small for gestational age from our sample (Streimish et al., 2012). This limitation may explain why the correlation between PMA and HRF-typicality following partial correlation analysis controlling for GA was only marginally significant. Intrauterine environment may have acted as a cofounding factor in the partial analysis. However, a more appropriate interpretation of the marginal significance is that GA did impact on HRF-typicality in addition to PMA. Even with neural maturation as the infants get older, lower GA may still slow their brain development. Previous EEG studies on speech perception in preterm infants have consistently reported that brain maturation (equivalent to PMA) is more significant than duration of language exposure (PNA) (Pena et al., 2010; Bisiacchi et al., 2009; Pena et al., 2012). Our study examining both GA and chronological age may add to the evidence that GA rather than chronological age influence the cerebral basis of speech perception. This issue should be explored in future research.

Another limitation of this study is the lack of consideration of potential differences in the rate of complications and neurotoxic interventions in the participants. The risk of significant complications and neurotoxic interventions is higher for very premature infants than for late preterm infants, thus biasing GA and/or PMA quality. We also need to consider the effect of complications, including patent ductus arteriosus, BPD, and intraventricular hemorrhage. However, we excluded infants with complications, including congenital anomalies (e.g. congenital heart anomalies), moderate and severe BPD, grade 2–4 intraventricular hemorrhage, periventricular leukomalacia, NEC, and deafness. This is because we aimed to exclude risk factors other than premature birth itself that can influence hemodynamic regulations and/or cognitive development. Accordingly, we made it a criterion that ductus arteriosus was closed in all infants, and no participants received supplemental oxygen for BPD at the time of fNIRS measurement. Although we included 9 infants with moderate BPD (5 infants in the group of 33–35 weeks of PMA, 1 infant in the group of 36–38 weeks, 3 infants in the group of 39–41 weeks, and no infants in the term group, respectively), all infants were examined after the cessation of supplemental oxygen. Because the proportion of infants with mild BPD among groups was not significantly different ($p = 0.116$, Fisher's exact test), it is unlikely that inclusion of BPD had an effect on the hemodynamic response. Although grade I intraventricular hemorrhage was included for the participants' recruitment criteria, the final dataset of this study resulted in involving no patients with grade I intraventricular hemorrhage. Our exclusion criteria may have decreased the effect of such risk factors on our results. Many previous studies share similar limitations to those outlined here (Mwaniki et al., 2012; Luu et al., 2009; Aarnoudse-Moens et al., 2009; Bisiacchi et al., 2009). Likewise, the present study intended to examine the general tendency of preterm infants, rather than examining traits of any specific subgroup. The effects of specific traits—such as BPD and the maturity of cerebrovascular autoregulation, with regard to intraventricular hemorrhage—on the development of hemodynamic response discussed in this study should be further investigated in future research.

5. Conclusions

The present study has provided new evidence that hemodynamic regulation of the speech-evoked cerebral response and its functional systems develops in preterm infants as PMA increases and will typically catch up to term infants by their projected due dates. While an atypical HRF was frequently observed in these infants before 39 weeks of PMA, their HRF became matured by their projected due dates. Furthermore, functional hemispheric specialization of temporal regions responsible for prosodic processing became similar in preterm infants from 39 weeks of PMA, suggesting an efficient network for prosodic processing at this age. These data showing the maturation process of the hemodynamic response may represent a developmental milestone in higher brain functions, such as language processing, in preterm infants and may highlight the efficacy of early intervention for developmental cognitive delay. Further neurocognitive studies such as this can contribute to the understanding of physiological mechanisms of higher brain dysfunction in preterm infants.

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Disclosure

The authors have no relevant financial relationships to disclose. The authors have no conflicts of interest to declare.

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Symbolic time series analysis of fNIRS signals in brain development assessment

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Abstract

Objective. Assessing an infant's brain development remains a challenge for neuroscientists and pediatricians despite great technological advances. As a non-invasive neuroimaging tool, functional near-infrared spectroscopy (fNIRS) has great advantages in monitoring an infant's brain activity. To explore the dynamic features of hemodynamic changes in infants, in-pattern exponent (IPE), anti-pattern exponent (APE), as well as permutation cross-mutual information (PCMI) based on symbolic dynamics are proposed to measure the phase differences and coupling strength in oxyhemoglobin (HbO) and deoxyhemoglobin (Hb) signals from fNIRS. *Approach.* First, simulated sinusoidal oscillation signals and four coupled nonlinear systems were employed for performance assessments. Hilbert transform based measurements of hemoglobin phase oxygenation and deoxygenation (hPod) and phase-locking index of hPod (*hPodL*) were calculated for comparison. Then, the IPE, APE and PCMI indices from resting state fNIRS data of preterm, term infants and adults were calculated to estimate the phase difference and coupling of HbO and Hb. All indices' performance was assessed by the degree of monotonicity (DoM). The box plots and coefficients of variation (CV) were employed to assess the measurements and robustness in the results. *Main results.* In the simulation analysis, IPE and APE can distinguish the phase difference of two sinusoidal oscillation signals. Both *hPodL* and PCMI can track the strength of two coupled nonlinear systems. Compared to *hPodL*, the PCMI had higher DoM indices in measuring the coupling of two nonlinear systems. In the fNIRS data analysis, similar to hPod, the IPE and APE can distinguish preterm, term infants, and adults in 0.01–0.05 Hz, 0.05–0.1 Hz, and 0.01–0.1 Hz frequency bands, respectively. PCMI more effectively distinguished the term and preterm infants than *hPodL* in the 0.05–0.1 Hz frequency band. As symbolic time series measures, the IPE and APE were able to detect the brain developmental changes in subjects of different ages. PCMI can assess the resting-state HbO and Hb coupling changes across different developmental ages, which may reflect the metabolic and neurovascular development. *Significance.* The symbolic-based methodologies are promising measures for fNIRS in estimating the brain development, especially in assessing newborns' brain developmental status.

Keywords: brain development, symbolic dynamic, fNIRS, in-pattern exponent and anti-pattern exponent, permutation cross mutual information

S Supplementary material for this article is available online

(Some figures may appear in colour only in the online journal)

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1. Introduction

Evaluating brain development is always a challenge in neuroscience and a clinical concern for the pediatricians. Existing studies indicate that earlier exposure to the extra-uterine environment (Watanabe *et al* 2017), postmenstrual age (Arimitsu *et al* 2018), birth weight (Streimish *et al* 2012), and the intrauterine/neonatal insults (Mwaniki *et al* 2012, Thomason *et al* 2017) may influence preterm infants' brain developmental trajectories. Preterm infants have a higher rate of neurodevelopmental diseases than term infants (Volpe 2009, Watanabe *et al* 2017). However, present studies still lack effective methods to access neonates' brain development status.

Functional near-infrared spectroscopy (fNIRS) is an optical brain imaging tool used in neuroscience. With the portable and non-invasive characteristics, as well as the merit of being tolerated by infants and children, the fNIRS is more suitable for assessing neonates' brain development (Quaresima *et al* 2012, Issard and Gervain 2018). fNIRS also allows bedside monitoring for long periods. All these features give unique advantages of fNIRS over functional Magnetic Resonance Imaging (fMRI) in the studies of newborns (Benavides-Varela *et al* 2017, Issard and Gervain 2017).

In developmental neuroscience, fNIRS studies of infants have shown that the hemodynamic response has canonical and non-canonical responses and changes with age in different cognitive tasks and brain regions (Lloyd-Fox *et al* 2017, Issard and Gervain 2018). In term and preterm infants, Watanabe *et al* found that the time-averaged phase differences between oxyhemoglobin (HbO) and deoxyhemoglobin (Hb) in spontaneous low-frequency oscillation ($<$0.1 Hz) were highly correlated with the chronological age (CA) (Watanabe *et al* 2017). The phase of oxygenation and deoxygenation hemoglobin (hPod) changes from in-phase to anti-phase as the CA increases. More fluctuations in hPod values were found in early preterm infants than in late preterm and term infants before 40 weeks postmenstrual age. However, early preterm infants had a slower development at later CAs (i.e. after eight–13 weeks). Furthermore, Taga *et al* employed the hPod and the phase-locking index of hPod ($hPod_L$) to investigate the spatial variation in infants' developing brain cortex (Taga *et al* 2018). They found that hPod exhibited spatial dependency in different brain development stages. Significant $hPod_L$ increases occurred in three-month-old infants compared to the neonate group. All these studies suggest that the dynamic phase difference between HbO and Hb have potential value in assessing the development of underlying neurovascular functions, as well as hemodynamic and metabolic changes, in infants.

In these studies, the instantaneous phase estimated in hPod and $hPod_L$ methodologies are based on the Hilbert transform, which is based on the assumption that the signal has narrow frequency band and stationary (Cohen *et al* 1999, Oliveira and Barroso 1999). However, brain development is a complex process that may be influenced by nonlinear circulatory and neurovascular developmental changes in different states, especially in infants (Norman and O'Kusky 1986, Franceschini *et al* 2007, Roche-Labarbe *et al* 2010). Many studies have shown that brain activities' dynamic responses measured by fNIRS signals are very likely to be nonlinear (Khoa *et al* 2008, Pouliot *et al* 2012). Nonlinearity from neural activity, blood flow, and metabolism makes the evaluations based on linear analyzing methods inadequate (Bießmann *et al* 2011, Fantini 2014, Sassaroli *et al* 2016). Moreover, oscillations are a prevalent feature of neuronal and hemodynamic recordings. Some methods used to analyze these physiological oscillations assume that they are largely sinusoidal (Cole and Voytek 2017). However, physiological oscillations are usually pseudo-periodic and contain multiple physiological fluctuations (Cole and Voytek 2017). Phase synchronization measurement is an important methodology used to interpret the mechanisms of electrophysiological and hemodynamic variations in cognitive neuroscience and mental diseases. Unfortunately, most phase synchronization analytical methods based on the Fourier transform and Hilbert transform cannot optimally represent a non-stationary signal (Li *et al* 2011).

The biological system's nonlinear characteristics have motivated researchers to investigate its underlying mechanism via nonlinear methodologies. Various measurements have been proposed for fNIRS signal analysis, such as wavelet phase coherence (Tan *et al* 2016), graph theory (Homae *et al* 2010), entropy (Gu *et al* 2017, Perpetuini *et al* 2018), and mutual information (Dalmis and Akin 2015, Yin *et al* 2015). In all these nonlinear measures, the symbolic dynamic analysis is an important nonlinear measurement, which has been widely applied to physiological system analysis (Edwards *et al* 2001, Daw *et al* 2003, Ray 2004, Bießmann *et al* 2011). A central procedure of the symbolic dynamic analysis is discretizing unprocessed time-series records into a corresponding sequence of symbols by comparing neighboring time-series (Bandt and Pompe 2002). Amigo *et al* stated that the signal's ordinal patterns are not only ad hoc symbols but also contain quantitative information regarding the underlying data's temporal scale (Amigo *et al* 2015). Due to the advantages described above, various symbolic dynamic-based measurements, such as permutation entropy, symbolic transfer entropy, and permutation min-entropy, have been widely used in neurological disease diagnosis and brain state monitoring (Martini *et al* 2011, Ferlazzo *et al* 2014, Zunino *et al* 2015), especially in fNIRS recording analysis (Gu *et al* 2017). A multi-scale symbolic information-theory approach has also been proposed to discriminate delayed synchronization and anticipated synchronization (Montani *et al* 2015). In this study, we propose two new exponents based on the patterns of symbolic dynamics, namely in-pattern exponent (IPE) and anti-pattern exponent (APE), to measure the phase relationship between HbO and Hb.

Although many synchronization measurements have been proposed, detecting the weak couplings in physiological recordings remains challenging considering the complex, nonlinear, and nonstationary characteristics of a physiological system (Palus and Vejmelka 2007, Bahraminasab *et al* 2008). Symbolic dynamic-based permutation analysis and conditional mutual information were proposed to estimate the weak coupling in two cardiorespiratory series (Bahraminasab *et al* 2008). The similar approaches have been used to estimate neuronal population coupling during seizures (Li and Ouyang 2010) and EEG oscillations in patients under anesthesia (Liang *et al* 2015). It was suggested that the permutation cross mutual information (PCMI) approach can track time-dependent coupling strength changes, which is associated with a better anti-noise effect. This encouraged us to utilize the PCMI in measuring HbO and Hb coupling in fNIRS and apply it to distinguishing brain development at different stages.

In this study, we used the IPE and APE, as well as PCMI, which are derived from symbolic dynamics and information theory to assess the brain development changes at different stages. These methods were applied to the same data as the hPod and $hPod_L$ methods proposed in the previous literature (Watanabe *et al* 2017, Taga *et al* 2018). The whole process is described below: section 2 presents IPE, APE, PCMI, hPod, $hPod_L$ and statistical analysis methods used in detail. In section 3, comparisons are made based on simulated sinusoidal oscillations, coupled nonlinear models are described in detail. An analysis of fNIRS recordings in preterm and term infants and adults based on these measures is detailed in section 4. Finally, the discussion and conclusions are presented in section 5.

2. Methods

2.1. IPE and APE

Symbolic dynamic measurements used to encode nonlinear systems based on time-series analysis have been systematically described in previous studies(Daw *et al* 2003, Ray 2004). In this study, we explored the temporal interrelationship of specific patterns in two time-series (i.e. HbO and Hb signals). The resulting exponent was used to evaluate the degree of in-phase or anti-phase in these two time-series. The percentage of in-phase and anti-phase measurements was calculated as an exponent to measure synchronization in these two time-series. We termed these two indices IPE and APE, to separate from the phase measures of the Hilbert transform. An algorithm of the diagram was shown in figure 1. When the embedding dimension $m = 3$, there are $3! = 6$ patterns (as shown in figure 1(A)). We termed these 6 patterns as $M\#1$ to $M\#6$. For these 6 patterns, the anti-pattern pairs and in-pattern pairs were shown in figure 1(B). The calculation of IPE and APE is straightforward. For two time series, such as HbO and Hb, the symbolic patterns can be constructed at each time point using a moving window. Then, the number of in-pattern pairs N_i and anti-pattern pairs N_a can be achieved. If the data length is L, the maximum number of in-pattern pair or anti-pattern pairs would be $L - m + 1$. Finally, the IPE and APE can be calculated as shown below:

$$\begin{cases} \mathrm{IPE} = \frac{N_i}{L-m+1} \times 100\% \\ \mathrm{APE} = \frac{N_a}{L-m+1} \times 100\%. \end{cases} \quad (1)$$

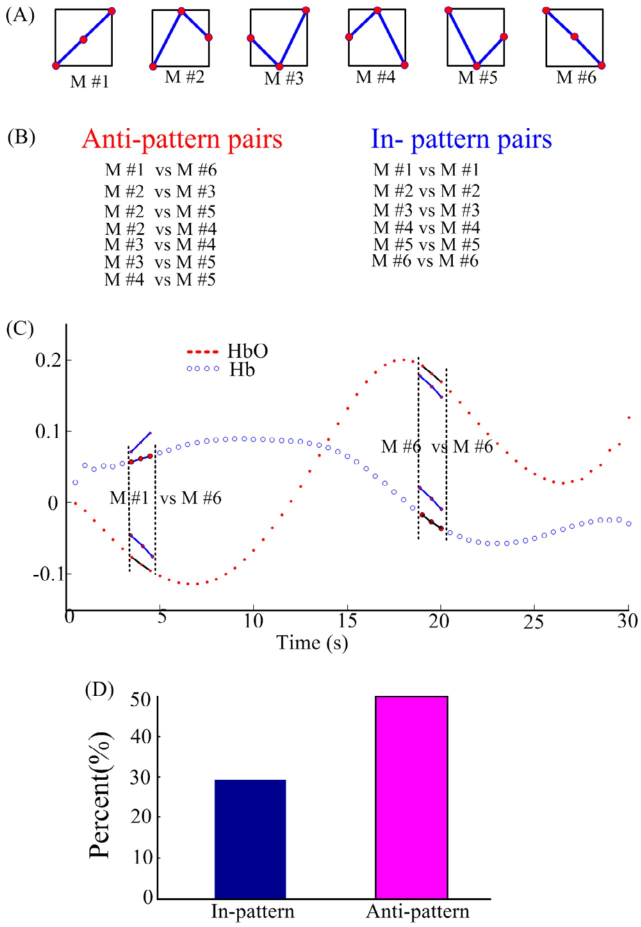

Figure 1. The diagram of anti-pattern and in-pattern percent measurements. (A) The motifs of the order 3 (3!). (B) The lists of the anti-pattern and in-pattern pairs. (C) Two original hemodynamic parameters (HbO and Hb) epochs of 30 s segments. In the time point near 5 s, the patterns of HbO and Hb are anti-pattern with each other ($M\#1$ versus $M\#6$). While the patterns of HbO and Hb are in-pattern with each other at the time near 20 s ($M\#6$ versus $M\#6$). (D) The in-pattern and anti-pattern percent of the signal in (C).

When $m \geqslant 4$ the symbolic patterns can describe more sophisticated signals, however, the in-pattern pairs and anti-pattern pairs will become much more complicated than when $m = 3$. Since the hemodynamic changes are relatively slow, the choice of $m = 3$ is sufficient. A more detailed description of the parameter selection was shown in supplementary appendix B (stacks.iop.org/JNE/15/066013/mmedia).

2.2. Permutation cross mutual information (PCMI)

Mutual information is a measurement of synchronization based on information theory, which calculates the amount of shared information between two time-series (Paluš 1996). The PCMI proposed by Li *et al* (Li and Ouyang 2010) has been applied to estimate the synchronization between two EEG signals (Liang *et al* 2015, 2016b). The details of PCMI are described as follows:

(i) A phase space reconstruction method was used to construct the vectors $X_t[x_t, x_{t+\tau}, \ldots, x_{t+m\tau}]$ and

$Y_t[y_t, y_{t+\tau}, \ldots, y_{t+m\tau}]$ based on two time series of $x(t)$ and $y(t)$, $t = 1, 2, \ldots n$ where m and τ are the embedding dimension and time lag, respectively.

(ii) X_t and Y_t were ranked in increasing order, $[x_{t+(j_1-1)\tau} \leqslant x_{t+(j_2-1)\tau} \leqslant \cdots \leqslant x_{t+(j_m-1)\tau}]$ and $[y_{t+(j_1-1)\tau} \leqslant y_{t+(j_2-1)\tau} \leqslant \cdots \leqslant y_{t+(j_m-1)\tau}]$, respectively.

(iii) Probability distribution functions of the time series $x(t)$ and $y(t)$ were calculate based on the emerged probability of ordinal patterns and termed $p(x)$ and $p(y)$.

The entropy of X_t and Y_t is defined as follows:

$$H(X) = -\sum_{j=1}^{J} p_j(x) \log p_j(x) \tag{2}$$

and

$$H(Y) = -\sum_{j=1}^{J} p_j(y) \log p_j(y) \tag{3}$$

(iv) The joint probability function of X_t and Y_t is termed as $p(x, y)$. The joint entropy of $H(X, Y)$ is defined as

$$H(X, Y) = -\sum_{x \in X} \sum_{y \in Y} p(x, y) \log p(x, y). \tag{4}$$

(v) The PCMI of time series X_t and Y_t is described as

$$\mathrm{PCMI}(X; Y) = H(X) + H(Y) - H(X, Y). \tag{5}$$

The embedding dimension m is crucial in PCMI calculation, same as the lag τ that is the number of sample points spanned by each section of the motif (Li and Ouyang 2010). A detailed description of the parameters' selections is shown in supplementary appendix C.

2.3. hPod and $hPod_L$

hPod and $hPod_L$ are the two measurements of phase synchronization. The hPod algorithms described in Watanabe *et al* (2017) are similar to the spatial analytic phase difference index presented in Pockett *et al* (2009). And the $hPod_L$ measurement is a classical phase-locking value proposed by Lachaux *et al* (1999) and has been widely used in the neurophysiological signal analysis (Li *et al* 2011, Wang *et al* 2014). Considering two time-series of $x(t)$ and $y(t)$, the calculations of hPod and $hPod_L$ are described as below.

(1) The analytic signal representation of $x(t)$ and $y(t)$ was calculate based on the Hilbert transform.

$$\begin{cases} x_a(t) = x(t) + jHT[x(t)] \\ y_a(t) = y(t) + jHT[y(t)] \end{cases}. \tag{6}$$

Where the $HT[\cdot]$ is the Hilbert transform.

(2) The signal's instantaneous phase (IP) was estimated:

$$\varphi_x(t) = \tan^{-1}\frac{\mathrm{Im}(x_a(t))}{\mathrm{Re}(x_a(t))} \quad \text{and} \quad \varphi_y(t) = \tan^{-1}\frac{\mathrm{Im}(y_a(t))}{\mathrm{Re}(y_a(t))}.$$

(3) hPod was calculated based on the IP. Because the IP is wrapped around $[-\pi,\pi]$, we needed to unwrap the IP on the real axis. Firstly, we estimated the absolute difference between the IP of φ_x and φ_y, termed $\Delta\varphi_{xy}$. Then, $\Delta\varphi_{xy}$ was projected into the interval $[0,2\pi]$. Finally, to achieve a consistent phase range with the measure in Watanabe *et al* (2017), the phase differences in the $[0, \pi]$ range were projected into the $[\pi,2\pi]$ range.

(4) $hPod_L$ was calculated. The measurement of $hPod_L$ is defined as:

$$hPod_L = \frac{1}{N}\left|\sum_{t=1}^{N} e^{j\Delta\phi_{xy}(t)}\right|. \tag{7}$$

Where the N is the length of the time series $x(t)$ and $y(t)$. The $hPod_L$ is bounded between 0 and 1.

2.4. Statistical analysis

The aim of this study was to (1) evaluate the performance of symbolic measurements (i.e. IPE, APE, and PCMI) in assessing the brain developmental stages, and (2) compare them with calculated hPod and $hPod_L$. Given the indices of hPod are angle values (i.e. different from numerical values), a circular statistics toolbox was used to perform statistical analysis (Berens 2009). The Watson–Williams test was used to evaluate whether the mean phase of two or more groups is identical, and the parametric Watson–Williams multi-sample test was used to determine the significant differences between groups. For other indices, the Liliefors test (*lillietest.m*) was performed to determine whether the data had a normal distribution. Kruskal–Wallis test (*kruskalwallis.m*) and multiple comparison tests (*multcomare.m*) were used to determine the significant differences between the indices in different age groups. The Bonferroni correction was used to prevent multiple comparison problems with $p < 0.05$/(number of channels). The coefficient of variation (CV), calculated from the ratio of the standard deviation (SD) over the mean, was employed to assess the index stability in brain development measurements (Li *et al* 2008).

3. Stimulation and results

3.1. The simulated signals

To evaluate IPE's and APE's performance in phase difference estimation, we simulated two time-series by combining two sinusoid waves with different frequencies across three situations (i.e. in-phase, anti-phase, and orthogonal-phase). Furthermore, two random time-series were used to assess the index's performance in evaluating the noise signals' impact. All the formulas are described as follows:

(1) In phase sinusoid equations

$$\begin{cases} x(t) = 20\sin(0.4\pi t) + 15\sin(0.2\pi t) \\ y(t) = 0.3x(t). \end{cases} \quad (8)$$

(2) Anti-phase sinusoid equations

$$\begin{cases} x(t) = 20\sin(0.4\pi t) + 15\sin(0.2\pi t) \\ y(t) = 20\sin(0.4\pi t - \pi) + 15\sin(0.2\pi t - \pi). \end{cases} \quad (9)$$

(3) Orthogonal-phase sinusoid equations

$$\begin{cases} x(t) = 20\sin(0.4\pi t) + 15\sin(0.2\pi t) \\ y(t) = 20\sin(0.4\pi t + 0.5\pi) + 15\sin(0.2\pi t + 0.5\pi). \end{cases} \quad (10)$$

Random signals were generated by the MATLAB function *randn.m*. The amplitude of the signal $y(t)$ is three times larger than $x(t)$. The data length of all the simulation signals is 500 s.

3.2. The coupling models

In this study, we employed four models to evaluate the coupling performance of PCMI and $hPod_L$. The coupling strength of bivariate dynamics was controlled by one continuous parameter. The first is the Rossler–Lorenz model (Andrzejak *et al* 2003):

$$\begin{cases} \dot{x}_1 = -6\,(x_2 + x_3) \\ \dot{x}_2 = 6\,(x_1 + 0.2x_2) \\ \dot{x}_3 = 6\,[(x_1 - 5.7)\,x_3 + 0.2] \\ \dot{y}_1 = 10\,(-y_1 + y_2) \\ \dot{y}_2 = 28y_1 - y_2 - y_1y_3 + \varepsilon x_2^2 \\ \dot{y}_3 = y_1y_2 - \frac{8}{3}y_3. \end{cases} \quad (11)$$

The coupling strength parameter ranged from $\varepsilon = 0$ to $\varepsilon = 5$ in a step of 0.2. The discrete time series X_n and Y_n from x_1 and y_1 were resampled at the sampling rate at 40 Hz (Liang *et al* 2015).

The second model system consisted of two coupled Henon maps proposed in the literature (Schiff *et al* 1996). The third and fourth models were made by two coupled Rossler (Palus and Stefanovska 2003) and Lorenz systems (Kreuz *et al* 2007), respectively. In this study, the coupling strength parameter in Henon was ranged from 0 to 0.8 with a step of 0.01. The coupling strength parameters in Rossler and Lorenz systems were set from 0 to 2 in step of 0.025 (Liang *et al* 2016a).

3.3. Evaluation of the model

We hypothesized that an increased coupling strength is linearly correlated with increased of synchronization. The degree of monotonicity (DoM) was used to evaluate the dependence of $hPod_L$and PCMI measures on the coupling strength ε (Kreuz *et al* 2007).

The formula of DoM is as follows:

$$\mathrm{DoM} = \frac{2}{r(r-1)} \sum_{i=1}^{r-1} \sum_{j=i+1}^{r} \mathrm{sign}(s_j - s_i). \quad (12)$$

Where s_i and s_j are the coupling measure indices (i.e. $hPod_L$ and PCMI) at monotonously-increased coupling strengths. $i,j = 1,2\ldots,r$ where the parameter r is the number of the discretized coupling strengths. If indices of s monotonically increased with the enhancing coupling strength ε, then $s_i < s_j$, $i \leqslant j$. DoM = 1 when the sequence of $s_1, s_2, \cdots, s_r$ is strictly monotonous increases with the enhanced coupling strengths, while DoM = −1 when the indices monotonically decrease with the increasing coupling strengths.

3.4. Results

To compare IPE's and APE's performance with hPod via the phase relationship between two time-series, we employed simulated and random noise signals. $hPod_L$ and PCMI were also compared in estimating coupling strength in different coupled models. We studied the anti-phases, in-phases, and orthogonal-phases of two sinusoidal signals, which were shown in figures 2(A), S1(A) and S2(A), respectively. Two random noise signals, which had random phase and no coupling between them, were used for assessment (see figure S3(A)). The hPod index was able to accurately reflect anti-phases, in-phases, and orthogonal-phases (see figures 2(B), S1(B) and S2(B)). Like hPod, the IPE and APE can precisely measure the same phase difference between these three situations. The IPEs were equal to 1 and 0 in in-phase and anti-phase patterns, respectively (see figures 2(D) and S1(D)). For the orthogonal phase relationship, IPE and APE were distributed around 0.42, which means the percent of anti-patterns and in-patterns in this situation is close to 0.5 (see figure S2(D)). All these results illustrate that the IPE and APE have similar performance in measuring phase differences.

For the coupling strength measurement, the $hPod_L$ indices remained 1 at in-phase, anti-phase, and orthogonal-phase scenarios (see figures 2(C), S1(C) and S2(C)). The analysis of parameter selection presented in supplementary appendix C shows that PCMI with an embedding dimension of $m = 3$, combined with lag $\tau = 11$ is the optimal selection. The PCMI indices in in-phase, anti-phase, and orthogonal-phase patterns were about 1.68, 1.68, and 0.64, respectively. Unlike $hPod_L$, the PCMI measurement regards the orthogonal-phase pattern to be a different coupling pattern from the in-phase and anti-phase patterns. We calculated the cross-correlation index of these two orthogonal-phase signals and we found that the correlation coefficient was equal to 0 when the lag = 0 s. The different results for PCMI, $hPod_L$, and cross-correlation may be derived from the different calculation principles and mechanisms while estimating synchronization (Liang *et al* 2016b).

Furthermore, the random noise simulation showed that the hPod indices were randomly distributed around the circle (see in figure S3(B)). The $hPod_L$ indices calculated from this time course are ranged from 0 to 0.2, which means that the two

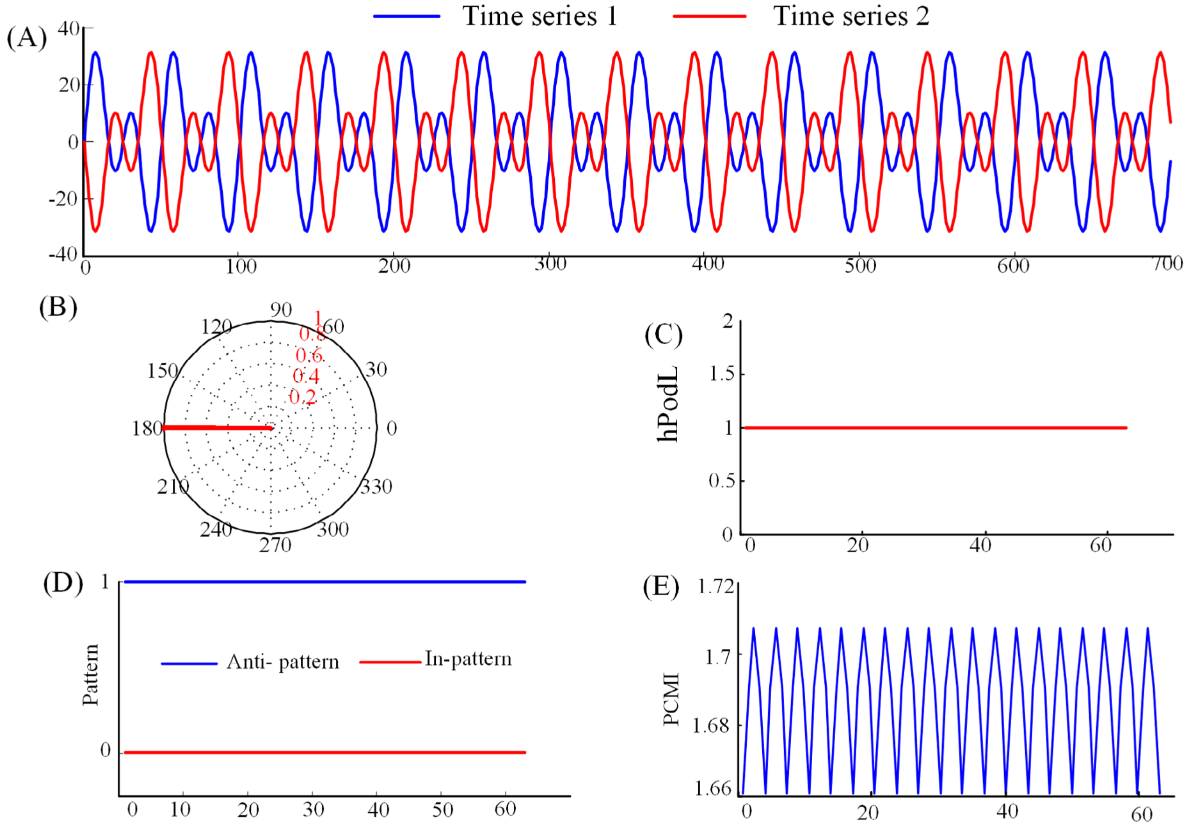

Figure 2. The comparison of the hPod and symbolic dynamic based measurements. (A) Two in-phase time series. (B) The hPod indices of the two time series in (A). (C) The hPod length of the time series in (A). (D) The anti-pattern percent and in-pattern percent values of the two time series. (D) The PCMI indices of the two time series.

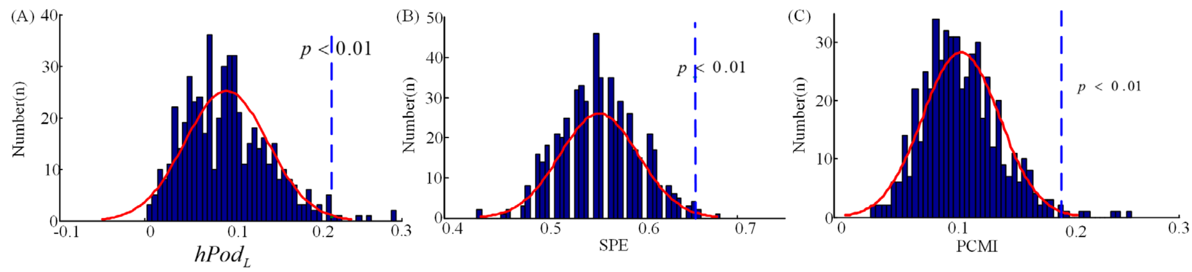

Figure 3. The histogram distributions of $hPod_L$ (A), SPE (B) and PCMI (C) derived from the 500 random time series epochs.

time-series are not correlated with each other. Hence, in this situation, the hPod values are invalid. The IPE and APE of these two random noise signals ranged in 0.1–0.3 and 0.3–0.5, respectively. The PCMI indices ranged from 0.02 to 0.1.

Additionally, to analyze the indices' range in all these measures at random time series, we calculated 500 pairs random noise segments. The distributions of $hPod_L$, as well as the sums of IPE, APE (SPE), and PCMI were presented in figures 3(A)–(C), respectively. Based on these distributions, we proposed a significant threshold for each measure ($p < 0.01$) to avoid spurious results. The significant thresholds of $hPod_L$, SPE and PCMI are 0.20, 0.64 and 0.19, respectively.

$hPod_L$'s and PCMI's performance in tracking the coupling strength was assessed further in four coupled nonlinear systems. Figures 4(A) and (B) showed the two simulated datasets in a coupled Rossler–Lorenz system, where coupling strength varied from 0 to 5 with a step of 0.2. The time series at the coupling strength of $\varepsilon = 0$ and 5 were presented in figures 4(C) and (D). Figure 4(E) showed the $hPod_L$, and PCMI of a coupled Rossler–Lorenz system at different coupling strengths. All three indices showed a rising trend with an increase in coupling strength. However, we also observed an abrupt increase in the coupling strength value around 2.2 that gradually decreased when the coupling strength value was greater than 3.5 in the $hPod_L$ curve (figure 4(E)).

DoM was used to evaluate $hPod_L$'s and PCMI's dependence on the coupling strength. DoM values of $hPod_L$ and PCMI for the coupled Hénon, Rössler, Lorenz, and Rossler–Lorenz (R–L) systems were shown in figure 5. All the DoM values were shown in table 1. Notably, the DoM values of PCMI were higher than those of $hPod_L$ in every model. The results illustrate that the PCMI more accurately assessed coupling strength than $hPod_L$.

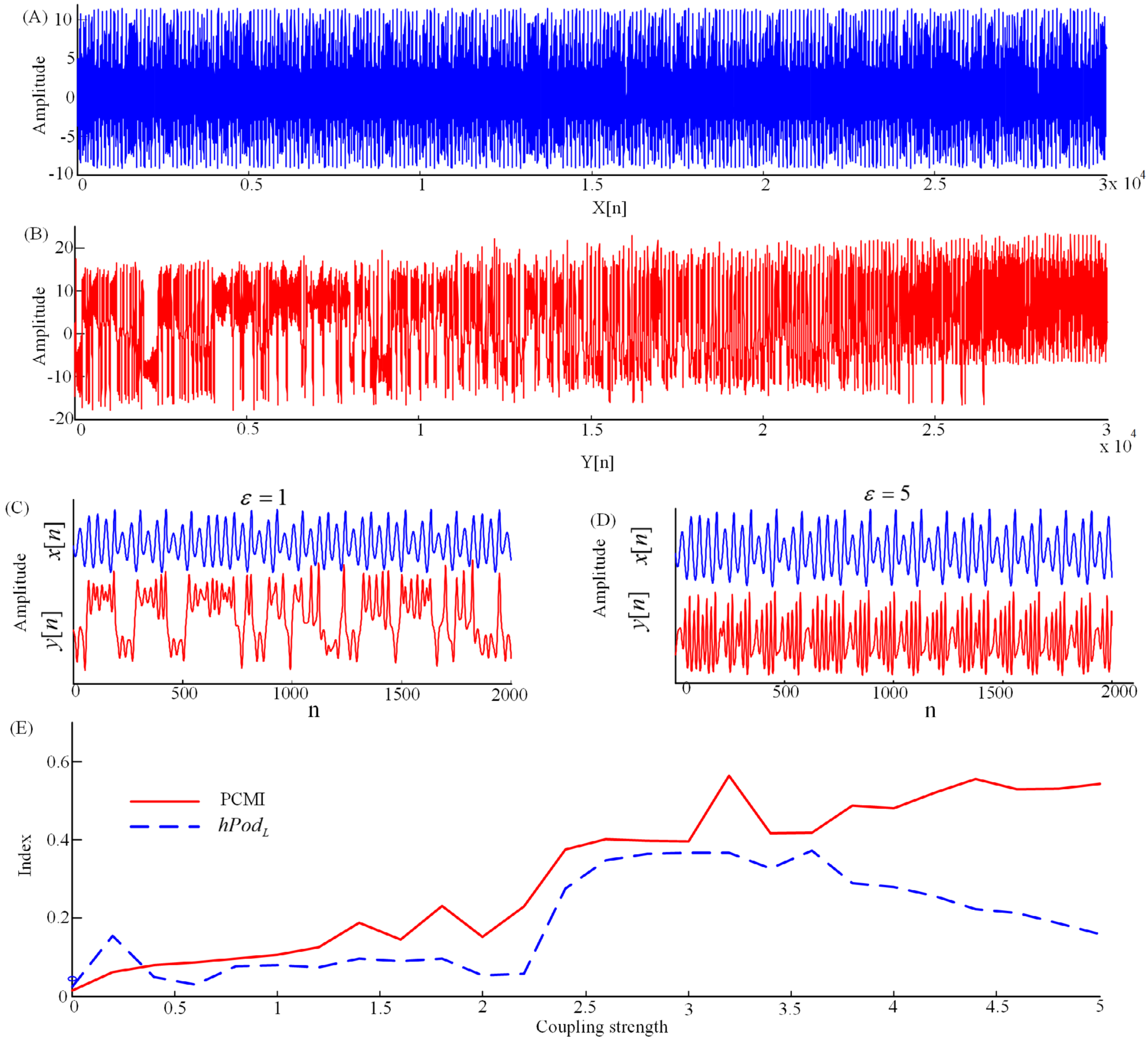

Figure 4. The simulation data generated based on the coupled Rossler–Lorenz model. (A) and (B) are the time series from the variables of v_1 and w_1 in Rossler–Lorenz model with $dt = 0.025$. (C)–(D) Time series of X_n and Y_n at two specific coupling strength $\varepsilon = 0$ and 5. (E) The $hPod_L$ and PCMI indices versus different coupling strength of Rossler–Lorenz system.

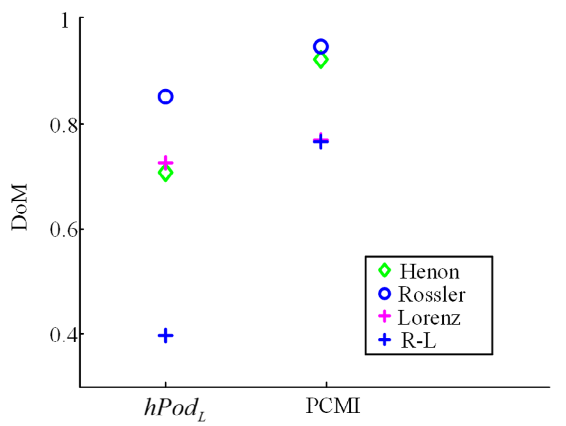

Figure 5. The DoM of $hPod_L$ and PCMI indices for the coupled Henon, Rossler, Lorenz and Rossler–Lorenz systems.

Table 1. The DoM values of $hPod_L$ and PCMI in measuring the model of coupled Henon, Rossler, Lorenz and R–L.

	$hPod_L$	PCMI
Henon	0.70	0.96
Rossler	0.85	0.94
Lorenz	0.73	0.77
R–L	0.40	0.77

4. Applications in fNIRS

4.1. fNIRS data recordings

We analyzed data from ten term infants (six boys and four girls), and ten preterm infants (five boys and five girls) during sleep. A detailed description of the participants was presented

Table 2. Demographic characteristics of the neonates.

Characteristics	Preterm	Term
Total (boy/girl)	10(6/4)	10(5/5)
GA (mean(min-max)) (wk)	32.5 (30.1–33.4)	38.3 (37–39.9)
PNA (day)	23.7 (17–35)	4.2 (3–6)
Birth weight (mean(min-max)) (g)	1644.3(1302–1887)	2874.8 (2476–3936)

GA = Gestational age.
PNA = Post natal age.
wk = week.

in table 2. Ethical approval was obtained from the ethical committee of Keio University Hospital (No. 20090189), and written informed consent was acquired from the participants' parent(s) prior to beginning the test. All the neonates were tested in a dimly-lit room when they were in active sleeping status as judged by their frequent motor activity and rapid eye movements.

A NIRS system (ETG-4000, Hitachi Medical Corporation) with 46 channels was used to measure the relative fluctuations of HbO and Hb concentrations (millimolar millimeter (mM $*$ mm)). Two sets of 3 $*$ 3 array probes were mounted on the left and right temporal regions. And one 3 $*$ 5 holder was mounted on the frontal region. The distance between the source and detector was about 2 cm. The sampling rate of the fNIRS recording was 10 Hz and the wavelengths of NIR lights were 695 and 830 nm. fNIRS coverage included frontal and temporal areas.

To compare developing and mature brains, we enrolled eight adult volunteers (aged 22–40 years, seven male, one female) for resting state testing. A fNIRS neuroimaging system (NIRx, NIRx Medical Technologies, LLC) was used for the experiment. All the volunteers were asked to close their eyes and lay flat on the bed in a dimly-lit room. Volunteers signed the written informed consent approved by the Purdue University ethics committee. The duration of the resting-state NIRS measurement was 15 min and a total of 20 channels were used to cover the prefrontal brain area.

4.2. Data preprocessing

Motion artifact is a major source of noises in fNIRS, especially in clinical tests. In this study, we used a kurtosis-based wavelet filtering for motion artifact correction (Chiarelli *et al* 2015). Figure 6 showed the denoising process of HbO and Hb from one channel. Figure 6(A) presented the HbO and Hb time series before and after denoising. In one example, the transient noise caused by motion was detected at around 250 s. Figure 6(B) showed an example of motion correction for HbO and Hb (between 210 s–270 s). To analyze hemodynamic changes in preterm and term infants and adults, we used a zero-phase digital filter (Matlab function of *filtfilt.m,* the order of butterworth = 3) for band-pass filtering. All the data were motion corrected and resampled to 2 Hz for the further calculation (Pinti *et al* 2015).

In a previous study (Watanabe *et al* 2017), the authors analyzed the hPod of three frequency bands: 0.05–0.1 Hz (main frequency), 0.01–0.05 Hz (low frequency), and 0.1–5 Hz (high frequency, which is dominated by pulsation/respiration and not the focus of our study). To be consistent with the previous study, we analyzed the phase difference and coupling of HbO and Hb in the 0.01–0.05 Hz, 0.05–0.1 Hz, 0.01–0.1 Hz frequency bands. Considering the low cut-off frequency of 0.01 Hz, the data length of IPE, APE, PCMI, hPod, and $hPod_L$ used in the calculation was set as 120 s in 0.01–0.05 Hz and 0.01–0.1 Hz frequency bands. However, in the frequency band of 0.05–0.1 Hz, we have found that the minimum length of the data (i.e. experiment) can be as short as 30 s, which is preferable in the studies of infants. Detailed evaluations can be found in supplementary appendix C and D (we only showed PCMI, which is the most complicated parameter).

4.3. Results

Figure 7 showed the distributions of APE versus IPE for preterm and term infants and adults in the 0.01–0.05 Hz (A), 0.05–0.1 Hz (B) and 0.01–0.1 Hz (C) frequency bands. We averaged the indices for all the channels and each circle represented the scatter distribution of one subject. The distributions of the adults' data were clearly separated from the other two groups (i.e. term and preterm infants) in all three frequency bands. Because IPE and APE are complementary measures, the sum of the in-phase pattern and anti-phase proportions is close to 1 under the slow oscillations of HbO and Hb. For this reason, the IPE and APE indices were mostly scattered around the backslash line, which is a feature of the method we used and does not reflect physiological information. The clear separation of the clustering of IPE and APE along the line indicates the power of the method rather than the line itself. Figure 8 presented the hpod and $hPod_L$ of preterm and term infants and adult subjects in the 0.01–0.05 Hz, 0.05–0.1 Hz, and 0.01–0.1 Hz frequency bands. It was shown that hPod indices of adults are near phase π in all these frequency bands, while the indices of the term and preterm infants are close to $3\pi/2$, especially in the 0.05–0.1 Hz frequency band. The results are similar to those in Watanabe *et al* (2017) and Taga *et al* (2018).

To further investigate the ability of different measures to assess brain development, especially in the term and preterm infants, the indices of each measurement in each channel were considered samples for statistical analysis. A corresponding box plot was presented in figures 9 and 10 for each measurement in each frequency band. In this study, the number of fNIRS recording channels in neonates (preterm and term) and adults are 46 and 20, respectively. To identify significant differences between them, we set the p-value at $p < 0.05/46 = 0.001$. The indices were not normally distributed, so the statistics of the different groups were expressed as medians (min-max), as shown in tables 3–5. The box plots in figure 9 showed that the hPod, IPE and APE of the term and preterm infants and adults differed significantly ($p < 0.0002$). Notably, hPod, IPE, and APE more precisely demarcated

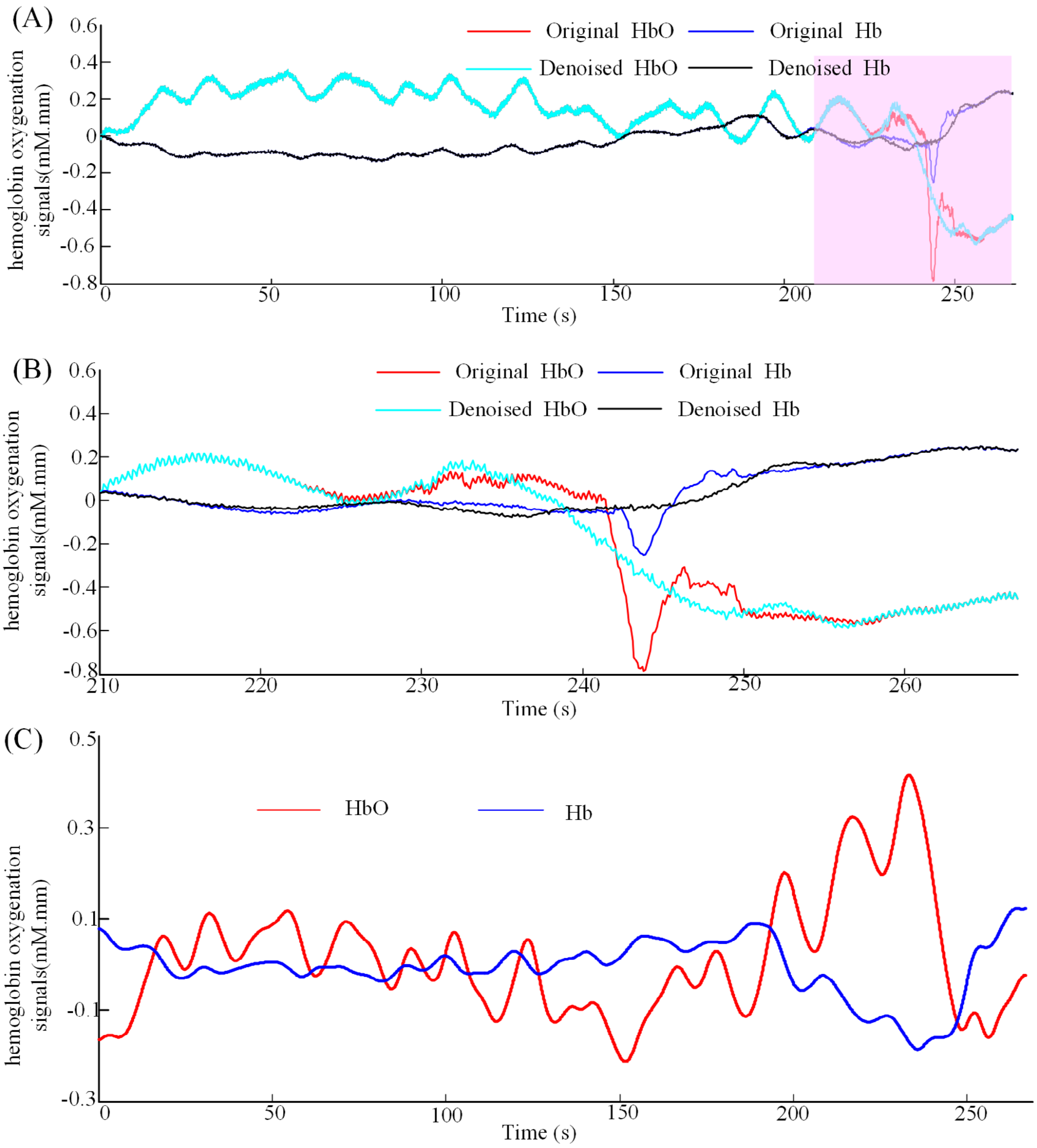

Figure 6. The motion denoising and bandpass filtering of HbO and Hb for one channel. (A) The motion artifact detection and denoising based on the Kurtosis-based wavelet algorithm. The red and blue curves are the original HbO and Hb, respectively. The cyan and black curves are the signals after removal of motion noise. The signals in the time range from 210 s to 270 s (pink rectangle) were contaminated by head movement. (B) The enlarged signals from the time range from 210 s to 270 s. (C) The low frequency band signals (0.01–0.1 Hz) of HbO (red) and Hb (blue), respectively.

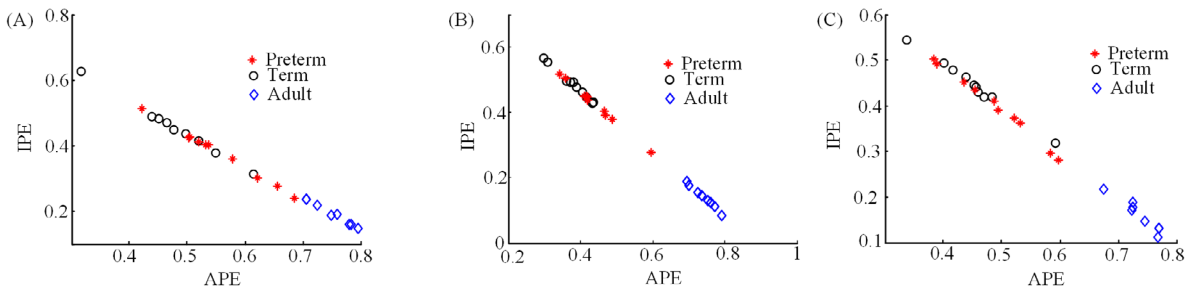

Figure 7. The scatter plot of in-pattern percent versus anti-pattern percent of preterm, term, and adult in 0.01–0.05 Hz (A), 0.05–0.1 Hz (B) and 0.01–0.1 Hz (C), respectively.

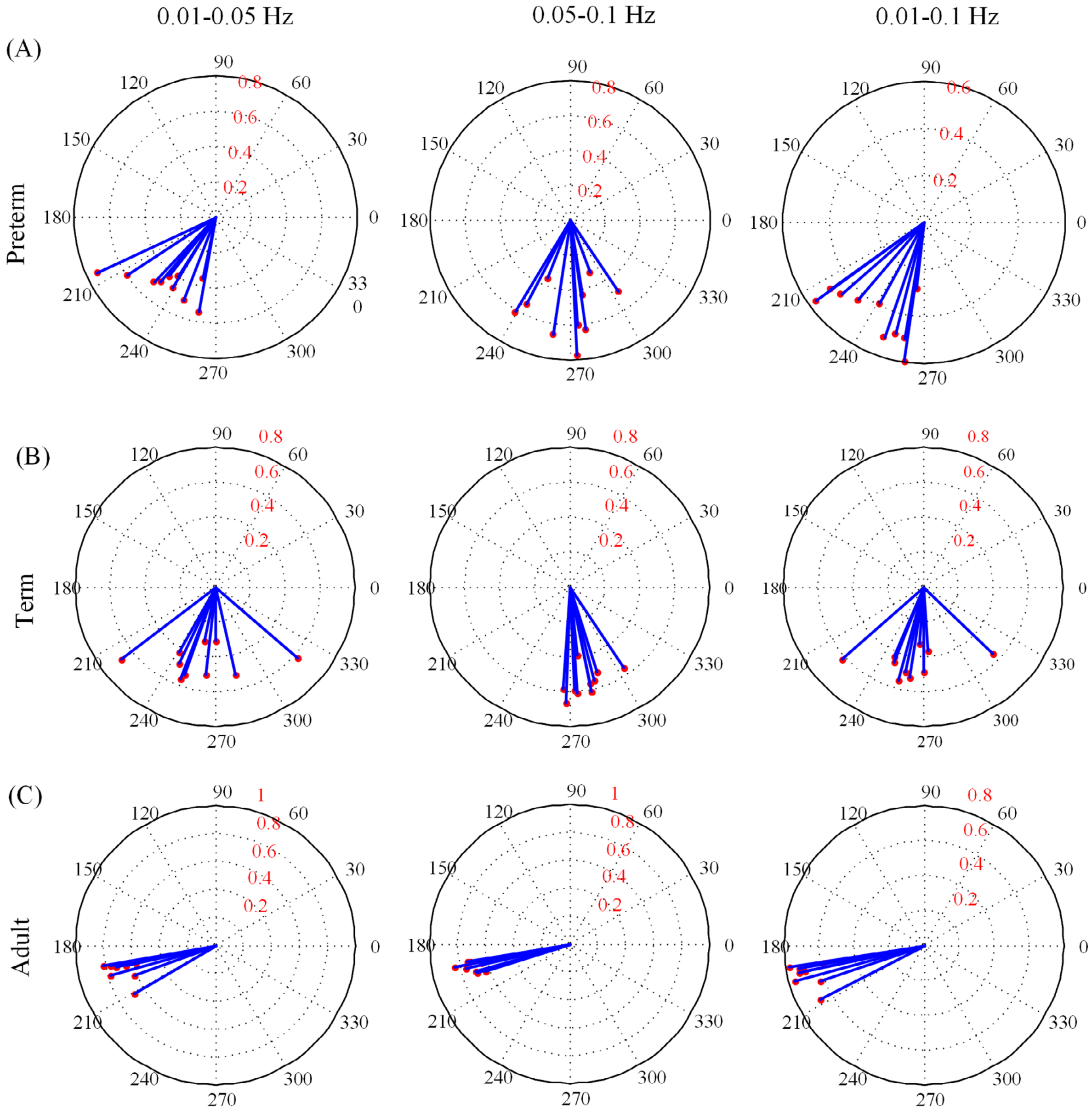

Figure 8. Vector representation of hPod and $hPod_L$ (length of the vector) for preterm (A), term (B) and adults (C) in 0.01–0.05 Hz, 0.05–0.1 Hz, and 0.01–0.1 Hz, respectively.

different brain development states. The overlaps of these three types of measures (i.e. hPod, IPE, and APE) between the adults and neonates (i.e. both term and preterm) were smaller than those between the term and preterm infants. Compared to the phase difference measures, the coupling strength measures (i.e. $hPod_L$ and PCMI) were less precise in distinguishing the preterm and term (see figure 10) neonates except for PCMI in the 0.05–0.1 Hz frequency band. The significant p-values of all indices were shown in table 6. PCMI with epoch lengths of the 30 s, 60 s, and 90 s can distinguish preterm and term stages in the 0.05–0.1 Hz frequency band, which is better than the parallel measure of $hPod_L$ (see figures 10 and S6).

Furthermore, the index assessments' robustness in different states is important in assessing brain development, especially in neonates. We calculated the CV of all measurements within all subjects in different frequency bands. The CV values were shown in tables 7–9. Because the CV value is vulnerable to the mean and SD, to compare the CV of IPE, APE, and hPod consistently, we projected the hPod indices into the range of 0–1 (Liang *et al* 2016b). All the CV values of IPE and APE were smaller than those of hPod in all frequency bands and the PCMI values in the 0.05–0.1 Hz frequency band, while the 30 s epoch length had the lowest CVs among all the measurements (0.07, 0.08, and 0.09). These results illustrated that IPE, APE, and PCMI had a higher tolerance for noise than hPod and $hPod_L$.

Spatial differences are also an important issue in brain development evaluation. We analyzed all the measurements in the prefrontal and left and right temporal areas of the infants. However, in this study, the fNIRS data were collected only

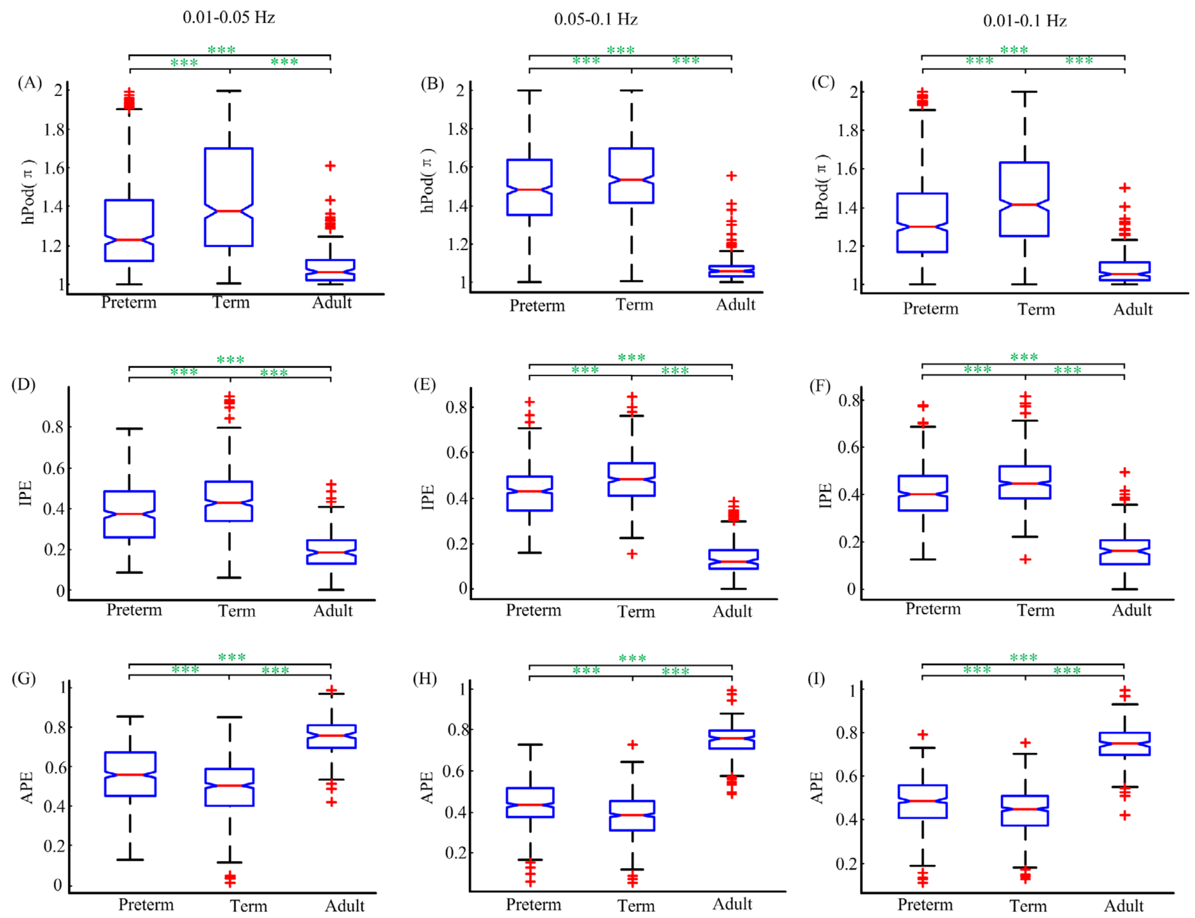

Figure 9. The statistics of the phase relationship measures indices. (A)–(C) The box plots of the hPod indices for preterm, term, and adults in 0.01–0.05 Hz, 0.05–0.1 Hz and 0.01–0.1 Hz, respectively. (D)–(F) The box plots of IPE indices for preterm, term and adults in the similar frequency bands with (A)–(C). (G)–(I) The box plots of IPE indices for preterm, term, and adult in the similar frequency bands with (A)–(C). The symbol of '∗∗∗' in each legend means that the *p*-value $p < 0.001/46 = 0.00002$.

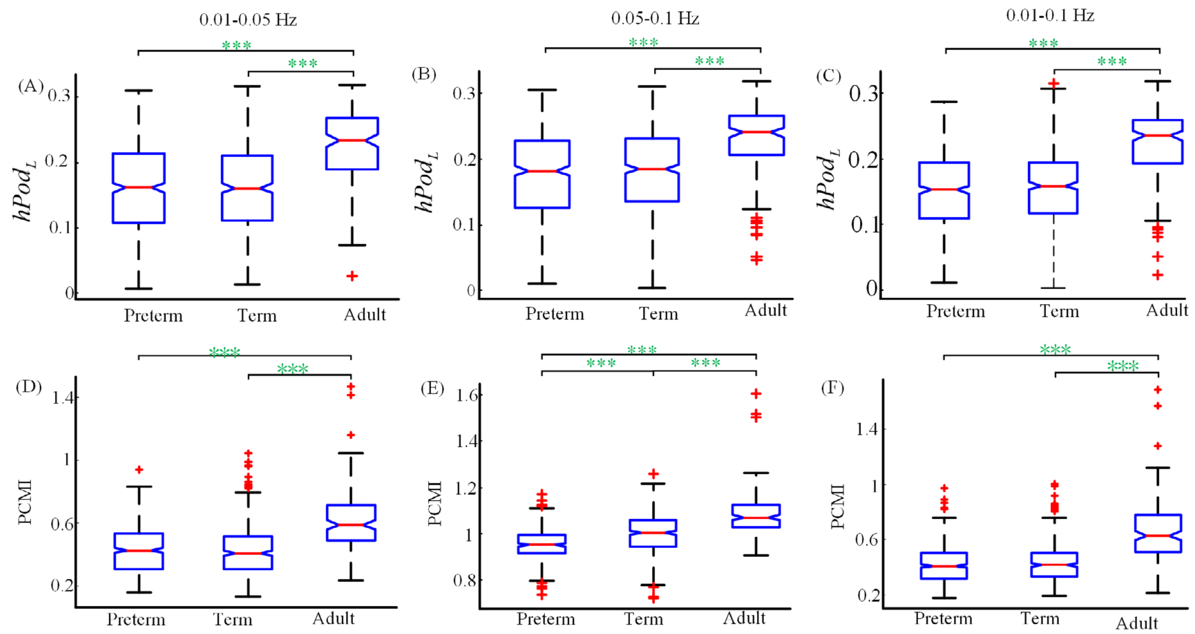

Figure 10. The statistics of the coupling strength measurements indices. (A)–(C) The box plots of $hPod_L$ indices for preterm, term, and adults in 0.01–0.05 Hz, 0.05–0.1 Hz and 0.01–0.1 Hz, respectively. (D)–(F) The box plots of PCMI indices for preterm, term, and adults in the similar frequency bands with (A)–(C). The symbol of '∗∗∗' in each legend means that the *p*-value $p < 0.001/46 = 0.00002$.

Table 3. The statistics of different measurements with preterm, term, and adults in 0.01–0.05 Hz.

	Preterm	Term	Adults
	Median (min-max)	Median (min-max)	Median (min-max)
hPod	1.23 (1.00–1.99)	1.37 (1.00–1.99)	1.06 (1.00–1.61)
IPE	0.37 (0.09–0.79)	0.43 (0.06–0.95)	0.18 (0–0.52)
APE	0.56 (0.13–0.85)	0.51 (0.01–0.85)	0.75 (0.42–0.98)
$hPod_L$	0.51 (0.02–0.97)	0.50 (0.04–0.99)	0.73 (0.08–0.99)
PCMI	0.43 (0.16–0.94)	0.41 (0.13–1.04)	0.59 (0.23–1.46)

hPod = hemoglobin phase of oxygenation and deoxygenation.
IPE = in-pattern exponent.
APE = anti-pattern exponent.
$hPod_L$ = phase-locking index of hPod.
PCMI = permutation cross mutual information with $m = 3, \tau = 11$.

Table 4. The statistics of different measurements with preterm, term, and adults in 0.05–0.1 Hz.

	Preterm	Term	Adults
	Median (min-max)	Median (min-max)	Median (min-max)
hPod	1.48 (1.00–1.99)	1.53 (1.00–1.99)	1.05 (1.00–1.56)
IPE	0.43 (0.16–0.82)	0.48 (0.16–0.85)	0.12 (0–0.39)
APE	0.43 (0.06–0.72)	0.38 (0.05–0.73)	0.75 (0.49–0.99)
$hPod_L$	0.57 (0.03–0.95)	0.58 (0.01–0.97)	0.75 (0.14–0.99)
PCMI	0.95 (0.74–1.17)	1.00 (0.74–1.26)	1.07 (0.91–1.60)

from the prefrontal area of adults. Hence, we can only compare the prefrontal area measurements of infants and adults. The arrangement of fNIRS channels and brain partition in infants are shown in figure S7, and a detailed analysis of all measurements was presented in supplementary appendix E. There were significant differences in the prefrontal area among preterm term neonates and adults based on the phase difference measurements (i.e. APE, IPE, and hPod) ($p < 0.00002$). However, these indices were not consistent with each other in distinguishing preterm and term infants in the left and right temporal regions. The coupling strength measurements ($hPod_L$ and PCMI) can also differentiate between infant and adult brains in the prefrontal area, although there was no significant difference between preterm and term. Only the PCMI in the 0.05–0.1 Hz frequency band more precisely distinguished between preterm and term infants in the left and right temporal areas (see figure S12).

5. Discussion and conclusions

Although brain development in neonates has been studied for a long time, and many fNIRS/fMRI algorithms have been proposed, no widely accepted theory has been established (Gu *et al* 2017, Watanabe *et al* 2017, Taga *et al* 2018). The fNIRS and fMRI literature indicated that the hemodynamic response curve changes with age (Issard and Gervain 2018) and the relative phase between the HbO and Hb can reflect complex interactions in neurovascular and metabolic development (Fantini 2002, Obrig and Villringer 2003, Boas *et al* 2008). There are

Table 5. The statistics of different measurements with preterm, term, and adults in 0.01–0.1 Hz.

	Preterm	Term	Adults
	Median (min-max)	Median (min-max)	Median (min-max)
hPod	1.29 (1.00–1.99)	1.41 (1.00–1.99)	1.05 (1.00–1.56)
IPE	0.40 (0.13–0.78)	0.45 (0.12–0.81)	0.16 (0–0.49)
APE	0.49 (0.11–0.79)	0.45 (0.13–0.75)	0.75 (0.42–0.99)
$hPod_L$	0.48 (0.03–0.90)	0.50 (0.01–0.99)	0.73 (0.07–0.99)
PCMI	0.41 (0.17–0.97)	0.42 (0.19–1.00)	0.63 (0.21–1.68)

Table 6. The *p*-values of different measurements with preterm, term, and adults in 0.01–0.1 Hz, 0.05–0.1 Hz and 0.01–0.1 Hz.

	Preterm-term	Preterm-adults	Term-adults
hPod	∗∗∗/∗∗/∗∗∗	∗∗∗/∗∗∗/∗∗∗	∗∗∗/∗∗∗/∗∗∗
IPE	∗∗∗/∗∗∗/∗∗∗	∗∗∗/∗∗∗/∗∗∗	∗∗∗/∗∗∗/∗∗∗
APE	∗∗∗/∗∗∗/∗∗∗	∗∗∗/∗∗∗/∗∗∗	∗∗∗/∗∗∗/∗∗∗
$hPod_L$	o/o/o	∗∗∗/∗∗∗/∗∗∗	∗∗∗/∗∗∗/∗∗∗
PCMI	o/ ∗∗∗/ o	∗∗∗/∗∗∗/∗∗∗	∗∗∗/∗∗∗/∗∗∗

The symbols, ‘o’, ‘∗’, ‘∗∗’ and ‘∗∗∗’ indicate the *p*-values $p > 0.05/46 = 0.001$, $p < 0.05/46 = 0.001$, $p < 0.01/46 = 0.0002$ and $p < 0.001/46 = 0.00002$, respectively. The combination symbols ‘∗∗∗/∗∗/∗∗∗’ represent the *p*-values in 0.01–0.05 Hz, 0.05–0.1 Hz and 0.01–0.1 Hz, respectively. The Kruskal–Wallis test and Multiple comparison were applied.

Table 7. The CV indices of different measurements with preterm, term, and adults in 0.01–0.05 Hz.

	Preterm	Term	Adults
hPod	0.80	0.65	1.08
IPE	0.36	0.32	0.48
APE	0.24	0.29	0.12
$hPod_L$	0.44	0.41	0.25
PCMI	0.34	0.37	0.30

many different ways to measure age-dependent phase changes in neonates, especially the phase synchronization methodology based on the Hilbert transform (Taga *et al* 2000, Imai *et al* 2014). The goal of these studies was to investigate more effective and robust methodologies to evaluate brain development. Motivated by this goal, in this study, we attempted to evaluate several novel methods (i.e. IPE, APE, and PCMI) based on symbolic dynamics and information theory in assessing brain development. IPE's, APE's and PCMI's performance were compared to those of hPod and $hPod_L$ indices in both simulated and real fNIRS data. Results indicated that IPE and APE can effectively demarcate preterm and term infants and adults, and had smaller CV indices in all three different frequency bands than hPod. Furthermore, PCMI was superior in distinguishing neonates and adults than $hPod_L$, especially in the 0.05–0.1 Hz frequency band. A comparison and statistical analysis based on coupled nonlinear models also showed that symbolic dynamics-based measurements made more accurate predictions in tracking coupling strength.

One possible explanation is that IPE, APE, and PCMI are calculated based on the time series' order patterns, which

Table 8. The CV indices of different measurements with preterm, term, and adults in 0.05–0.1 Hz.

	Preterm	Term	Adults
hPod	0.43	0.37	1.04
IPE	0.26	0.21	0.57
APE	0.25	0.26	0.12
$hPod_L$	0.40	0.36	0.24
PCMI	0.07	0.08	0.09

Table 9. The CV indices of different measurements with preterm, term, and adults in 0.01–0.1 Hz.

	Preterm	Term	Adults
hPod	0.67	0.57	1.04
IPE	0.25	0.22	0.51
APE	0.22	0.23	0.11
$hPod_L$	0.40	0.37	0.25
PCMI	0.32	0.32	0..34

combines mutual information, symbolic dynamics, and nonlinear system theories. hPod and $hPod_L$ are based on the FFT and Hilbert transform, which implicitly assumes that the physiological records are sums of periodical stationary signals. However, IPE, APE, and PCMI are based on the patterns' sequential information, so this symbolic transform focuses on the temporal relationship between neighboring points instead of the oscillation magnitude (Bandt and Pompe 2002). Hence, the phase relationship (APE and IPE) and coupling strength (PCMI) obtained from HbO and Hb signals at different stages will be presented in symbolic synchronization and mutual information. Moreover, compared to FFT and Hilbert transform based algorithms (hPod and $hPod_L$), symbolic dynamics and mutual information methodologies are nonparametric and required limited computing power (Bahraminasab *et al* 2008). Furthermore, it does not need any underlying assumption that the time series or oscillations are stationary or sinusoidal (Talebinejad *et al* 2011). More importantly, mutual information and symbolic transform analysis offer a unique perspective to estimate complex hemodynamic and neurovascular changes during brain development (e.g. the coupling strength of the HbO and Hb become stronger as the cerebral vascular system and neurovascular and metabolic functions develop). Lastly, as described in our previous studies, the symbolic dynamic and mutual information measures were insensitive to the time series' amplitude, making them more tolerant to noise (Abásolo *et al* 2006, Ferenets *et al* 2006, Liang *et al* 2015). Therefore, all these merits indicated the great potential of IPE, APE, and PCMI to be outstanding nonlinear measurements in evaluating brain development changes using fNIRS signals.

Although fNIRS can not measure neuronal activation directly, it can measure HbO and Hb concentration changes, which can be caused by changes in blood flow/volume, or neuronal activation through the neurovascular coupling. In this study, we systematically measured phase changes between Hb and HbO among infants during sleep (no stimulation). We will interpret the results from the perspective of the cerebrovascular development. From a previous study, it is known that brain development will cause the following vascular changes. (1) increased blood volume due to growing capillary density; (2) increased capillary and venous blood flow; and (3) increased mean arterial pressure (limited by cerebral auto-regulation (Greisen 2005)). In addition to these vascular changes, Franceschini *et al* found that there were regionally specific increases in oxygen consumption in healthy infants during their first year (Franceschini *et al* 2007). Interestingly, based on the model (Fantini 2014), increased cerebral blood volume has an in-phase contribution to the phase difference of HbO and Hb, whereas increases in the partial pressure of oxygen, oxygen utilization rate, and speed of blood flow have an anti-phase effect (Watanabe *et al* 2017). In this study, we found that infants with a higher post-natal age (preterm infants (mean: 23.7 d, range: 17–35 d) have a higher anti-phase trend (compared to term infants with mean: 4.2 d, range: 3–6 d). Thus, our study implies that growth of the partial pressure of oxygen, oxygen utilization rate and speed of blood flow is the dominant effect in infants' development, which outweigh that of cerebral blood volume increase. This growth likely stabilizes after six months, resulting in a constant phase difference between HbO and Hb that are maintained into adulthood (Watanabe *et al* 2017).

We reached the conclusions that the hPod, IPE, and APE indices have the similar group mean values in 0.01–0.05 Hz and 0.05–0.1 Hz frequency bands, which are consistent with a previous study (Watanabe *et al* 2017). From the perspective of coupling measurement, the coupling measure of PCMI indices shows a significant difference between term and preterm infants only in the 0.05–0.1 Hz frequency band (see figures 10 and S6) ($p < 0.0002$). However, we do not know what underlying physiological changes made the 0.05–0.1 Hz signal more sensitive to brain development for PCMI. Frequency dependence is an open question in fNIRS and fMRI resting-state studies. We believe that multimodal studies using EEG and fNIRS/fMRI, or animal studies could be exploited to deepen our understanding of this issue.

In this study, the most important finding is the identification of parameters that can distinguish term and preterm infants. For these two groups of infants, channel locations, measurement devices, and recording durations were exactly the same. The fNIRS measurements of adults only covered the prefrontal area, which was not ideal. However, we do not think it would change the results for the following reasons. First, many studies of healthy adults have observed the same anti-phase relationship of HbO and Hb oscillations in many regions of the brain in both resting and task experiments (Issard and Gervain 2017, Lloyd-Fox *et al* 2017, Watanabe *et al* 2017). The measurements we performed should only be served as an example. Second, in this study, we found that the prefrontal region gave the most robust results for many parameters (e.g. IPE, APE, and hPod). This region was shared by infants and adults. Third, although different measurement devices were used for infants and adults, all the indices we analyzed were based on the phase or symbolic pattern of the signal, which is less sensitive to device selection. Finally, in both infants and adults, the measurement times extended beyond 2 min, which has been proven sufficient to obtain a robust index.

However, there are some limitations that should be addressed. First, in this study, the number of datasets is relatively small and the preterm data set only contains early preterm neonates. In future studies, more subjects from a wider age range should be recruited. Second, the adults' experimental conditions were different from those of the infants, which may make direct comparisons difficult. More consistent experimental conditions will be sought in future studies.

In conclusion, the symbolic dynamic-based measures, IPE, APE, and PCMI, can measure brain development changes based on fNIRS signals. PCMI reflects the coupling strength of hemodynamic signals and, to some extent, reveals the underlying mechanisms of brain development. The potential of IPE, APE, and PCMI in estimating brain development has been demonstrated in this study. Furthermore, our new methods (IPE, APE, and PCMI) can be applied to fMRI data. However, instead of measuring HbO and Hb phase differences within one channel, these parameters can be used to assess coupling strength or phase differences between channels (voxels/regions of interest). We believe it will approach interesting brain interactions from a new perspective.

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Disclosure

The authors declare no conflict of interest.

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Infant word segmentation recruits the cerebral network of phonological short-term memory

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ABSTRACT

Segmenting word units from running speech is a fundamental skill infants must develop in order to acquire language. Despite ample behavioral evidence of this skill, its neurocognitive basis remains unclear. Using behavioral testing and functional near-infrared spectroscopy, we aimed to uncover the neurocognitive substrates of word segmentation and its development. Of three age-groups of Japanese infants (5–6, 7–8, and 9–10 months of age), the two older age-groups showed significantly larger temporo-parietal (particularly supramarginal gyrus) responses to target words repeatedly presented for training, than to control words. After the training, they also exhibited stronger inferior frontal responses to target words embedded in sentences. These findings suggest that word segmentation largely involves a cerebral circuit of phonological (phonetic) short-term memory. The dorsal pathway involved in encoding and decoding phonological representation may start to function stably at around 7 months of age to facilitate the growth of the infant's vocabulary.

1. Introduction

Unlike written language, conversational speech does not have noticeable spaces between words. Indeed, speech hardly has any salient acoustic cues to indicate word boundaries. This becomes an obstacle for infants in identifying a spoken word unit. Similar to listening to an unknown language for adults, the native language that infants hear probably sounds like a running sound stream. Hence, a primary step of word acquisition in infants is the ability to segment words from continuous speech. This type of language skill, known as "word segmentation", is one of the significant landmarks in language development in the first year of life.

How does an infant determine where one word ends and another starts? Extensive studies have been performed on this issue, chiefly using the head-turn preference procedure (HPP). Jusczyk and colleagues performed a series of studies and identified several factors that guide infants to segment words such as phonotactic rules, coarticulation, and stress (Jusczyk & Aslin, 1995; Jusczyk, Hohne, & Bauman, 1999; Jusczyk, Houston, & Newsome, 1999). Among them, stress appears to play a significant role in many languages. For example, Jusczyk, Houston, et al. (1999) showed that 7.5-month-old infants were able to identify familiarized English words with a Strong–Weak pattern but not those with a Weak–Strong pattern. Infants whose native language is Dutch show a similar tendency at 9 months of age (Houston, Jusczyk, Kuijpers, Coolen, & Cutler, 2000). However, languages without any stress accents appear to have different developmental word segmentation processes. French contains no lexical accents, and provides no clear acoustic indications to infants. These results in infants being unable to segment a final syllable by 8 months of age, or find the boundary of a whole word by 16 months of age (Nazzi, Iakimova, Bertoncini, Frédonie, & Alcantara, 2006).

In the case of Japanese, whose primary acoustic cue to a lexical accent is a pitch pattern, infants start to segment Japanese words with particular phonemic and accentual context around 8–10 months of age (Kajikawa & Masataka, 2003; Sato, Kajikawa, Sakamoto, & Matsumoto, 2007). Specifically, words starting with a High (H) pitch followed by a Low (L) pitch (HL, initial accented pattern) are more easily segmented, whereas those with a Low–High pattern (no initial accentuation) are more difficult to segment. Note that in standard Japanese, a mora with H pitch following a decrement of pitch (i.e. a mora with L pitch) represents an accented mora (e.g. HLL initial accent, LHL second mora accented, LHH no accentuation when the next word starts with H pitch). Vowel qualities of the first and second morae also contribute to saliency of these two successive initial morae, such that an

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open-closed vowel sequence is easier to detect than any other sequence. By analyzing the acoustic features of words that are well segmented by 9 months, Sato et al. (2007) concluded that acoustic differences in amplitude and duration between the first and second morae provide a strong cue for infants in finding a boundary. Altogether, Japanese 9-month-old infants have a tendency to segment words under an initial HL accent condition and an open-closed vowel sequence with enough acoustic differences between both morae (Sato et al., 2007). These studies imply that similar to English-learning infants, Japanese infants make use of the acoustic sequence of "Strong–Weak" as a salient cue to initially identify words. Additionally, since Japanese is an agglutinative language, it has case marking auxiliary words, such as topic and subject markers. It has been suggested that these markers also contribute to word segmentation (Kajikawa & Haryu, 2007). Finally, subsequent research after a series of studies by Jusczyk and colleagues showed that depending on the type of stimulus presentation and training method, young infants can segment words earlier (Bergmann & Cristia, 2015; Bortfeld, Morgan, Golinkoff, & Rathbun, 2005; Nishibayashi, Goyet, & Nazzi, 2015; Seidl & Johnson, 2006). For example, word–object pairing training with real social interaction enhances word learning, and results in the capability to segment trained words, even for 5–6-month-old Japanese infants (Hakuno, Omori, Yamamoto, & Minagawa, 2017). Here, to compare the accumulating results of previous studies, we focus on a typical word-segmentation task that only uses auditory cues.

Apart from the abovementioned behavioral studies, Kooijman, Hagoort, and Cutler (2005) attempted to investigate the neural basis of word segmentation in infants using event-related potentials (ERP). Employing a similar paradigm as the one by Jusczyk and Aslin (1995), they found a differential electrophysiological signature between trained and control unfamiliar words. During the training phase, positive electrophysiological responses gradually decreased as infants were familiarized with target words, a neural indication of habituation to the word. Accordingly, in the test phase, learned words elicited more negative deflections (around 350–500 ms) in Dutch 7- and 10-month-old infants (Kooijman et al., 2005). HPP shows the earliest evidence for segmentation in Dutch infants is 9 months of age; therefore, ERP is a more sensitive methodology to examine word segmentation. Additionally, Goyet, de Schonen, and Nazzi (2010) tested French 12-month-old infants with no behavioral indication of bisyllabic word segmentation in French (Nazzi et al., 2006), and they showed negative deflections around 350–500 ms in response to familiarized words. Given that these ERP responses are similar to the neural correlate of segmentation observed in the study of Kooijman et al. (2005), French infants were also shown to segment words 4 months earlier by electrophysiological measures than with behavioral measures.

Although these studies crucially reveal the cerebral correlate of word segmentation from continuous speech, ERP cannot precisely detect the brain region engaged in specific cognitive processing. Consequently, the brain mechanism or network underlying word segmentation still remains unclear. Further, it is possible that a brain signature is more sensitive than behavioral results, thus a much younger infants' brain (e.g., 5–6 months of age) may already be responsive to familiarized words inserted in sentences. fNIRS studies of word familiarization strongly support this view, suggesting that neonates exhibit some form of sound memory by presenting isolated words (Benavides-Varela, Hochmann, Macagno, Nespor, & Mehler, 2012). To explore these issues in the present study, we investigated cerebral activation in infants during word training and word segmentation of learned words using both a behavioral method (described in Experiment 1) and a neuroimaging method, specifically, functional near-infrared spectroscopy (fNIRS) (described in Experiment 2). We aimed to reveal: (1) at what age Japanese infants start to segment whole words, as assessed by hemodynamic brain responses and behavioral testing; and (2) what brain network underlies the process of word learning and segmentation, and thus what cognitive processes are engaged within the network.

2. Experiment 1: Materials and methods

In experiment 1, we examined the behavioral performance of an infant's ability to segment whole words from continuous speech. The targeted stimulus words were Japanese three mora words with HLL accents, which are easier to segment (as already explained). Accordingly, we used a forced-choice preferential looking (FPL) paradigm (McCleery, Allman, Carver, & Dobkins, 2007; Teller, 1979) to test Japanese infants from three age groups (5–6, 7–8, and 9–10 months of age).

2.1. Participants

Fifty-four Japanese infants from three age groups (5–6 months: $N = 18$, 14 boys, mean age = 181 days, SD = 22.7; 7–8 months: $N = 18$, 10 boys, mean age = 238 days, SD = 15.2; and 9–10 months: $N = 18$, 13 boys, mean age = 288 days, SD = 14.7) were included in the final data set. They had no hearing or developmental problems, nor significant exposure to foreign languages. There were 21 additional infants, but 15 were excluded because they did not reach the criterion for minimum looking time (2 s) on all 12 test trials. Other exclusions were due to fussiness (5 infants) or insufficient exposure to Japanese at home (1 infant). Parents signed an informed consent form approved by the ethics committee of Keio University, Faculty of Letters [No. 09049].

2.2. Stimuli

The stimulus words used as target words were "*tanishi*" (mud snail or Pilidae) and "*zakuro*" (pomegranate). On the basis of our preliminary study and a previous study (Sato et al., 2007), we used the following two criteria to select these stimulus words. First, our stimulus words were initially accented 3-mora (sub-syllabic unit) nouns with the vowel sequences "a-i" or "a-u" in the first and second morae. Second, the stimulus words had low familiarity scores ranging from 5.0 to 5.5 points, according to the database for spoken words created by Amano and Kondo (1999). The first criterion was chosen on the basis of previous studies, and facilitates infant word identification from sentences. As stated above, Sato et al. (2007) reported that an initial word sequence of "a-u" is easier to detect than "u-a" due to the strong amplitude at the initial mora. This is consistent with our pilot study, where we found a tendency towards easier segmentation of broad–narrow vowel sequences than closed–open vowels in the context of an initially accented word. The second criterion was chosen to ensure that stimulus words were not already familiar to the participants.

For the training session, one of the target words (zakuro or tanishi) was used for each participant. In the test session, the previously familiarized words (zakuro or tanishi) were used as target words, as well as unfamiliarized control words, specifically, "*gaika*" (foreign money) and "*aruji*" (master). These control words adhered to the same criteria for word context as the target words. The combination of familiarized and unfamiliarized control words and frequency of combination use were counterbalanced for each age group as much as possible. Specifically, either "*gaika*" and "*aruji*" was used as the control word for half of the infants in each age group. For test session stimuli, each stimulus word was embedded in six different sentences (Table 1), resulting in a total of 24 sentences. For the stimulus recording, three female native Japanese

Table 1
Stimulus materials used in experiment 1 and 2, with literal English translation.

Target words and sentences used for the test session (Exp.1&2)	
zakuro (Pomegranate)	tanishi (mud snail)
anozakurowakikaraochimashita	*akai tanishi wa takumashii kai desu*
That pomegranate has fallen from a tree.	Red mud snails are robust snails.
fuyunimichidemitazakuro	*kappatsu de chiisa na tanishi*
The pomegranate that I saw on the path in winter.	Little and active mud snails.
okaasanwachiisanazakurookiri mashita	*tanishi no kara wa katai desu*
Mom cut the little pomegranate.	The shell of a mud snail is hard.
zakuro wa oishii kudamonodesu	*kesa kawa de mita tanishi*
Pomegranates are tasty fruits.	The mud snail that I saw this morning by the river.
mizumizushiiakaizakuro	*tanishi wa suna ni moguri masu*
A fresh, juicy and red pomegranate.	Mud snails go under the sand.
zakuro nomiwakireidesu	*kodomo wa ano tanishi o tori mashita*
The fruit of pomegranate is beautiful.	The child has caught that mud snail.
Control words and sentences used for the test session (Exp.1&2)	
gaika (foreign currency)	aruji (master)
chiisanagaikawamachide tsukai masu	*ano aruji wa youki na seikaku desu*
They use small foreign currency in the town.	That master has a cheerful character.
kichou naanogaika	*yoru ni yado de mita aruji*
That precious foreign currency.	The master that I saw at a hotel in the evening.
gaikawajuuyouna okanedesu	*aruji wa heya o kataduke masu*
Foreign currency is important money.	The master put rooms in order.
ojiwaakaigaikaosagashimashita	*aruji no hanashi wa yukai desu*
My uncle looked for a red foreign bill.	The master's talk is funny.
gaikanoshuruiwaooidesu	*musume wa akai aruji o tashiname mashita*
There are many kinds of foreign currency.	The daughter reproved the master having his face red.
kyoukuukoudemita gaika	*shinsetsu de chiisa na aruji*
The foreign currency that I saw at the airport.	The kind little master.

speakers pronounced the stimulus list in an infant-directed fashion. To edit the auditory stimuli, ten different tokens of recordings were selected for each word or sentence from each speaker. Acoustic information for the stimulus words is displayed in Table 2 and Fig. 1. There were no statistically significant differences between the target and control stimuli in their averaged pitch, pitch range and duration.

2.3. Experimental setup and design

The FPL paradigm can be explained as a modified version of HPP. To measure an infant's preference to audio stimuli, traditional HPP uses a flashing light on the right or left side that corresponds to the audio stimulus source (speaker). However, the FPL paradigm uses animation on either side of the monitor instead of light. The FPL paradigm is based on the fact that infants will look longer at a patterned stimulus with audio-visual correspondence on one side of the monitor, compared with nothing on the other side. In each trial, the visual stimulus appears on the left or right side of the monitor with an audio stimulus on the same side. An experimenter observes the infant's eye gaze behavior through a video camera monitor to judge how long the infant attends to the stimulus. This FPL technique is often used to assess visual acuity in infancy (McCleery et al., 2007), although Hakuno, Omori, Yamamoto, and Minagawa-Kawai (2012) showed that this approach is also applicable to test an infant's preference to auditory stimuli by replicating a previous result obtained by HPP.

The behavioral experiment was performed in a quiet testing room. The infant sat on the mother's lap, facing a monitor 40 cm away from the infant's eyes at the height of the infant's head. Auditory stimuli were presented from one of two loudspeakers mounted on either side of the monitor (ca. 70 dB sound-pressure level, SPL). Visual stimuli were presented on a 19-inch monitor controlled by a computer. A video camera was mounted behind the monitor to record the infant's eye gaze during the experiment. An experimenter observed the infant's behavior through another monitor connected to a video camera in the observation area. From the observation area (in the testing room), an experimenter monitored the infant's eye gaze and controlled stimuli presentation using a computer. The observation area and testing area were divided by a thick curtain. The parent and experimenter were blind to the auditory stimuli presented.

Training session. Prior to the test session, infants participated in a training session, and were trained to learn one of the target words (i.e., tanishi or zakuro). The trial started by attracting the infant's attention using animated moving ducks accompanied by fanfare. After the infant's attention had shifted to the screen, 12 target words were presented along with animated visual stimuli (moving alligator or bat) for each trial. Although the target words within one session were the same in terms of linguistic structure, the acoustic characteristics were different for each stimulus because different recordings were used from three speakers. The target words were presented with a stimulus onset asynchrony (SOA) of 1 s and each trial lasted 12 s. Participants completed five trials, and therefore listened to 60 tokens of the target word.

Test session. Participants performed the test session immediately after the completion of the training session. In the FPL experiment, each trial began with presentation of a fixation point on the monitor and a fanfare sound from two speakers on the right and left side. As soon as the infant's gaze fixed on the monitor, the movie clip of a puppet appeared on the right or left side of the display. Shortly after the infant had moved their eyes to the visual stimulus, auditory stimuli (sentences containing either familiarized or unfamiliarized new words) were presented from the speaker on the same side as the visual stimulus. The time spent looking at the stimuli was measured for each trial that lasted 26 s at maximum. When the infant looked away from the visual stimulus for more than 2 s or continued to look at the stimulus for longer than 26 s from the beginning, the trial ended and the

Table 2
Acoustic properties of target and control words. Average value of stimulus tokens and standard error of mean (in parenthesis) are indicated. F0 = fundamental frequency.

	Training session				Test session							
	Target words in isolation				Target words in sentences				Control words in sentences			
	zakuro		tanishi		zakuro		tanishi		gaika		aruji	
Duration (ms)	547	(5.2)	623	(5.1)	462	(8.8)	459	(12.2)	451	(10.0)	472	(7.5)
F0 (Hz) mean	237	(2.9)	266	(1.4)	238	(6.7)	234	(10.3)	240	(8.5)	248	(9.3)
Maximum	318	(3.4)	339	(2.1)	311	(9.8)	303	(11.2)	302	(13.7)	310	(13.3)
Range	146	(3.0)	160	(3.2)	125	(10.7)	129	(8.5)	131	(14.1)	125	(10.8)

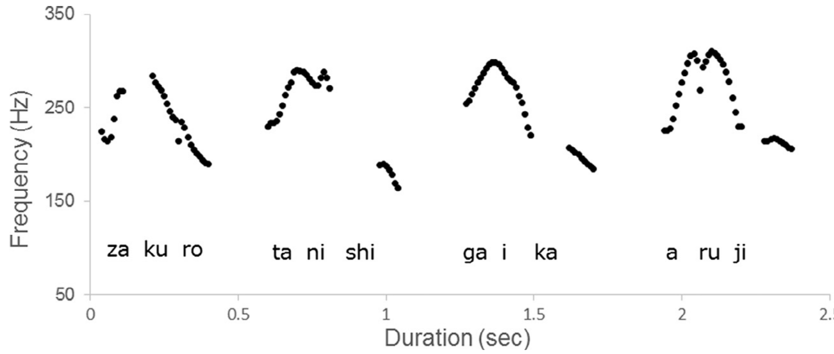

Fig. 1. Examples of pitch contours contained in stimulus words. These words are extracted from the sentences of the test condition. HLL pitch (initial accent) was assigned to all the words. Japanese pitch accent has a phenomenon called "late fall" as observed from the second "L" mora having slow declination.

experimenter stopped the stimulus presentation. Each target word condition and control condition with a new word had 6 trials, resulting in 12 trials in total. Each trial consisted of acoustically different sentences spoken by different speakers, but some sentences were identical in linguistic form. The presentation order of the two conditions and presenting side was counterbalanced within one session and within participants. The time infants looked at each visual stimulus was recorded by the experimenter.

2.4. Data analysis

An experienced coder was responsible for coding fixation duration on visual stimuli by judging an infants' eye position and movements at 100 ms intervals using behavioral coding software (GenobsX, Tokyo, Japan). Each participant's mean fixation duration for target and control words was obtained by averaging the corresponding six trials. To ensure reliability of the coder, another coder who was blind to the experiment performed 31% (16 infants) of the entire video coding. The kappa coefficient value was determined by Cohen's test to compare the coding results between both coders for each infant's recording. The averaged kappa coefficient value was 0.88 (S.D. 0.03), showing reliability of the first coder.

3. Experiment 1: Results

Fig. 2 shows the average time spent looking in target and control trials for the three different age groups. The younger age groups did not show much difference in looking time between target and control conditions, while the oldest group looked for longer in the target condition. Two-way analysis of variance (ANOVA) with condition (target and control) as the between-subject factor and age group as the within-subject factor revealed a significant main effect for condition [$F(1,51) = 4.77$, $p = 0.033$] and a marginal significant condition × group interaction [$F(2,51) = 3.00$, $p = 0.058$]. A straightforward test of the main effect indicated that this interaction was due to the longer looking time in the target condition in 9–10-month-old infants only [$F(1,51) = 8.00$, $p = 0.006$]. This means that although there is a global tendency to attend for longer to sentences with target words, this is only significant in the oldest age group. This suggests that 9–10-month old infants have learnt the target words and are able to segment these words within sentences. We also found a tendency for a main effect of age group [$F(2,51) = 2.50$, $p = 0.091$], but no significant difference among the three age groups was revealed by post hoc analysis.

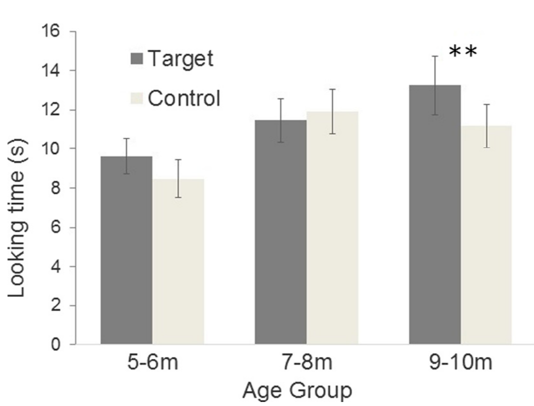

Fig. 2. Looking time to target and control word conditions during the behavioral auditory word segmentation task. ** p < 0.01.

4. Experiment 1: Discussion

Although our behavioral method was different from that of Sato et al. (2007), which used HPP, our results are fairly consistent. Indeed, our results provide further evidence that the FPL paradigm is a reliable behavioral method for testing infant preference to auditory stimuli, as already shown (Hakuno et al., 2012). Our looking time data found that Japanese infants begin to segment whole words from sentences at 9 months of age. This timing is relatively slower than infants whose ambient language is English (7.5 months) and German (8 months) (Höhle & Weissenborn, 2003; Jusczyk & Aslin, 1995) but earlier than French infants (12 months) (Nazzi et al., 2006). Although general tendency towards looking longer in the target condition compared with the control condition was significant among all participants, only 9–10-month-old infants exhibited a significant difference between the conditions. However, because the neural marker of word segmentation is more sensitive than the behavioral one (Goyet et al., 2010; Kooijman et al., 2005), it may be that infants in these two age groups can segment words. Experiment 2 explores this possibility with a stronger focus on examining the cerebral basis of word segmentation in the perisylvian area.

5. Experiment 2: Materials and methods

In experiment 2, we investigated the neural correlate of word segmentation in infants from 5 to 10 months of age. Employing the same stimulus words and a similar paradigm as in the behavioral test, we aimed to identify cerebral activity during learning of words and segmenting or recognizing words from running speech.

5.1. Participants

Japanese monolingual infants were recruited as paid participants in three age groups ranging from 5 to 10 months. The participants were different from those in experiment 1. Final data samples for participants undertaking fNIRS recordings included 5–6 months ($N = 28$, 16 boys, mean age = 179.7 days, SD = 19.3), 7–8 months ($N = 22$, 14 boys, mean age = 242.8 days, SD = 20.3), and 9–10 months ($N = 19$, 10 boys, mean age = 297.6 days, SD = 18.8). Basically, two experimental conditions (i.e. training and test conditions) used this data set, the data sets for two conditions were not completely identical because some infants' data were not usable due to the artifact for either one of the conditions. Parental reports revealed no hearing or developmental problems nor significant exposure to other foreign languages. Although an additional 82 infants participated in the sessions, their data were excluded from the final data set because of rejection of the NIRS probe cap (17), cessation of the session due to fussiness (19), or insufficient trials because of motion artifacts (46). Parents signed an informed consent form approved by the ethics committee of Keio University, Faculty of Letters [No. 09049].

5.2. Experimental design

The experiment consisted of both training and test sessions. The training session detected brain activation in infants as they listened to (1) one target word repetitively presented and spoken by various speakers, and (2) various types of words, which are impossible to learn, as the control condition. The test session examined brain responses to (1) various sentences, each of which had the target word learnt in the training session, as the target condition and (2) various sentences, each of which had one control word the infants had never heard, as the control condition. The control word was fixed in the same manner as Experiment 1, because repetitive presentation of the same word in only the target condition may cause biases in the brain response elicited by learning. Target and control words were paired in the same manner as Experiment 1. For each group, half of the participants listened to tanishi and another half listened to zakuro as the target word. Each of them was paired with either gaika or aruji as the control word approximately 50% of the time.

5.3. Stimuli

The stimulus words for both conditions were the same as used in the behavioral experiment apart from additional control words in the training session. The stimulus words used in the training session were "zakuro" and "tanishi" for the target condition as well as 84 additional 3-mora words for the control condition. In the test session, two previously familiarized words (zakuro and tanishi) were used as target words, and unfamiliarized words (gaika and / aruji) as control stimuli. Unfamiliarized words adhered to the same criteria in relation to word context as those for the target words.

Stimulus words were presented in different contexts in two separate sessions. Specifically, in the training session, they were presented in isolation in both the target and control blocks. One block involved 12 words pronounced by three female speakers in an infant-directed fashion. Each word was physically unique within one block, with no acoustically identical token, because various tokens (even for the same word) were recorded from each speaker. Each block had in principle unique word (token) presentation order for one session. In the target block, one of the target words was continuously presented for 12 s, while in the control block, various words were randomly presented.

In the test session, the familiarized target word was embedded in six different sentences for the target block (Table 1). While for the control block, one of the unfamiliarized words was spoken in the same sentence context as the test session of Experiment 1. The sentences were randomly presented for approximately 12 s. Similar to the training session, a multiple token method was used, with each sentence within one block being acoustically unique.

In both sessions, two types of blocks (target or control) were pseudo-randomly presented 8 times for each, with jittered (8–16 s) silent baseline blocks between them. Furthermore, target and control blocks were acoustically matched for sound amplitude (route mean square, RMS).

5.4. fNIRS recordings

Our study used NIRS (ETG-7000, Hitachi Medical Co., Japan), which measures brain hemoglobin (Hb) concentration changes in optical paths between the nearest pair of incident and detection probes, which are positioned 3 cm apart on the scalp surface (Watanabe et al., 1998; Yamashita, Maki, & Koizumi, 1996). This separation allows hemodynamic changes within the brain (2.5–3 cm deep from the head surface) to be detected, and corresponds to the gray matter on the outer brain surface (Fukui, Ajichi, & Okada, 2003). The NIRS system emits two wavelengths (approximately 780 nm and 830 nm) from continuous near infrared lasers, which are modulated at different frequencies depending on the channel and wavelength, and detected by sharp frequency lock-in amplifier filters (Watanabe et al., 1998).

5.5. Localization

For infants, four incident and four detection probes arranged in 2×4 square grids (10 channels) were fitted onto the temporal area on each side of the head using the International 10–20 system (see Fig. 3A for channel position). In particular, the line connecting T3, F7, F8, and T4 was horizontal to the lowest fNIRS probe line, and the center of the posterior probe in the lowest line corresponded to T3 or T4 (Fig. 3A). This provides good coverage of the superior temporal cortices, and extending upwards into the inferior frontal gyrus, precentral gyrus, and temporo-parietal junction. Brain areas corresponding to fNIRS channels were estimated according to the spatial registration procedure of fNIRS (Okamoto et al., 2004; Tsuzuki et al., 2007). Talairach Atlas was used to label regions in terms of Brodmann areas. Although this virtual registration is applicable to the adult brain, we used this method to estimate infant brain region by adjusting for differences in head size and emitter–detector separation length (inter-probe separation) between adults and infants. Specifically, infant head circumference is roughly 0.8 times smaller than an adult. Accordingly, a channel array was used with an inter-probe separation of 25 mm (0.83 times shorter than the 30 mm used in the virtual registration for adults) (Tsuzuki et al., 2007). Apart from occipital regions, brain region proportion does not change much between adults and 1-year-old infants (Matsui et al., 2014).

5.6. Procedures

The infant sat on their mother's lap in a sound attenuated room, at approximately 1.5 m from a loud speaker. Experimenters carefully positioned probe pads onto the infant's head using a reference point from the International 10–20 system. After the intensity level of all the channels had been checked, stimuli were presented using a program based on Visual Basic (Microsoft) via a loudspeaker (ca. 70 dB SPL). To reduce motion artifacts and restlessness, one experimenter entertained the infants using silent toys. During the session, both the mother and experimenter listened to other sounds through headphones to prevent any influence of the stimuli on

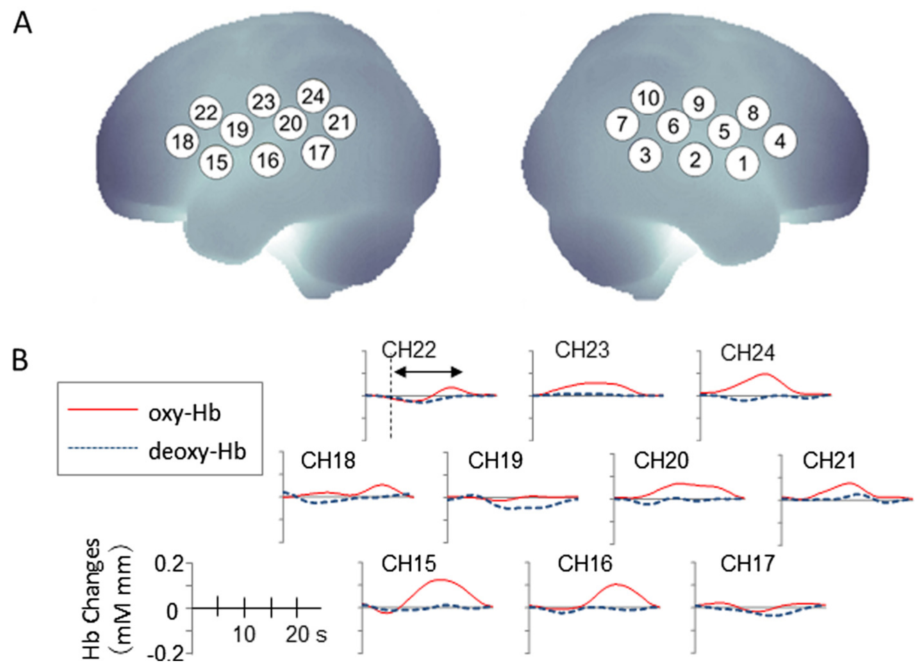

Fig. 3. Location of probe pads relative to surface landmarks (A) and averaged time course of hemodynamic responses on the left temporal area for training session in the 9–10-month-old group (B). Vertical dotted line indicates a stimulus onset and horizontal arrow indicates a task period (12 s).

their behavior. The test session immediately began, after the training session was complete.

5.7. Data analysis

Relative concentrations of oxygenated (oxy-) and deoxygenated (deoxy-) Hb were calculated from attenuation data of 780 and 830 nm laser beams sampled at 10 Hz. According to the criteria for rapid signal change (>0.2 mm changes within two consecutive data points), followed by further manual checks, inappropriately fitted channels and blocks (including motion artifacts) were removed. Infants who had more than five "bad" channels were excluded from the final data set. For each session, data containing more than four blocks for each of two conditions was included in the final data set. Thus, degrees of freedom vary across analysis sets involving condition and channel, even within the same age group. All data were averaged synchronously to target (or control) block onset and smoothed with a 5-s moving average. After normalizing the target block data with a 5-s baseline period immediately before the target (or control) block, averaged Hb values during a target block were calculated using a time windows of 6.5–12.5 s from onset. Statistical significance of each channel (CH) for each condition was assessed using *t*-tests to compare average Hb change for baseline and target (or control) periods. In this study, a false discovery rate (FDR) was applied to accommodate multiple comparisons across all channels for each condition (in addition to normal statistics without corrections). To compare responses between target and control conditions, *t*-tests using averaged Hb values during a target time window, subtracted by averaged Hb values during a 5-s baseline period for each condition were applied (i.e. target Hb during time window minus baseline Hb) vs (control Hb during time window minus baseline Hb). An FDR for *t*-tests was also applied across all channels. For further statistical analysis, ANOVA was used with the factors of age group and experimental condition for region of interest (ROI). Appropriate channels were determined according to the results of activation statistics. The ROI was set in the same brain area across different age groups, because we aimed to examine the developmental course of particular cognitive processes, such as memorizing and retrieving words, in the same brain regions typically responsible for that cognitive process in the mature human brain. Thus, the channel with the strongest Hb values in the target-control comparison of 9–10-month-old infants successful in the segmentation task (Experiment 1) was determined to be an ROI for each training and test session.

6. Experiment 2: Results

In general, infants showed an increase in oxy-Hb and slight decrease in deoxy-Hb during the stimulus period (Fig. 3B) for both training and test sessions. However, response amplitudes were different depending on the stimulus condition (brain region (CH) and age group), as indicated in Figs. 4 and 5. The training session consisted of familiarization and control conditions. Both conditions broadly activated bilateral temporal and parietal regions, but comparison of the response between them (familiar vs control) by limiting significant channels revealed an overall reduction in activation levels. In particular, activation around the superior temporal area [or superior temporal gyrus (STG)/inferior frontal gyrus (IFG)] (CH15) was generally decreased for familiar vs control, suggesting similar activation in both conditions in this area. In contrast, Hb response around the inferior parietal and posterior STG areas (CH 20 and 24 marked in Fig. 4) remained partly significant particularly for 7–8- and 9–10-month old infants. In addition, area CH6 (right posterior STG) exhibited a strong response, even compared with the control condition, exclusively for 7–8-month-old infants. Among them, we selected CH24 (supra marginal gyrus, SMG) as a ROI (Fig. 6A), because the response amplitude was consistently highest for the 9–10-month-old groups. Two way ANOVA was performed with condition as the within-subject factor and group as the between-subject factor. The results revealed a significant main effect for condition [$F(1,58) = 10.33$, $p = 0.0021$] and marginal significance for an interaction between both factors [$F(2,58) = 3.00$, $p = 0.057$]. Further analysis showed that the interaction was due to a significantly greater response to the target

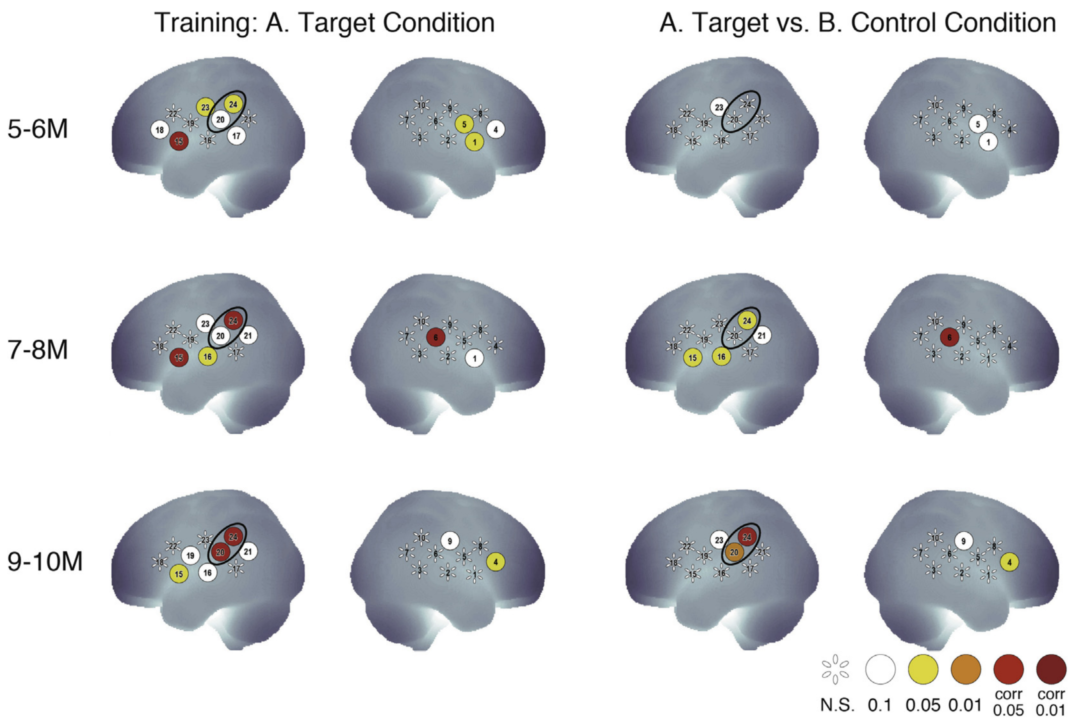

Fig. 4. Activation map (*p*-values) in all three age groups in response to target stimuli (A) and target vs. control (B) for the training session. Channel labels are shown in different colors according to statistical values of $p < 0.01$ and $p < 0.05$ in those corrected for multiple comparisons and $p < 0.01$, $p < 0.05$, and $p < 0.1$ in those without corrections. Uncorrected p-values and marginal values ($p < 0.1$) were considered as channel labels to enable both activation foci and overall activation tendency to be observed.

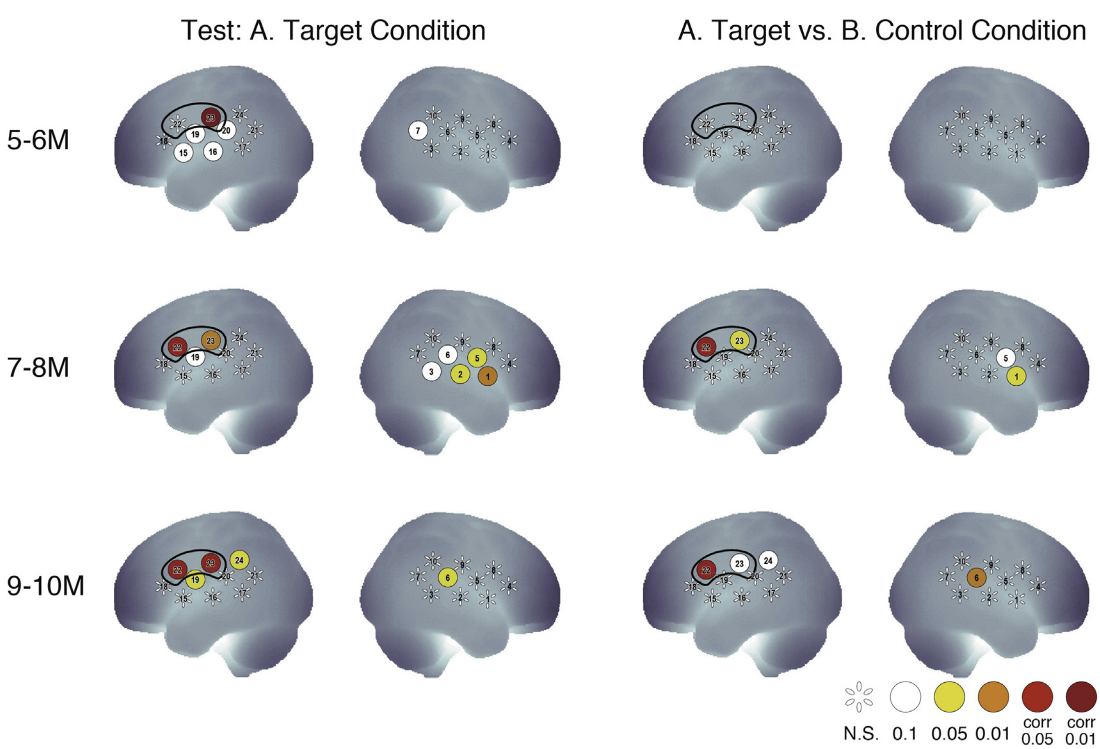

Fig. 5. Activation map (*p*-values) in all three age groups in response to target stimuli (A) and target word vs. control (B) for the test session. See legend of Fig. 4 for details of channel labels.

condition in the 7–8- [$F(1,58) = 7.04$, $p = 0.010$] and 9–10- [$F(1,58) = 9.28$, $p = 0.003$] month-old groups.

In the test session, consisting of the condition with the target word and control condition with an unknown word, infants also showed bilateral activation in temporal, frontal, and parietal regions. While target vs control detected almost no significant channels for the youngest group, 7–8- and 9–10-month-old infants showed a similarly strong response around IFG and premotor areas

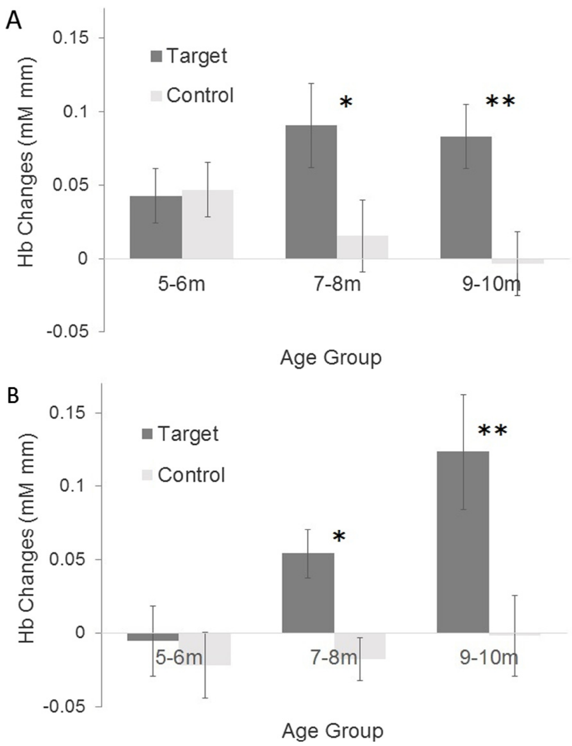

Fig. 6. Differences in oxy-Hb response between target and control conditions in three different age groups at CH24 (SMG) for the training session (A) and at CH22 (IFG) for the test session (B). * $p < 0.05$, ** $p < 0.01$.

on the left side (CH22 and 23 marked in Fig. 5). To compare the response among age groups, CH22 (which chiefly encompasses IFG) was chosen as the ROI as it had the strongest response. As shown in Fig. 6B, the two older groups showed a stronger response to target stimuli than control stimuli. Consistently, ANOVA detected a significant main effect for group [$F(2,53) = 3.62$, $p = 0.033$] and condition [$F(1,53) = 18.19$, $p = 0.0001$]. A group × condition interaction was also significant [$F(2,53) = 3.53$, $p = 0.036$]. This was due to a significant difference between target and control conditions for 7–8- [$F(1,53) = 6.20$, $p = 0.015$] and 9–10- [$F(1,53) = 18.72$, $p = 0.0001$] month-old groups.

7. Experiment 2: Discussion

Using fNIRS, we have identified a localized brain area engaged in whole word segmentation in infants. We examined two processes, a word training session where infants learned/encoded the target word, and a test session where they recognized/retrieved the memorized word. These two sessions were distinct in neural processes of the perisylvian area: the training (familiarization) task activated a more posterior part involving STG and SMG, whereas the test session more engaged the prefrontal brain. However, this pattern of localization was not clearly observed in the youngest age group of 5–6-month-old infants. In the training session, 5–6-month-old infants appeared to process repetitively presented words using the left IFG and temporo-parietal area. Nevertheless, this activation diminished when compared with the control condition, suggesting there is no specific neurocognitive difference between learning a word and listening to various different words that cannot be learnt. In the test session, the two older age groups exhibited strong left-lateralized frontal activation, even for target vs control analysis. We assume this frontal activation is a neurophysiological basis for word segmentation in infants. We will discuss previous evidence that supports this interpretation in Section 8, although at this point, it should be highlighted that 5–6-month-old infants lack this frontal activation, potentially explaining their inability to correctly segment words.

To date, an infants' cerebral basis for word segmentation has been exclusively investigated by ERP (Goyet et al., 2010; Kooijman, Hagoort, & Cutler, 2009; Kooijman et al., 2005). Although we should be cautious in comparing results due to the methodological differences, our results appear to be generally consistent with these studies, with respect to the activated brain regions. Although the previously observed response distributions involve relatively larger areas due to the limited spatial resolution of ERP, the evoked responses appear to originate from roughly similar brain areas as our study. Specifically, while evoked responses to training were distributed in the frontal, front-central, and front-temporal areas in the ERP studies (Kooijman et al., 2005, 2009), Hb responses for the training block were elucidated from IFG and temporo-parietal areas in our study. A minor difference is that fNIRS detected slightly more left-lateralized activation with stronger foci on the parietal area (which is presumed to be SMG). In the test session, a left-lateralized response from frontal-temporal electrodes was obtained by ERP (Kooijman et al., 2005, 2009). Although our test vs control results show that the rather limited brain area engaged in retrieving words is the IFG area, our results are not dissimilar to those obtained by ERP.

8. General discussion

Using behavioral and neuroimaging experiments, our present study identified the cerebral basis for word segmentation abilities and its developmental change in infants. fNIRS measurement of perisylvian areas found differential activation between training and test sessions, in which infants performed word segmentation of learnt words. While the neuronal substrate for learning words was primarily based on the temporo-parietal area, word segmentation localized to the inferior frontal/precentral areas. In this section, we will first discuss the developmental timing at which infants start to segment whole words by examining the behavioral and fNIRS results from both experiments. Next, we will examine the brain network that underlies the process of word segmentation, including word learning and word retrieval. By examining the role of the activation areas observed in this study, we will then provide our interpretation, specifically, that functional cerebral organization for word segmentation may partly recruit a cerebral network of phonological short-term memory (STM).

We found dissociation between our behavioral and fNIRS results. Our behavioral test showed that 9–10-month-old infants were capable of word segmentation, while our fNIRS evidence suggested an earlier age (7–8-month-old infants), as discussed in Experiment 2. How can we interpret this difference? We can assume that a neurophysiological measure more sensitively tracks an infants' word segmentation ability than a behavioral measure, which may be influenced by various noise factors. This improved sensitivity of neurophysiological measures has repeatedly been reported for both ERP and fNIRS in infant studies (e.g., Gervain, Macagno, Cogoi, Pena, and Mehler (2008)) showing a specific response to certain types of grammar in neonates). Although in some cases, behavioral measures have been shown to be superior (e.g., Mazuka, Cao, Dupoux, and Christophe (2011) and Minagawa-Kawai et al. (2013) for the phonotactic rule). Previous ERP studies on word segmentation strongly support interpretation of the former view. Both Dutch- and French-learning infants show earlier sensitivity to ERP response than a behavioral measure (Goyet et al., 2010; Kooijman et al., 2005, 2009). Similar distribution of evoked responses in these studies and our own further strengthens our interpretation.

Our fNIRS experiment consisted of training and test sessions, and here we will focus on the neurocognitive process of the training session, namely word learning. In the training session, infants repeatedly listened to target words, which were learned as the target condition. Conversely, to prevent learning in the control condition, they listened to various types of words without any repetition. In order to avoid habituation and facilitate general learning, we used multiple tokens pronounced by different speakers with various recording tokens for target word presentation. In response to target word learning, infants showed hemodynamic activation encompassing STG, SMG, IFG, and the sensory-motor area of the left hemisphere, regardless of age. This may reflect a dorsal language pathway in processing receptive speech (Hickok & Poeppel, 2007; Rauschecker & Scott, 2009). However, apart from activation in the temporo-parietal region, this pattern of activation disappears when contrasted with the control condition in 7–8- and 9–10-month-old infants. This shows that the control condition similarly activates IFG and parietal regions, while the temporo-parietal region is specific to the target condition, suggesting a role for learning words. SMG and STG correspond to part of the posterior language area, and particularly play a significant role in encoding and storing phonological STM processes. Early neuroimaging studies (Celsis et al., 1999; Paulesu, Frith, & Frackowiak, 1993) show that SMG engages in constructing, as well as storing, phonological representations. Although the neuronal basis of phonological storage has traditionally been postulated in parietal areas, later interpretations favor temporo-parietal regions, including STG (Buchsbaum & D'Esposito, 2008). Examining the relationship between speech processing and phonological STM by literature review, Jacquemot and Scott (2006) proposed that the cortical candidate of a speech input buffer is SMG, the posterior part of the superior temporal sulcus (pSTS), and planum temporale (PT). Although fNIRS cannot detect deep brain responses, activation in CH16 (mostly from STG) and CH20 (mostly from posterior STG) may likely include responses from pSTS and PT. Thus, these results indicate that infants older than 7 months, who exhibit specific SMG and STG activation to learning words, may have shaped phonological or phonetic representation and stored it through stimulus exposure. In contrast, the youngest group seemed not to have firmly established this cerebral network for phonological encoding, as suggested by the lack of significant activation in these areas. While this pattern of brain activation was observed exclusively in the left hemisphere, 7–8-month-old infants showed strong responses to the target word in the right posterior STG. This suggests that the cerebral circuits for phonetic encoding in 7–8-month-olds and 9–10-month-olds are not completely identical. The different activation foci in the left STG between these groups also support this view. Differential cerebral network may be employed until the network for phonological encoding is firmly established.

The test session also evoked similar cerebral activities in 7–8- and 9–10-month-old infants. These two age groups showed significant responses in IFG, SMG/postcentral, and STG to the target word condition. Even after subtraction of the control condition, IFG and SMG/postcentral activation remained significant. These activations can also be explained by the phonological STM network. Namely, IFG activity as observed in CH 22, engages in phonological output storage (Chein & Fiez, 2001). The cerebral response of CH23, which correspond to SMG/postcentral, is assumingly related to phonological input buffer, as explained for the training session, although the region in this case is anterior SMG. Our results are in agreement with an adult fMRI study of syllable segmentation using transitional probabilities (McNealy, Mazziotta, & Dapretto, 2006). Listening to words implicitly learnt through artificial language exposure, implicated posterior superior left IFG, SMG, and STG. Similarly, 10-year-old children also show comparable brain activation during the same word segmentation task (McNealy, Mazziotta, & Dapretto, 2010). Unlike their study, our segmentation task did not involve grammatical processing (i.e., transitional probability), therefore IFG may have played a particular role here in phonological storage output.

Although fMRI studies have revealed in detail the IFG region uniquely engaged in grammatical processing (e.g., pars opercularis), semantic processing, and STM (Demb et al., 1995; Makuuchi, Bahlmann, Anwander, & Friederici, 2009), our present fNIRS study, with a spatial resolution of only 20–30 mm, cannot pinpoint the exact area within IFG. Nevertheless, CH15 partly includes ventral IFG, and did not show strong activation. Consequently, the significant response in CH22 to trained words appears to originate chiefly from dorsal IFG. This is indeed consistent with previous fMRI studies, which found that dorsal IFG (including the inferior frontal sulcus) was engaged in working memory processing (Hautzel et al., 2002; Makuuchi et al., 2009).

While word segmentation discussed here is not rule-based segmentation (cf. Saffran, Aslin, & Newport, 1996) but whole word segmentation, this type of segmentation may require building up a robust acoustical or phonological representation of word-form during learning. Such learning processes are mediated by the dorsal pathway, as observed in both older groups for the training session. We assume that once such a robust memory trace of phonological representation is constructed, infants can easily detect it from the continuous speech stream. This is because each age group shows consistently significant (or non-significant) activation across training and test conditions. Namely, if infants show temporo-parietal activation during learning, they always show IFG activation during the test condition, indicating successful retrieval. Furthermore, behavioral studies indicate that acoustic salient words are easier to detect (Jusczyk, Hohne, et al., 1999; Jusczyk, Houston, et al., 1999). This also means that acoustic salient words, such as those with a Strong-Weak accent, can easily be learnt as a robust phonological representation, and thereby facilitate word segmentation. Thus, we assume that a stable and precise processing ability of phonological working memory largely contributes to successful word segmentation. It should be noted that this unit of segmentation may not necessarily be a whole word. Behavioral studies reported that young French infants used the rhythmic unit (a syllable) to segment the speech stream (Nazzi et al., 2006). Under certain conditions, young French infants have been reported to find a word border only by using an initial syllabic cue (Nishibayashi et al., 2015). Similarly, the Japanese infants in the present study may have created a memory trace of the initial bimoraic unit assigned by the HL pitch, rather than the whole word. Although our experiment was not designed to examine this issue, our findings and the previous behavioral studies mentioned above suggest that a small part of a word that is an acoustically salient unit (e.g. trochaic unit and/or a rhythmic unit), may serve as a significant cue for segmentation. Development of the dorsal stream of the language network (Rauschecker & Scott, 2009) which involves the phonological STM appears to play a crucial role in this process.

It is possible that "phonological STM" is not a suitable term for infants less than 1–year-old, because they have not completely acquired the phonological system for their language at this age. This means that their development of phonemic perception is still underway and acoustic memory traces may not accurately fit with the phonological system in their language. Because their perception may thus be more "phonetic" rather than "phonological", "phonetic STM" may be a more accurate term. However, infants acquire a native vowel system by 6 months-old and their perception subsequently becomes largely language-specific. Infants older than 8 months-old are typically able to produce canonical babbling. Furthermore, the capacity of actual articulatory gestures is not a prerequisite for the articulatory rehearsal in phonological STM (Vallar & Cappa, 1987; Waters, Rochon, & Caplan, 1992). Thus, the phonological system of 7–10-month-old infants may be matured enough to implement phonological STM, probably at a primitive level. Consequently, we have used the term "phonological STM" in this paper for a consistency with the literature on memory in adults. In addition, we used this terminology because we hypothesize that the phonetic STM system in these infants will eventually develop into a mature phonological STM system. On the one hand, we speculate that the phonetic memory system in young infants particularly before 6-month-old, does not necessarily accompany either articulatory rehearsal or phonological STM, as assumed from neonate neuroimaging studies (Benavides-Varela et al., 2011, 2012). It may be that encoding and retrieving speech is more facilitated when infants acquire the memory system with phonological STM.

Our results for two different conditions suggests that phonological STM processes (including input and output) are involved in word segmentation processing in infants. Indeed, STM is one of the crucial cognitive factors that enables humans to implement the language faculty, and this ability appears to develop, probably at an early stage, in the course of language acquisition. In particular, our study shows that such a STM system starts to function efficiently at the age of 7–8 months. Obviously, phonological STM used by infants in the present task does not comprise real word meaning, and thus the processing is likely to be within a prelexical level. However, the ability to segment phonetic representation is itself significant for lexical learning, which infants will eventually be facing. Although we identified a cerebral substrate of a "phonological template (scaffold)" to memorize word-form representation, at some point this network will connect to the lexical network in the temporal area as real word learning proceeds. An ERP study on lexical processing reported clear lateralization to the left hemisphere for N400 emerging around 20 months old (Mills, Coffey-Corina, & Neville, 1997). It is plausible that this is the stage when the phonological STM network implemented in the dorsal pathway has made a firm connection with the ventral pathway in the temporal area where lexical items are stored. In this sense, this STM system plays a fundamental basis in vocabulary growth.

9. Conclusion

The present behavioral and neurocognitive studies show that: (1) Japanese infants are able to segment words at 7–8 months of age, as judged from hemodynamic measures, which is 2 months earlier than observed by behavioral measures; and (2) segmentation largely involves the cerebral basis of phonological STM in the dorsal language stream. The temporo-parietal language area, including SMG and pSTG, are associated with word-form learning, whereas IFG and SMG are related to segmentation or decoding of learned words. These two processes clearly correspond to the neurocognitive bases for the input and output systems of phonological STM. Thus, the neurocognitive system of phonological STM, which begins to function around 7 months of age, plays a fundamental role in language faculty development.

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Which epenthetic vowel? Phonetic categories versus acoustic detail in perceptual vowel epenthesis

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Abstract: This study aims to quantify the relative contributions of phonetic categories and acoustic detail on phonotactically induced perceptual vowel epenthesis in Japanese listeners. A vowel identification task tested whether a vowel was perceived within illegal consonant clusters and, if so, which vowel was heard. Cross-spliced stimuli were used in which vowel coarticulation present in the cluster did not match the quality of the flanking vowel. Two clusters were used, /hp/ and /kp/, the former containing larger amounts of resonances of the preceding vowel. While both flanking vowel and coarticulation influenced vowel quality, the influence of coarticulation was larger, especially for /hp/.

[QJF]
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1. Introduction

Our auditory perceptual system is tuned to the sound system of our native language, resulting in impoverished perception of nonnative sounds and sound sequences (Sebastián-Gallés, 2005). For instance, in Japanese, a vowel can only be followed by a moraic nasal consonant or by a geminate consonant. As a consequence, Japanese listeners tend to perceive an illusory, epenthetic, /u/ within illegal consonant clusters (Dupoux *et al.*, 1999; Dehaene-Lambertz *et al.*, 2000; Dupoux *et al.*, 2001; Monahan *et al.*, 2009; Dupoux *et al.*, 2011; Guevara-Rukoz *et al.*, 2017) and it is evident in loanword adaptation as well (e.g., the word "sphynx" is borrowed in Japanese as /sufiNkusu/). Similar effects have been documented in other languages, with different epenthetic vowels [/ɨ/ in Korean (Kabak and Idsardi, 2007; Berent *et al.*, 2008; de Jong and Park, 2012); schwa in English (Berent *et al.*, 2007; Davidson and Shaw, 2012); /i/ in Brazilian Portuguese (Dupoux *et al.*, 2011; Guevara-Rukoz *et al.*, 2017); and /e/ in Spanish (Hallé *et al.*, 2014)]. Even within languages, there sometimes is variation in the quality of the epenthetic vowel; for instance, in Japanese, the epenthetic vowel can in certain contexts be /i/ or /o/ (Mattingley *et al.*, 2015; Guevara-Rukoz *et al.*, 2017).

The factors that determine the quality of the epenthetic vowel are still unclear. There is evidence that local acoustic cues in the form of vowel coarticulation play a

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role. Specifically, using artificial consonant clusters obtained by completely removing an inter-consonantal vowel, Dupoux *et al.* (2011) found that the quality of the removed vowel—traces of which are present in the neighboring consonants—influences the quality of the epenthetic vowel. Other studies, however, have argued for an influence of phonological factors, such as the legality of the resulting repair at the phonotactic level (Mattingley *et al.*, 2015) or the presence of phonological alternations in the language (Durvasula and Kahng, 2015). Determining the source of epenthetic vowel quality is important at a theoretical level, because it can shed light on the computational mechanisms underlying the perception of speech sounds. For instance, Dupoux *et al.* (2011) argued that coarticulation effects cannot be accounted for by two-step models, in which the repair of illegal sequences follows that of phoneme categorization, while they are in accordance with one-step models, in which phoneme categorization takes phonotactic probabilities into account.[1] However, Dupoux *et al.* (2011) only assessed the presence of acoustic effects, without investigating a possible role of categorical effects. Here, our aim is to quantify the relative contributions of categorical and acoustic effects on epenthetic vowel quality by directly comparing these two types of effect.

We focus on perceptual vowel epenthesis following /h/. This case is ideally suited for our objective as in Japanese loanwords these fricatives are typically adapted by adding a "copy" of the preceding vowel when they occur in a syllable coda. For instance, "Bach," "(van) Gogh," and "Ich-Roman" are adapted as /bahːa/, /gohːo/, and /ihːiroman/. In work on loanword adaptations, cases of vowel copy in epenthesis have been explained as a result of the spreading of phonological features from the preceding vowel onto the epenthetic vowel (i.e., vowel harmony), for instance, in Shona, Sranan, and Samoan (Uffmann, 2006), and Sesotho (Rose and Demuth, 2006). In speech perception, however, this pattern could be based either on phonetic categories, i.e., the preceding vowel itself, or on acoustic detail, i.e., traces of this vowel that are present in /h/, as laryngeal fricatives such as /h/ contain acoustic information relative to formants of surrounding vowels (Keating, 1988). Using an identification task, we tease apart these two explanations by independently manipulating the categorical context in which /h/ occurs and the acoustic realization of this segment, using cross-splicing. As a control, we also use stimuli with /k/, which are expected to give rise to more default /u/-epenthesis because they contain less coarticulation.

2. Methods

2.1 Participants

Twenty-five native Japanese speakers were tested in Tokyo, Japan (mean age 24 ± 3.5; 13 female). All were students at Keio University, and none had lived abroad.

2.2 Stimuli

We constructed a set of 20 base items, 10 disyllabic ones of the form $V_1C_1C_2V_1$ and 10 matched trisyllabic ones of the form $V_1C_1V_1C_2V_1$, with V_1 a vowel in the set /a, e, i, o, u/ (henceforth, flanking vowel), C_1 /h/ or /k/, and C_2 a fixed consonant, /p/, e.g., /ahpa/, /ekpe/, /ohopo/, /ikipi/. Three trained phoneticians, native speakers of Dutch, American English, and Argentinian Spanish, respectively, recorded all items with stress on the first syllable. All /kp/ stimuli presented release bursts. For each disyllabic item, we used one token per speaker as a natural control stimulus. By systematically replacing the /C_1C_2/-cluster in these items by the same cluster out of the other disyllabic items produced by the same speaker but with a different vowel, we created spliced test stimuli such as /ah_opa/ and /ek_ipe/, where the small vowel denotes vowel coarticulation present in the consonant cluster. Similarly, by replacing the /C_1C_2/-cluster in the disyllabic items by the same cluster out of the second token of the same items, we created spliced control stimuli in which the vowel coarticulation matched the flanking vowel, e.g., /ah_apa/, /ek_epe/. We also created trisyllabic fillers in which the middle vowel either matched or mismatched the flanking vowel, e.g., /ahapa/, /ekepe/, /ahopa/, /ekipe/ (these were also created by splicing, as they served as test stimuli in an experiment not reported in this article). Overall, each speaker thus contributed 40 test stimuli (5 flanking vowels $\times$ 4 vowel coarticulations $\times$ 2 consonant clusters), 20 control stimuli (5 flanking vowels $\times$ 2 consonant clusters, all both in a natural and a spliced form), and 50 fillers. Ten additional training items were recorded by a fourth speaker. Their structure was similar, but included only phonotactically legal nasal + stop sequences with or without an intervening copy vowel (e.g., /ampa/, /enepe/).

2.3 Procedure

Participants were tested individually in a soundproof room. At each trial, they heard a stimulus over headphones and were asked to identify the vowel between the two consonants, if any. They were provided with a transcription of the item on screen, containing a question mark between the two consonants (e.g., "*ah?pa*") in Latin characters (as non-CV syllables cannot be transcribed using Japanese characters), as well as the list of possible responses: "*none, a, i, u, e, o*." Participants responded by pressing labelled keys on a keyboard. Participants were familiarised with the procedure with 10 training trials in which they received on-screen feedback.

The 330 stimuli were presented in a pseudo-randomised order: Consecutive stimuli were produced by different speakers, and a stimulus could not be followed by a stimulus with the same combination of vowel coarticulation and consonant. Trials were presented in two blocks, with each stimulus appearing once per block, for a total of 660 trials. The experiment lasted approximately 40 min.

3. Results

Test and control trials with responses that were either too fast (before the medial portion of the stimulus could be perceived and processed, <400 ms) or too slow (>3 SD: 3238 ms) were excluded from the analyses. This concerned 736 trials (4.5%).

3.1 Control items

Participants experienced perceptual epenthesis in 57% of control items in which the flanking vowel and coarticulation are of the same quality (/hp/: 52%, /kp/: 61%). Recall that in loanwords, the default epenthetic vowel is /u/, while after voiceless laryngeal fricatives it is a copy of the preceding vowel. Focusing on trials with an epenthetic response, we examined whether the choice of epenthetic vowel reflected this pattern.

First, a generalised mixed-effects model with a declared binomial distribution (Bates *et al.*, 2015) was used to examine a possible effect of consonant cluster on default /u/-epenthesis. Thus, we analyzed the proportion of default /u/, using participant, speaker, experimental block, and trial as random effects, and consonant cluster (/kp/ vs /hp/; contrast coded) as fixed effect. This model was compared to a reduced model with no fixed effect. The full model was found to explain significantly more variance than the reduced model [$\beta = -4.2$, $SE = 1.2$, $\chi^2(1) = 9.9$, $p < 0.01$], showing that participants experienced significantly less default /u/-epenthesis in /hp/- than /kp/-items (39% vs 86% of all trials with epenthesis, respectively).

Next, we examined whether epenthesized vowels shared the quality of the flanking vowel more often in /hp/- than in /kp/-clusters. Given that for items with flanking vowel /u/ it is impossible to know if /u/-epenthesis is due to vowel copy or to default epenthesis, these items were excluded. As before, a generalised mixed-effects model with a declared binomial distribution was used. We analyzed the proportion of vowel copy (i.e., whether the flanking vowel and epenthetic vowel shared quality), using participant, speaker, experimental block, and trial as random effects, and consonant cluster (/kp/ vs /hp/; contrast coded) as fixed effect. Comparing this full model to a reduced model with no fixed effects revealed a significant effect of consonant cluster [$\beta = 3.7$, $SE = 1.2$, $\chi^2(1) = 7.4$, $p < 0.01$]. Therefore, participants epenthesized a vowel that matched the flanking vowel more often in /hp/-clusters (53%) than in /kp/-clusters (13%).

Thus, analysis of control items revealed that, similarly to the loanword pattern, participants perceived the vowel /u/ more often in /kp/- than in /hp/-clusters, and they perceived a vowel copy more often in /hp/- than in /kp/-clusters.

3.2 Test items

Figure 1 shows trial counts, separated according to response category, consonant cluster, flanking vowel, and vowel coarticulation for test and control trials. Within the individual rectangles, vertical lines are indicative of a larger influence of flanking vowels compared to vowel coarticulation. Horizontal lines, by contrast, are indicative of a larger influence of vowel coarticulation. Finally, uniform colouring indicates that neither flanking vowels nor vowel coarticulation have the upper hand in influencing the quality of the epenthetic vowel. Note that except for the rectangles with "none" and "u" responses where colouring is more uniform, horizontal lines are more visually prominent than vertical lines. Thus, the epenthetic vowel's quality generally depends mostly on acoustic details present in the consonant cluster.

Focusing on the test trials eliciting epenthesis (/hp/: 62%, /kp/: 66%), we quantify the respective influence of flanking vowel and vowel coarticulation (explanatory

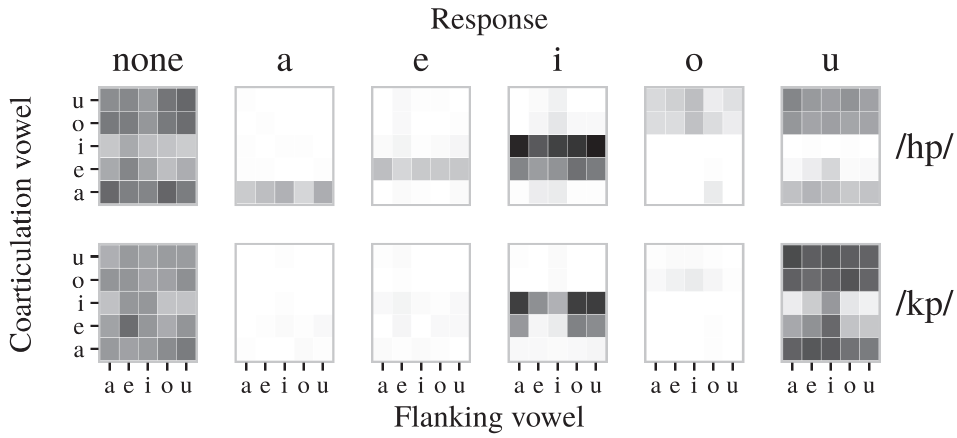

Fig. 1. Counts of responses for the test and spliced control items. Top: /hp/-items; bottom: /kp/-items. Within each rectangle, flanking vowels and vowel coarticulation are given in the horizontal and vertical axes, respectively. Darker colours indicate higher counts. A figure showing counts separated by speaker can be found in Guevara-Rukoz (2017).

variables, EV) on the epenthetic vowel (response variable, RV), using two measures from information theory, mutual information (MI) and information gain (IG) (see Daland *et al.*, 2015, for a comprehensive description of these measures). MI and IG are derived from entropy, which is the "uncertainty" in the value of a RV at a given trial. The lower the entropy $H[X]$ of a variable X, the easier it is to predict the outcome of a trial. The MI $I[X; Y]$ of variables X and Y represents the reduction in uncertainty of the trial outcome for RV X, given that the value of EV Y is known (and vice versa). This corresponds to the maximum amount of influence that Y can have over X, without removing contributions from other variables. IG $H[X|Z] - H[X|Y,Z]$ represents the minimum amount of influence of variable Y on X. This corresponds to the reduction in uncertainty as to the value of X that arises from knowing the value of Y, after removing all uncertainty explained by variable Z.

As in Daland *et al.* (2015), we compute accidental information introduced to MI and IG, which corresponds to inaccuracies introduced to our measurements by the process of inferring underlying probability distributions from samples, i.e., sampling error (as when one does not obtain 50 tails and 50 heads when flipping a fair coin 100 times). We can estimate the accidental information by recomputing MI and IG after having removed the dependencies between the EV and the RV. We can do so by shuffling the values of the EV within each participant. For instance, in order to compute the accidental information introduced to MI and IG for the EV "vowel coarticulation," we randomly shuffle the vowel coarticulation labels of all of our trials, per participant, while leaving the EV "flanking vowel" untouched. We then compute MI and IG as for the real data. In order to obtain a better estimate of accidental information from an average value, we do this 1000 times (i.e., Monte Carlo shuffling process).

To recapitulate, for both coarticulation vowel and flanking vowel, we compute "sample" and "accidental" MI and IG. The "true" values of these measures are obtained by removing mean accidental information from sample information. Following Daland *et al.* (2015), we consider the set of shuffled datasets (i.e., accidental MI and IG) as probability distributions given by the null hypotheses that neither coarticulation nor the flanking vowel influence the responses.

As shown in Table 1, all sample lower bounds are greater than their respective accidental information gains on all 1000 shufflings, for which the ranges are given in brackets. Therefore, the true lower bounds for both coarticulation and flanking vowel influence on epenthesis are greater than 0 with $p < 0.001$, showing that both coarticulation and flanking vowel quality influence participant responses. However, the amount of influence differs greatly: a larger information gain is yielded by considering vowel coarticulation than by considering the flanking vowel. This is true both for /hp/-items, which are heavily coarticulated, and for /kp/-items, where coarticulation is mainly only present in the burst, even though the influence of coarticulation on epenthetic vowel quality is higher for the former (/hp/: [0.86, 0.92] vs /kp/: [0.44, 0.52]). (The range of variation within shuffles of accidental information was about 0.03; thus any difference of 0.06 or bigger is significant, including differences between MI and IG values, respectively.) In summary, both vowel coarticulation and the flanking vowel influence

Table 1. Quantified influence of vowel coarticulation and flanking vowel on vowel epenthesis measured with information gain (IG) and mutual information (MI). Ranges for Monte Carlo simulations of the null hypothesis (i.e., accidental information) are given in square brackets. Values are given in bits.

	Vowel coarticulation				Flanking vowel			
	IG		MI		IG		MI	
	data	null	data	null	data	null	data	null
/hp/	0.90	0.04 [0.02, 0.05]	0.93	0.01 [0, 0.02]	0.07	0.03 [0.02, 0.05]	0.09	0.01 [0, 0.02]
/kp/	0.47	0.03 [0.02, 0.05]	0.53	0.01 [0, 0.02]	0.07	0.03 [0.02, 0.04]	0.13	0.01 [0, 0.02]

epenthetic vowel quality, but this influence is greater for vowel coarticulation; response patterns are more predictable when the value of this variable is known than when the value of the flanking vowel variable is known.

4. Discussion and conclusion

We used an identification task to assess the quality of epenthetic vowels perceived by Japanese listeners in illegal consonant clusters with varying amounts of coarticulation. Our findings can be summarized as follows: First, we were able to replicate the perception of illusory vowels within phonotactically illegal clusters by Japanese listeners (64% of all test trials).[2,3] Second, when the flanking vowel and coarticulation match, the quality of the perceived vowel patterned in the same way as in loanword adaptation data. That is, for /kp/-clusters, the predominant epenthetic vowel was the standard default vowel for Japanese (/u/), while for /hp/-clusters, it was a copy of the flanking vowel. Finally, and most importantly, in items where the coarticulation and flanking vowel differed, the quality of the epenthetic vowel was significantly influenced by both variables, but the influence of the former was much larger than that of the latter, especially in the case of /hp/. Our discussion focuses on this last finding.

Before discussing its theoretical relevance, let us comment on the numerically small—yet significant—influence of flanking vowel on epenthesis for /hp/-clusters, where vowel coarticulation is maximal. This result suggests a contribution of categorical variables on epenthetic vowel quality (i.e., copy effect). A similar effect, though, was also found for /kp/-clusters, for which loanword adaptation patterns provide no particular reason to propose the existence of a categorical copy phenomenon; indeed, in loanwords, coda-/k/ generally triggers default /u/-epenthesis. Therefore, it is possible that this effect results from a response bias due to task demands: given a perceptually uncertain stimulus, the flanking vowel could prime a copy response, for instance, because it was visually available on-screen at each trial (e.g., "ah?pa"). Further work using different tasks is necessary to examine the perceptual reality of this "vowel copy" effect.

Keeping in mind that this work focuses on the choice of epenthetic vowel, while not directly addressing questions related to why phonologically illegal clusters are repaired, or what the role of phonotactics in epenthesis is, the finding that the quality of the epenthetic vowel is influenced more by coarticulation than by the flanking vowel calls for a perceptual repair mechanism in which acoustic details are taken into consideration. Two-step models in which epenthetic repair is performed after the consonant cluster in the acoustic input has been represented in terms of discrete phonetic categories are therefore ruled out. Rather, like Dupoux *et al.* (2011), we argue in favor of one-step models, in which epenthetic vowel quality is based on the similarity between local acoustic cues and prototypical properties of each vowel in the language, such that the closest matching vowel gets selected for insertion. This mechanism can account both for the coarticulation-induced vowel copy effect in items with a /hp/-cluster, as the voiceless glottal fricative /h/ contains strong coarticulation from the adjacent vowels (Keating, 1988; see Guevara-Rukoz, 2017, for acoustic analyses of our stimuli), and for the default /u/-epenthesis effect in items with a /kp/-cluster—which exhibit a lower degree of coarticulation—as /u/ is the phonetically shortest vowel in the language (Han, 1962) and is prone to be devoiced in certain contexts (see footnote 2).

Focusing on cases where the quality of the epenthetic vowel varies *within language* as a function of the type of cluster, previous studies have investigated whether language-specific phonotactic or phonological properties play a role for the quality of the epenthetic vowel. In Japanese, for instance, dental stops cannot be followed by /u/, and in loanwords this phonotactic constraint gives rise to adaptation by means of

/o/-epenthesis (e.g., *batman* → *batoman*). Using identification tasks, both Mattingley *et al.* (2015) and Guevara-Rukoz *et al.* (2017) report that the perceptual equivalent of this effect is only marginally present in Japanese listeners (10%–12% of /o/-epenthesis in /d/-initial clusters; see also Monahan *et al.*, 2009, for the absence of such an effect in a discrimination task). Thus, so far there is only weak evidence that the mechanism of phonotactic repair takes into account the legality of the resulting CVC-sequence. A stronger effect of cluster-dependent perceptual epenthesis has been reported in Korean listeners, who repair /eʃma/ and—to a lesser extent—/ec^{h}ma/ with an epenthetic /i/ instead of the default epenthetic vowel /ɨ/ (Durvasula and Kahng, 2015). This is argued to be due to the existence of an allophonic rule that palatalizes /s/ and /t^{h}/ before /i/, yielding [ʃi] and [c^{h}i], respectively. It is also possible, however, that this effect is (partly) due to coarticulation; for instance, acoustic cues in /ʃ/ and /c^{h}/ might be more suggestive of /i/ than of /ɨ/.

To conclude, we directly compared the relative contributions of acoustic and categorical effects on epenthetic vowel quality, and found that the former override the latter. This result thus strengthens those of Dupoux *et al.* (2011), who also established the presence of acoustic effects but without investigating possible categorical effects. More research is needed to investigate whether our findings generalize to other cases of perceptual epenthesis. This question can be addressed by two complementary approaches. One would be to run additional experiments with cross-spliced stimuli, as in the present study. Another one would be to measure the effective amount of coarticulation in experimental stimuli of previous studies, using a computational implementation of a one-step repair mechanism (see Dupoux *et al.*, 2011 and Wilson *et al.*, 2014 for propositions, and Schatz, 2016 for an implementation using Hidden Markov Models).

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References and links

[1]Due to a typo, the summary in the first-to-last paragraph of Dupoux *et al.* (2011) erroneously states the opposite.

[2]Note that whereas previous studies examined perceptual epenthesis within clusters with at least one voiced consonant, we presently focused on completely voiceless clusters, a context in which the high vowels /i/ and /u/ may be devoiced in Japanese (Han, 1962; Vance, 1987).

[3]As pointed out by an anonymous reviewer, the observed differences in rates of epenthesis by speaker (Dutch: 68%, American English: 58%, Argentinian Spanish: 66%) are consistent with an important role for acoustic factors in epenthesis, suggesting that participants interpret speakers' acoustic cues instead of responding based on abstract phonological categories (cf. Wilson *et al.*, 2014). This can also be seen in more detail when decomposing Fig. 1 by speaker, see Guevara-Rukoz (2017).

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Prefrontal Function Engaging in External-Focused Attention in 5- to 6-Month-Old Infants: A Suggestion for Default Mode Network

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The present study used functional near-infrared spectroscopy (fNIRS) to measure 5- to 6-month-old infants' hemodynamic response in the prefrontal cortex (PFC) to visual stimuli differing in saliency and social value. Nineteen Japanese 5- to 6-month-old infants watched video clips of Peek-a-Boo (social signal) performed by an anime character (AC) or a human, and hand movements without social signal performed by an AC. The PFC activity of infants was measured by 22-channel fNIRS, while behaviors including looking time were recorded simultaneously. NIRS data showed that infants' hemodynamic responses in the PFC generally decreased due to these stimuli, and the decrease was most prominent in the frontopolar (FP), covering medial PFC (MPFC), when infants were viewing Peek-a-Boo performed by an AC. Moreover, the decrease was more pronounced in the dorsolateral PFC (DLPFC) when infants were viewing Peek-a-Boo performed by an AC than by a human. Accordingly, behavioral data revealed significantly longer looking times when Peek-a-Boo was performed by an AC than by a human. No significant difference between Peek-a-Boo and non-Peek-a-Boo conditions was observed in either measure. These findings indicate that infants at this age may prefer stimuli with more salient features, which may be more effective in attracting their attentions. In conjunction with our previous findings on responses to self-name calling in infants of similar age, we hypothesize that the dynamic function of the MPFC and its vicinity (as part of default mode network (DMN): enhanced by self-focused stimuli, attenuated by externally focused stimuli), which is consistently observed in adults, may have already emerged in 5- to 6-month-old infants.

Keywords: fNIRS, attention, prefrontal cortex (PFC), infant, default mode network (DMN)

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INTRODUCTION

Humans are highly social creatures and develop communicative capacities via various interactions with others very early in life. Converging evidence from functional neuroimaging studies suggests that the medial prefrontal cortex (MPFC) plays a pivotal role in social cognition, especially self-related information processing, not only in adults, but also in young infants

(Kampe et al., 2003; Amodio and Frith, 2006; Northoff et al., 2006; Andrews-Hanna et al., 2010; Grossmann, 2013; Imafuku et al., 2014). Interestingly, neural activity of dorsal MPFC (DMPFC) and its peripheral areas has been shown to increase in tasks involving self-referential attention, and to decrease in tasks involving externally focused attention (Gusnard and Raichle, 2001). This phenomenon has been suggested to be related to the default mode network (DMN), which serves as a baseline between self-referential and externally focused states (Gusnard and Raichle, 2001; Raichle et al., 2001; Buckner et al., 2008). Such dynamic functional patterns have been consistently found in studies on adult subjects. However, at which point during development of brain function these dynamic patterns first occur remains to be elucidated.

To date, research on DMN has mainly focused on adults. Although some recent developmental studies have reported novel findings on DMN in infants and children, a comprehensive understanding of DMN development, especially during the first year of life when the brain undergoes the most dramatic development (Gao et al., 2015), has not yet been attained. Fransson et al. (2007) did not detect a DMN in preterm infants at a gestational age of 41 weeks. Xiao et al. (2016) found developmental changes of DMN subsystems between 3- and 5-year-olds. de Bie et al. (2012) reported that DMN is present but less mature in awake 5- to 8-year-olds compared with older children and adults. Fair et al. (2008) found an only sparsely connected DMN in 7- to 9-year-olds. Gao et al. (2009) focused their research on children of younger age filling the gap between the above-mentioned studies: in a resting-state fMRI study on children between 2 weeks and 2 years of age, evidence for a primitive and incomplete DMN structure in 2-week-old infants and for an adult-like DMN in 1- and 2-year-old children was found. Recently, Gao et al. (2015) further investigated neural networks of infants from <1 month to 1-year-old in 3-month steps, and found that the structure of DMN undergoes major changes during the first 3 months of life, continues development during the first year of life and becomes adult-like at 1-year of age.

Taken together, these findings approximately sketch out the developmental trajectory of DMN structure from early life. However, the early development of DMN function remains unclear, because most developmental studies examined resting-state (sleeping) children to effectively collect fMRI data. Based on findings of Gao et al. (2015) that the long distance synchronization of two typical hubs of the DMN, i.e., the MPFC and the posterior cingulate cortex (PCC), showed significant strengthening during the second half of the first year, we focused our infant functional studies on this critical age for structural development. To elucidate whether the aforementioned dynamic function of PFC has already emerged at this early age and to shed light on the functional development of primitive DMN, we designed two distinct sets of experiments. The first experiment, published in a previous report, focused on self-referential tasks and found increased hemodynamic responses in the DMPFC in 6-month-old infants in response to self-name calling (Imafuku et al., 2014).

In the present study, we focused on externally focused attention tasks in 5- to 6-month-old infants. Infant-directed social communication cues—Peek-a-Boo video clips performed either by a Japanese woman or an anime character (AC) "ANPANMAN", and video clips without Peek-a-Boo performed by an AC—were presented to healthy Japanese 5- to 6-month-old infants. Functional near-infrared spectroscopy (fNIRS) was used to measure the activity of PFC in infants while their behavior (looking time) was recorded simultaneously. If the functional activation in response to externally-directed (non-self-referential) stimuli of the PFC of 5- to 6-month-old infants resembled that of adults, we would expect an attenuated cerebral response in PFC elicited by stimuli with Peek-a-Boo. In addition, we predict that PFC activity may depend on other properties (saliency and social value) of the stimulus. Specifically, Peek-a-Boo performed by an AC might induce a more prominent hemodynamic response than Peek-a-Boo performed by a human, because of the saliently emphasized facial features of the AC (exaggerated facial parts, high brightness and strong contrast); and than non-meaningful hand-waving movements performed by an AC because of the social value of Peek-a-Boo.

MATERIALS AND METHODS

Participants

Nineteen 5- to 6-month-old Japanese infants (9 males and 10 females; mean age: 173.2 ± 14.3 (150∼196) days old) participated in this study. Another nine infants participated in the study, but were excluded from final analysis because of insufficient valid trials (at least three valid trials for each condition) attributable to extensive fussiness, motion artifacts or technical problems. All participants were full term infants at birth and had no history of serious diseases or disorders. All parents volunteered by responding to advertisements and were paid for participation of their child. Both parents of all infants' parents were Japanese. Informed consent was obtained from the parents before the study. The study protocol was approved by the Ethics Committee of Keio University, Faculty of Letters (No. 120223-1) and was in accordance with the latest version of the Declaration of Helsinki.

Stimuli

Full-color, life-size video clips of Peek-a-Boo performed by a human woman or an AC ("ANPANMAN") were used as social stimuli. The AC used in this study has exaggerated facial and body parts (eyebrows, eyes, cheeks, nose, mouth and hands), strong contrast, and high brightness (**Figure 1**). Other features of the AC and the human woman (size and movements of face and hands) were controlled to be comparable as much as possible. Vocal signals expressing Peek-a-Boo were recordings of a female voice actor speaking Japanese and were identical for AC and human Peek-a-Boo conditions. During the experiment, the vocal sound amplitude was adjusted to be around 70 dB SPL measured at the approximate location of each infant's head. Three types of video clips were used as experimental conditions: (A) Peek-a-Boo performed by an AC; (B) non-meaningful hand-waving

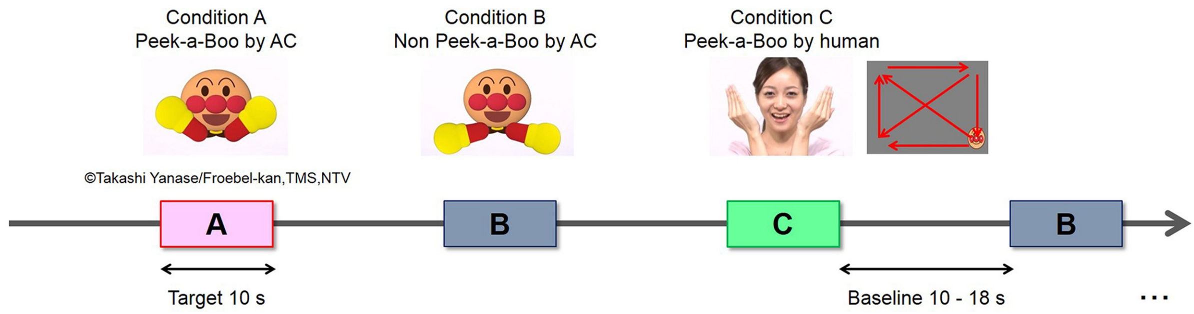

FIGURE 1 | Experimental design and stimuli.

movements performed by an AC; and (C) Peek-a-Boo performed by a human woman. A small-sized AC face moving slowly on a blank background served as the baseline. This stimulus contains no social signal and is able to maintain the infants' gazes at the screen.

Experimental Procedure

Prior to the experiment, all infants were screened for typical cognitive functioning using the Kyoto Scale of Psychological Development (KSPD; Ikuzawa et al., 2002). In addition, the infants' familiarity with the AC and Peek-a-Boo was examined. All questionnaires were completed by the infants' parents.

During the experiment, infants were seated on the lap of their mothers in a sound-attenuated chamber. Mothers wore headphones to prevent them from hearing the stimuli during the experiment. Video stimuli were presented at a viewing distance of approximately 40 cm on an 18.1″ LCD monitor controlled by a computer outside the sound-attenuated chamber. The loudspeaker was mounted on the monitor at about the height of the infant's head. Infants were encouraged to focus on the displayed stimuli, and experiments were terminated when infants became fussy or bored. A video camera was set behind the monitor to record the infants' behavior (e.g., body and eye movements) during the experiment. An experimenter outside the sound-attenuated chamber observed the infant's behavior during the experiment via another monitor connected to the video camera to monitor the progress of the experiment.

The experiment was block-designed. The sequence of stimulus presentation is shown in **Figure 1**. One experimental trial made up of a baseline period of 10∼18 s (randomly) and a target period of 10 s. Each of the three conditions was presented in seven target blocks. The total of 21 trials was pseudo-randomly arranged with the constraint that no two consecutive trials were of the same condition. Moreover, the presentation order of the 21 trials was counterbalanced across participants. The total time of the whole experiment was around 7∼9 min. Presentation of video stimuli was controlled using Visual Basic 6.0.

Data Acquisition

The infants' behavior was recorded on a DVD throughout the experiment for later assessment of movement artifacts and looking time at the stimulus. Hemodynamic responses in the PFC region were recorded using a multichannel NIRS system (ETG-7000, Hitachi Medical Co., Japan). The system emits continuous near-infrared lasers with fixed wavelengths of approximately 780 nm and 830 nm. Lasers are modulated at different frequencies depending on the wavelengths and the channels, and are detected using lock-in amplifiers (Watanabe et al., 1996). The device provides estimates of changes in hemoglobin (Hb) concentrations and their oxygenation levels of the optical paths in the underlying brain region between the nearest pairs of emitter and detector probes.

A silicon probe pad was used to arrange eight emitters and seven detector probes in a 3 × 5 rectangular lattice, forming 22 recording channels. Each pair of emitter and detector probes was separated by 20 mm, and the spatial resolution was estimated to be 15∼30 mm. It has been suggested that near-infrared light penetrates deeper into the cortex in infants than adults, because infant brains contain less myelinated and less reflective white matter (Fukui et al., 2003). Therefore, the 20 mm distance between each emitter and detector probes pair used in this study was able to capture cerebral activity in relatively deeper regions of infant PFC, around 20∼35 mm from the scalp-skin surface (Imafuku et al., 2014).

The 3 × 5 probe pad was placed on the infants' PFC region as shown in **Figure 2**. Specifically, the bottom border of the probes was placed in a direction horizontal to the line connecting T3, Fp1, Fp2 and T4 on the international 10-20 system, and the center of the channels was positioned across the nasion–inion line (Jasper, 1958). This probe arrangement enabled us to estimate the specific brain region of any localized cerebral activity based on the virtual registration method (Tsuzuki et al., 2007). After probe placement, the experimenter verified that each probe was in adequate contact with the scalp. Only after this verification NIRS recordings were initiated.

Behavioral Data Analysis

The recorded DVDs were used for the looking time analysis. Infants' gaze durations toward video clip stimuli during both baseline and target periods were estimated by two trained coders at 100 ms intervals using the behavior coding software GenobsX. Data from two infants was excluded from further

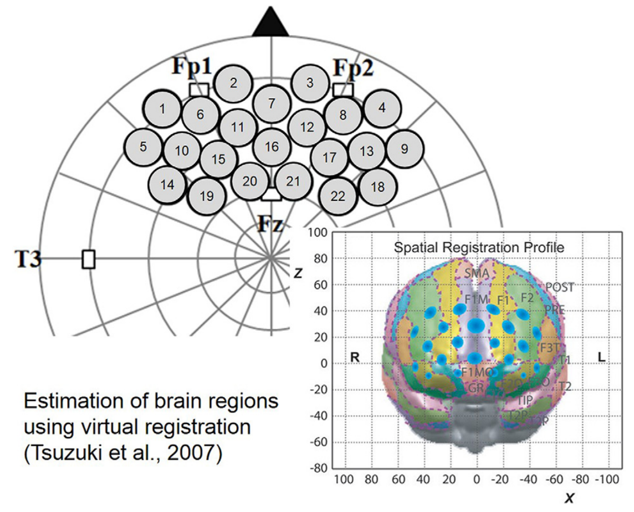

FIGURE 2 | Probe set and location on the brain.

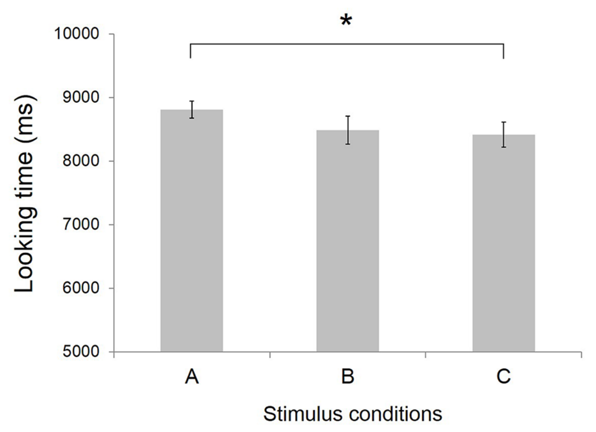

FIGURE 3 | Mean looking time at video clips stimuli (*N* = 17). Error bars indicate standard error of the mean. *$p < 0.05$. Conditions definition: **(A)** Peek-a-Boo by anime character (AC); **(B)** Non Peek-a-Boo by AC; and **(C)** Peek-a-Boo by human.

analysis because of technical problems. Valid behavioral data was obtained from 17 infants (**Figure 3**).

NIRS Data Analysis

NIRS data were analyzed using Platform for Optical Topography Analysis Tools (POTATo) developed by Research and Development Group, Hitachi, Ltd. in a Matlab 7.7 environment (The MathWorks, Inc., Natick, MA, USA). Changes in concentration of oxygenated (oxy-) Hb and deoxygenated (deoxy-) Hb were calculated from absorbance changes of 780 nm and 830 nm laser beams sampled at 10 Hz. For each participant, the raw oxy- and deoxy-Hb data in each channel were bandpass filtered (Butterworth) at 0.02–0.7 Hz separately for each trial to remove components of physiological nature (e.g., respiratory and cardiac activity) and body movements (Taga et al., 2003; Naoi et al., 2012). Trial rejection was based on two criteria. First, based on analysis of the behavioral data, any block containing failure of gazing, speaking or body movements exceeding 5 s in total was discarded. Second, any block containing oxy-Hb changes larger than 0.15 mM/mm within 200 ms was discarded. In addition, we also discarded the data of the nine lower channels (CH1–CH9) because the amplitudes of the changes in Hb concentrations were too large, synchronous and in the same direction, indicating loose attachment of probes in the lowest line. The loose attachment might have been caused by unfitted silicon probe pad against the lower part of the infant's forehead.

Further analysis focused on a 20 s epoch composed of 5 s pre-target baseline, 10 s target block and 5 s post-target. For each condition, Hb concentrations of all valid trials were averaged. Subsequently, a time course of the mean change in oxy-Hb and deoxy-Hb was compiled for each channel, condition and participant. These average time courses for each participant were then grand averaged to form time-dependent waveforms of the hemodynamic responses in each channel under each condition (**Figure 4**).

Peak Hb changes were observed approximately 5∼10 s after target stimulus onset across infants and channels. Therefore, we defined this period of interest as analysis window. For statistical analysis, mean oxy-Hb concentration changes during this time window were calculated and compared with mean oxy-Hb concentration changes during the 5 s pre-target baseline period for each channel, condition, and participant. To determine activated brain areas in each condition, differences in the changes of oxy-Hb concentrations between target and baseline periods were compared using a two-tailed paired *t*-test for each channel. False discovery rate (FDR) was used to correct for multiple comparisons across all channels. Brain regions underlying each channel were estimated using the virtual registration for NIRS channels (Okamoto et al., 2004; Okamoto and Dan, 2005; Tsuzuki et al., 2007). This method has been used consistently in the fNIRS literature (e.g., Minagawa-Kawai et al., 2009; Dan et al., 2013; Imafuku et al., 2014). A detailed account of the reliability of this method, especially for infants, can be found in our previous study (Imafuku et al., 2014). Further, to detect any difference in response between conditions, we applied a one-way analysis of variance (ANOVA) to the mean oxy-Hb concentration changes in the target period for each channel, with condition (Peek-a-Boo by AC vs. No Peek-a-Boo hand movements by AC vs. Peek-a-Boo by human) as within-subject factor. To control for between-condition discrepancies in global response magnitude, zero correction was performed on the response in the target period before ANOVA. Specifically, the response at the time of stimulus onset was adjusted to be zero for each condition. The tukey *post hoc* test was used to further clarify any significant main effects.

Last, correlations between the infants' behavioral responses and hemodynamic responses measured with NIRS were assessed. Pearson's correlation coefficients were calculated between the behavioral results (looking time, developmental score, familiarity with the AC and Peek-a-Boo) and the oxy-Hb concentration changes in significant channels.

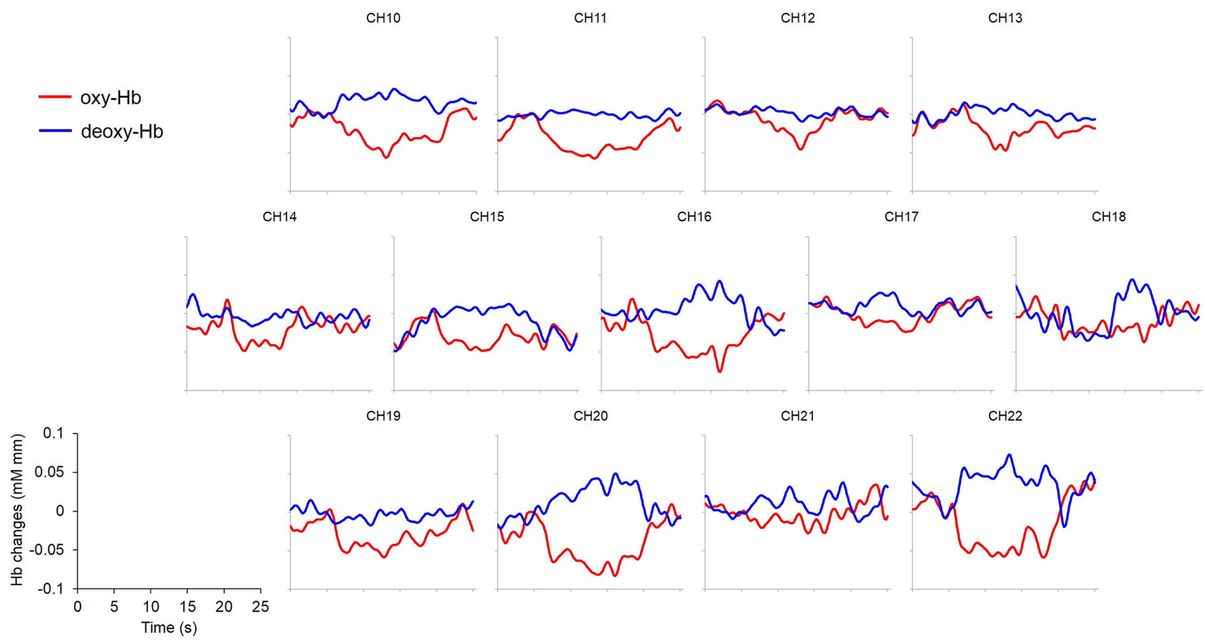

FIGURE 4 | Grand averaged (*N* = *19*) time courses of changes in oxy- and deoxy-Hb in response to condition (A) Peek-a-Boo by AC as an example. Channels 1~9 were not displayed because of excessive noises due to poor attachment to the infants' foreheads. Red lines: change of oxy-Hb; blue lines: change of deoxy-Hb. *x*- and *y*-axis scales and labels are shown in the lower left corner. Stimuli requiring externally focused attention elicited widespread decrease in oxy-Hb.

RESULTS

Behavioral Results

As shown in **Figure 3**, the mean looking time was 8.81 ± 0.13 s (mean ± SEM) for condition A Peek-a-Boo by AC, 8.49 ± 0.22 s for condition B No Peek-a-Boo hand movements by AC, and 8.42 ± 0.20 s for condition C Peek-a-Boo by human. A one-way ANOVA with stimulus condition as within subject factor showed a tendency for a main effect of stimulus condition ($F_{(2,16)} = 2.58$, $p = 0.092$). *Post hoc* tests revealed that infants' looking times at condition A was significantly ($t = 2.07$, $p < 0.05$) longer than at condition C, indicating the infants' preference for Peek-a-Boo performed by an AC over Peek-a-Boo performed by a human.

NIRS Results

An overall decrease in oxy-Hb concentration was observed in PFC areas regardless of condition. However, the decrease was of larger magnitude and was more widely spread in condition A Peek-a-Boo made by AC than in the other conditions (**Figure 4**).

Two-tailed paired *t*-tests were performed on the data as described in the "*NIRS Data Analysis*" Section. This analysis revealed different but overlapping channels showing a significant decrease in oxy-Hb concentration change in response to the different conditions. Specifically, oxy-Hb concentration change was significantly decreased in channels CH10, CH11, CH12, CH20 and CH22 for condition A; CH18 and CH22 for condition B; and CH12 for condition C (**Figure 5**). Using virtual registration for NIRS measurement, the corresponding brain regions for these channels were estimated to be frontopolar (FP), dorsal lateral PFC (DLPFC) and DMPFC for condition A; right DLPFC for condition B; and FP for condition C, respectively. After FDR correction for multiple comparisons, only oxy-Hb decrease in CH11 in condition A was significant (colored in purple in **Figure 5**). The corresponding estimated brain region of this channel was FP (FP 53%, DLPFC 47%). Please note that in infants, NIRS measurement captures hemodynamic responses from deeper regions in addition to the superficial part of cerebral cortex, owing to less myelinated and less reflective white matter (Fukui et al., 2003). Therefore, in case of the infants in our study, responses of deeper regions like the MPFC are likely to have formed part of the significant decrease of oxy-Hb response allocated to FP.

Furthermore, one-way ANOVA (with condition as within subject factor) performed on each channel revealed that CH15 ($F_{(2,54)} = 4.73$, $p = 0.01$) and CH22 ($F_{(2,54)} = 3.59$, $p = 0.04$) showed significant differences of oxy-Hb decrease between conditions (**Figure 6**). The estimated brain regions of these two channels were DLPFC for CH15 (DLPFC 65%, DMPFC 30%, FP 5%) and DLPFC for CH 22 (DLPFC 97%, DMPFC 3%). Tukey *post hoc* tests confirmed that both for CH15 ($p = 0.01$) and CH22 ($p = 0.03$), oxy-Hb decrease was significantly larger in condition A than in condition C, indicating that infants focused their attention more easily on Peek-a-Boo performed by an AC than by a human, and that DLPFC may reflect the degree of externally focused attention.

Finally, no significant correlation was found between oxy-Hb changes and behavior (looking time, developmental score, or familiarity with AC and Peek-a-Boo) in any channel.

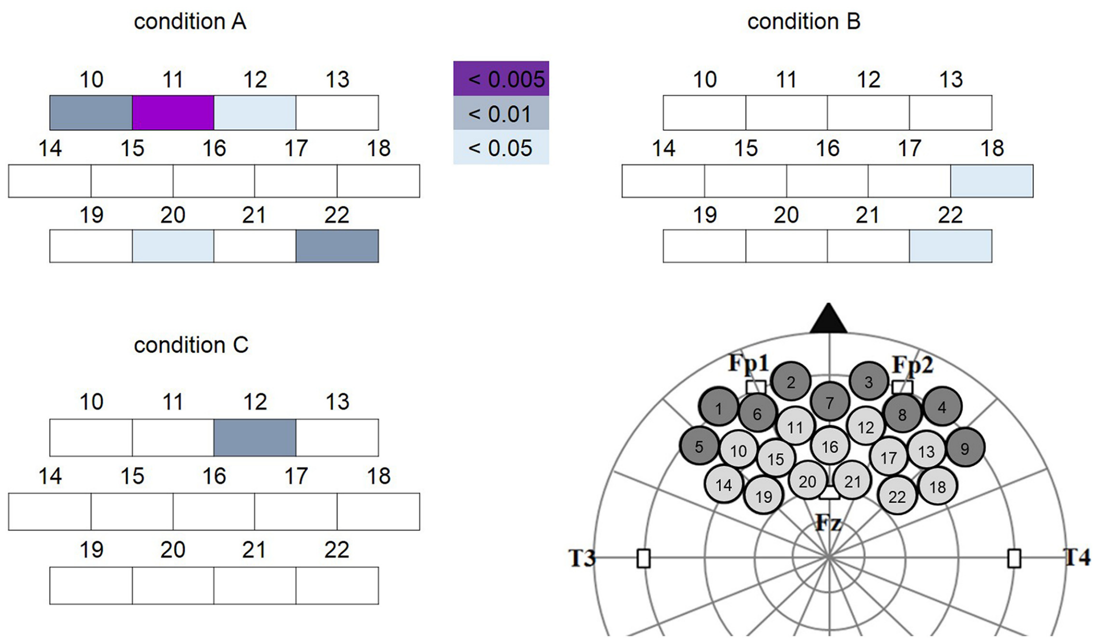

FIGURE 5 | Channels showing significant oxy-Hb decrease (target vs. baseline) in each condition. The colored boxes represent channels showing significant oxy-Hb decrease at different levels (purple: significant channel after false discovery rate (FDR) correction). Channels 1∼9 were excluded from analysis because of excessive noise. Location of each channel on the brain was illustrated in the lower right corner. Note that the oxy-Hb decrease was more widespread in condition A (Peek-a-Boo by AC) than in conditions B (Non Peek-a-Boo by AC) and C (Peek-a-Boo by human).

DISCUSSION

The present study employed behavioral and fNIRS recordings to examine 5- to 6-month-old infants' cerebral responses to externally focused stimuli with different social value (with or without Peek-a-Boo) and stimulus saliency (human or AC). Behavioral data showed that infants spent significantly more time looking at Peek-a-Boo performed by an AC than at Peek-a-Boo performed by a human, indicating more interest in the AC. The increased interest for the AC relative to the human may have been caused by the more salient facial features of the AC. NIRS data revealed that the hemodynamic response in the infant PFC generally decreased for the externally focused stimuli employed in this study. Peek-a-Boo performed by an AC induced the most widespread decrease among the three conditions and the decrease was most significant in FP including MPFC. Moreover, a significantly larger decreased response was observed when the infants viewed Peek-a-Boo performed by an AC than by a human in the DLPFC. We will discuss the implications of these decreased hemodynamic responses later on in this article.

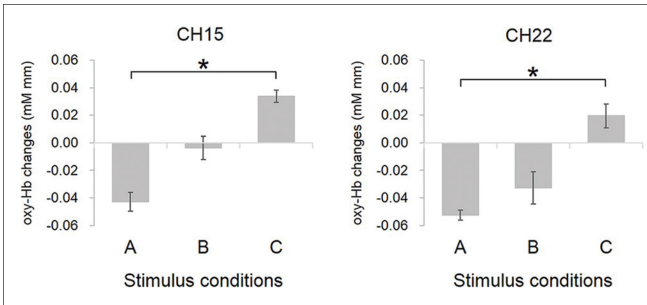

FIGURE 6 | Comparison of oxy-Hb changes in channels showing significant difference between conditions. Conditions definition: **(A)** Peek-a-Boo by AC; **(B)** Non Peek-a-Boo by AC; and **(C)** Peek-a-Boo by human. For both CH15 and CH22, the oxy-Hb response in condition A was significantly more decreased as compared to condition C. Error bars indicate one standard error of the mean (N = 19). *$p < 0.05$.

Since the development of neuroimaging methods, especially resting state fMRI (rsfMRI), an increasing number of studies focused on the structural development of the infant brain. However, functional studies of infants under 1-year of age (the most vital period for brain development) are scarce owing to the difficulty to make such young infants attend to certain stimuli obediently and motionlessly. Motion is detrimental to most neuroimaging methods. fNIRS is a promising method to investigate brain functions of children and infants because it is much lesser vulnerable to body and head motion. In addition, fNIRS is exceptionally safe. Functional studies of the infant brain using fNIRS have accumulated in recent years. However, studies investigating higher-order functions such as social cognition are still rare. A recent fNIRS study demonstrated increased response to social stimuli when compared to non-social stimuli in the temporal area (superior temporal sulcus (STS)) in 5-month-old infants, resembling the functional specialization in adults (Lloyd-Fox et al., 2009). Similar to the current study, this previous study used Peek-a-Boo performed by a human as a social stimulus, suggesting suitability of Peek-a-Boo to attract attention and serve as a social communicative cue for infants as young as 5-month old.

Our study employed similar social stimuli, but we focused on the cerebral responses of infants in another key region involved in social cognition, the MPFC (Grossmann, 2013). Moreover, we aimed not only to pinpoint the specialized region in the PFC responsible for processing social stimuli, but also to investigate how 5- to 6-month-old infants respond to stimuli that require externally focused (non-self-referential) attention, and whether responses recorded from infants resemble responses recorded from adults. Our fNIRS measurements demonstrated reduced PFC activity in response to stimuli that required externally focused attention, similar to previous neuroimaging studies on adults (Shulman et al., 1997; Gusnard and Raichle, 2001). Gusnard and Raichle (2001) have discussed such task-induced but task-independent decreases in PFC activity in depth based on the findings of several PET studies in adults. These functional studies employed stimuli from different domains involved in a wide variety of tasks, such as motoric activity, language processing, visual and auditory attention, etc. (Shulman et al., 1997; Mazoyer et al., 2001). However, the decreased responses hardly varied in their locations, suggesting the existence of a systematized mode of brain function—the default mode (Raichle et al., 2001), which is attenuated during externally directed behaviors. Furthermore, as Gusnard and Raichle (2001) have concluded from a number of functional neuroimaging studies, the DMPFC, a key part of the DMN (Gao et al., 2009; Andrews-Hanna et al., 2010; Xiao et al., 2016), may encompass a dynamic range of activity that is enhanced in tasks that involve self-referential mental activity (Castelli et al., 2000; Gusnard et al., 2001), and attenuated in tasks that require externally directed (non-self-referential) attention (Shulman et al., 1997).

Our group confirmed the presence of such dynamic functional activity in DMPFC and its vicinity of infants as young as 5- to 6-month of age. Specifically, our previous fNIRS study (Imafuku et al., 2014) demonstrated increased activity in the DMPFC of 6-month-olds (185 $\pm$ 21.9 days) in response to self-referential stimuli (self-name calling). Using the same instrument and probe arrangement, the present fNIRS study revealed that externally directed stimuli decreased responses relative to baseline in the PFC region including FP, DMPFC and DLPFC of infants of similar age (173.2 $\pm$ 14.3 days). This data indicates primitive DMN functioning in 5- to 6-month-old infants. rsfMRI studies in young infants lend further support to this possibility: Gao et al. (2009) found primitive DMN structure in 2-week-old infants, and approximately adult-like DMN structure, in particular the two key hubs (MPFC and PCC), in 1-year-old infants. Furthermore, Gao et al. (2015) suggested that DMN structure undergoes the most prominent development during the first 3 months of life and that the long-distance connectivity of MPFC and PCC strengthens to a large extent during the second half of the first year.

One may wonder: (1) why the supposed infant DMN structure reported here is so large, including not only MPFC, but also lateral frontal regions like DLPFC, which is known as a central region of executive control (MacDonald et al., 2000); and (2) how our study aligns with previous studies that have shown increased rather than decreased hemodynamic responses induced by attention-directing cues in DLPFC (e.g., Hopfinger et al., 2000).

Regarding the dynamic pattern of activity in infant DMN structure, two possible reasons may explain the seemingly broader activated region. First, even in studies of adult subjects, the decreased activity in response to externally focused attention covered a larger region including not only the DMPFC but also adjacent areas like the ventral MPFC (see Figure 5 from Raichle et al., 2001; Figure 4 from Gusnard et al., 2001; and Figure 1 from Gusnard and Raichle, 2001). In our study, after FDR correction for multiple comparisons, only response in CH11 in condition A was significantly decreased when compared to baseline. The estimated region for CH11 is FP, which includes partial ventral MPFC. Second, both in our present and previous infant studies using NIRS, the regions underlying each significant channel were estimated based on the virtual registration method for NIRS channels (Okamoto et al., 2004; Okamoto and Dan, 2005; Tsuzuki et al., 2007). This method principally projects superficial parts of cerebral cortex. NIRS light penetrates much deeper into the brains of infants than into the brains of adults owing to infants' less myelinated and less reflective white matter in addition to much thinner skull and scalp (Fukui et al., 2003). Therefore, the estimated DLPFC activity in the present study may also contain activity from deeper regions including DMPFC. According to these interpretations, the dynamic pattern of DMN activity is not necessarily restricted to DMPFC, at least for the decrease in activity accompanying externally focused attention. Therefore, we suggest that the dynamic DMN function observed in 5- to 6-month-old infants in our present (externally focused attention) and our previous (self-focused attention) study (Imafuku et al., 2014) is comparable to the dynamic DMN function observed in adults, which has been concluded from several independent functional neuroimaging studies as well (Shulman et al., 1997; Gusnard and Raichle, 2001; Gusnard et al., 2001; Raichle et al., 2001).

Regarding DLPFC activity, the decrease in the hemodynamic response was significantly larger for more salient Peek-a-Boo stimuli (larger for the AC than the human), indicating that DLPFC modulation may reflect the degree of attention. Many studies have found increased DLPFC hemodynamic response in attention tasks (e.g., Hopfinger et al., 2000). However, brain regions may respond differently to different task demands. In the present study, we may have found decreased hemodynamic responses because we used a passive viewing task for 5- to 6-month-old infants who are not able to perform attentional tasks at such a young age. Tasks requiring explicit execution may be quite another matter.

Interestingly, decreased hemodynamic responses were found to be more prominent when Peek-a-Boo was performed by an AC rather than by a human woman. Compared to the human face, the facial parts (eyebrows, eyes, cheeks, nose and mouth) of the AC were exaggerated; figure and color were emphasized and the AC showed a higher level of brightness and contrast.

These features made the AC face a more salient stimulus than the human face. Previous research has reported that the vision of young infants is not fully developed until 3-years of age (Held, 1979; Norcia and Tyler, 1985; Maurer and Lewis, 2001). Therefore, it is possible that stimuli with more outstanding features are best suited to attract infants' attention. In fact, face stimuli with salient features were found to be more attractive to infants at early developmental stage and such stimuli elicited strong activation in their frontal regions (Perkins, 1975; Rhodes et al., 1987; Ellis et al., 1992). The behavioral results of our study support this possibility: the infants spent significantly more time looking at Peek-a-Boo performed by an AC than at Peek-a-Boo performed by a human. Based on these reasons, we suggest that the DLPFC, where the most prominent difference in activity was found between conditions (A vs. C), may reflect the degree of attention focused on external stimuli by infants as young as 5–6 months old. Moreover, we propose that everyday learning may be facilitated in infants of this young age by using stimuli with salient features.

The present experimental design used Peek-a-Boo performed by an unknown woman. We hypothesize that if Peek-a-Boo was performed by the infants' mothers, the decrease in response in the infant's PFC would be strongest to the mother's Peek-a-Boo. Previous behavior and neuroimaging literature suggests that the mother is extremely important to infants' early life (Minagawa-Kawai et al., 2009; Imafuku et al., 2014). Therefore, mother-related stimuli may be special to young infants and elicit unique brain activity. We are planning to test this hypothesis in our future investigations.

In addition, to keep the infants' attention on the display, we presented a small-sized moving AC face rather than a blank screen with a cross mark (as used in studies on adult subjects) for fixation during the baseline period. One might suspect that the eye movements induced by this moving AC face might have activated the DPFC (e.g., frontal eye field) and have led to the decreased activity during the target period relative to the baseline period. Indeed, we tried to exclude such interference as far as possible: (1) movement of the small-sized AC face was much slower than the Peek-a-Boo movement during the target period; and (2) the range of movement of the small-sized AC face was controlled to be identical to the range of the Peek-a-Boo movement in the target period. Based on these precautions, we assume that eye-movement was comparable between baseline and target periods. Moreover, behavioral data showed that the mean looking time of infants was 6.43 ± 0.34 s (mean $\pm$ SEM) during the 10∼18 s baseline period, much shorter than that during the 10 s target period under the three different conditions (8∼9 s). Therefore, we conclude that the decreased hemodynamic responses in the PFC reflect externally focused attention rather than eye movements during the baseline period.

Last, we did not observe a significant difference between social and non-social stimuli performed by an AC, neither in the behavioral nor in the NIRS measurement. In contrast, Lloyd-Fox et al. (2009) found significantly more activation in response to social stimuli than to non-social stimuli in STS of infants of similar age. However, our study focused on a different brain region (the PFC). Therefore, our results do not need to be consistent with these previous findings. Rather, this discrepancy may reflect that 5- to 6-month-old infants have developed specialized regions for processing of social stimuli including the STS but not the PFC.

CONCLUSION

In this study we used fNIRS, a suitable and promising instrument for infant functional study, to investigate hemodynamic responses to tasks that require externally focused attention in 5- to 6-month-old infants. Our NIRS data revealed decreased PFC responses elicited by externally directed stimuli depending on stimulus property. Stimuli with more salient features induced decrease in response to a larger extent. In conjunction with our previous findings on enhanced PFC responses in infants of similar age performing tasks using self-referential stimuli (self-name calling), we suggest primitive functioning of DMN in 5- to 6-month-old infants.

AUTHOR CONTRIBUTIONS

HS, AM, MY, SM and YM designed research; YM performed research; EH, KY and YM analyzed data; and MX and YM wrote the article.

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【概要３-4】遠隔コミュニケーション事態における視聴覚間相互作用

遠隔コミュニケーション事態における視聴覚間相互作用

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1. 研究の背景と目的

インターネット等の通信技術を用いた遠隔コミュニケーションでは，視覚および聴覚情報が通信網に乗り，我々は相互の端末から再生された視聴覚刺激を知覚認知している。このとき，通信の相手側において同時に生じた視聴覚情報（例えば，カメラとマイクで収録された映像と音声）は，相手側の端末，通信網および自分の端末といった経路においてそれぞれ処理されることで，必然的に一定以上の遅延が生じる。このような感覚刺激間の同時性が必ずしも担保されない事態において，刺激間に時差が生じることが感覚間の統合的知覚にどのような影響を与えるかについて明らかにすることが，本研究の目的である。

多感覚情報処理における刺激間の時間情報については，時差をもった異種感覚刺激を継続的に呈示することによって，2 刺激間の時間順序判断（Temporal Order Judgment: TOJ）や同時性判断（Simultaneity Judgment: SJ）において 2 刺激の呈示タイミングを同時と判断する時差，すなわち主観的同時点（Point of Subjective Simultaneity: PSS）が変化することが知られている（Fujisaki et al., 2004; Vroomen et al., 2004)。時間的再較正と呼ばれるこの現象は，時差への順応が生起することで同一事象により同一タイミングで生起した物理刺激の伝達速度差 （King, 2005） や感覚情報の神経伝達速度差 （Sugita & Suzuki, 2003） を補償し，効率的な知覚・認知処理を促す情報処理を反映していると考えられる。時間的再較正はほとんどの報告において PSS は継続呈示された時差の方向へシフトすることが示されており，継続呈示時差を同時と見なすように判断分布が推移することが明らかになっている。一方で視聴覚統合事態においては，呈示時差方向への PSS シフトを示す「時差順応」メカニズムとその反対方向への PSS シフトを示す「ベイズ較正」メカニズムが両立することも示唆されており （Miyazaki et al., 2006)，感覚間時差への適応過程には複数の情報処理過程が同時に機能していると考えられる。

主観的同時性の適応的処理過程は，感覚情報の統合過程に貢献するものと考えられる (Vroomen & Keetels, 2010)。話声知覚が話者の口の動きにより変化するマガーク効果 (McGurk & MacDonald, 1976) や聴覚刺激呈示により視覚刺激の運動知覚が変化する交差／

反発錯覚（Sekuler et al., 1997）など，一方の感覚情報が他方の感覚知覚へ干渉する感覚間相互作用は，両感覚刺激呈示が時間的に近接するほど強く知覚されることが明らかになっている。Fujisaki et al.（2004）はSJ課題による時間的再較正に加えて，交差／反発錯覚の判断分布の推移も検討しており，時差順応手続きによってSJ判断分布だけでなく交差／反発判断分布も呈示時差方向へ推移することを明らかにしている（Fujisaki et al., 2004)。このことから，時間的再較正におけるPSSのシフトは，知覚タイミングの異なる感覚知覚を同時とみなすことで，感覚固有情報の統合過程メカニズムの時間的特性をも変化させ，情報統合を促進する働きを示していると考えられる。

しかしながら，主観的同時性がすなわち多感覚統合メカニズムの「時間窓」であるという解釈について，疑念を呈する報告もなされている。Freeman et al.（2013）は，TOJにおけるPSSとマガーク効果および交差／反発錯覚をもたらす時差が乖離することを報告しており，主観的同時性と感覚統合が互いに異なる時間情報処理メカニズムを基盤としていることを示唆している（Freeman et al., 2013)。さらに，TOJとSJではしばしば異なるPSS値が得られることから（van Eijk et al., 2008），主観的同時性それ自体においても判断課題によって異なる情報処理過程を反映している可能性がある。したがって，一連の多感覚統合過程においては，少なくともTOJとSJ・感覚間相互作用との間において，異なる時間情報処理が同時に機能しており，時間的再較正におけるPSSのシフトは必ずしも感覚統合メカニズムの情報処理変化を反映していないと考えられる。

TOJ，SJおよび感覚間相互作用の情報処理過程が異なるものであるとすれば，その適応過程についても異なる特性が反映される可能性がある。Heron et al.（2010）は視聴覚間のTOJにおける時間的再較正について，時差順応中に刺激間時間順序へ選択的注意を向ける条件では，視覚刺激特徴へ注意を向ける条件に比べ再較正量が増加することを報告している。彼らは同現象の説明として，時間順序への注意によって，時差情報ではなく刺激間時間構造の顕著性が上昇した状況で一定順序の刺激ペアを継続的に呈示されることで，時間構造についての判断であるTOJの判断分布推移が増加すると考察している。もし順応中の注意および課題と順応前後の判断課題の同一性が時差への適応過程において重要なものであるならば，刺激もしくは刺激間におけるどの情報へ選択的に注意を向けるかによって，それぞれの課題に応じた時間情報への適応特性が立ち現れる可能性がある。

本研究では，視聴覚間の時差を統制しやすく，また視聴覚の統合知覚が得られやすい交差／反発刺激を用い，TOJやSJなどの時間的判断と感覚統合の知覚判断をすることで，両判断課題の時間情報処理にどのような影響が見られるかについて検討した。時差順応中の注意対象を実験条件とすることで，順応前後の各課題における判断分布が条件によってどのように推移するかについて検討した。

2. 方法

2.1. 被験者

7名の学生（男性5名，平均年齢22.2±0.4歳）が実験に参加した。全被験者が健常な視力または矯正視力および聴力を有していた。

2.2. 刺激および装置

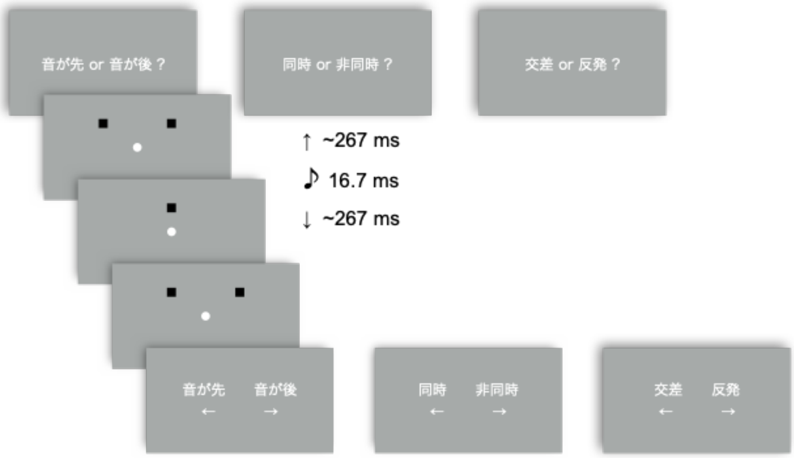

図1. 一試行の刺激呈示図

実験は防音処理が施された暗室で行われた。120 Hz液晶モニタ（XL2420TE, BenQ）を用い，全試行において視覚刺激として灰色の背景（1.36 cd/m^2）上で画面中央に呈示された白色の注視点（13.1 cd/m^2, 0.42 deg^2）の2.11 deg上方を黒色の正方形ペア（0.12 cd/m^2, 0.42 deg^2）が12.66 deg/cm^{2}の速度で通過する交差／反発（Stream/Bounce: SB）刺激を呈示した（図1）。被験者は頭部をあご台に固定し視距離60 cmで観察した。聴覚刺激としては密閉型ヘッドフォン（HDA200, Sennheiser）を用いて純音（600 Hz, 70 dB SPL）を，すべての課題において約16.7 ms間呈示した。視聴覚間時差として，順応および再順応フェイズでは平均150 msの視覚先行呈示となる3種類（-100, 150, 400 ms）の時差，事前および事後テストフェイズでは9種類の時差（±267, ±200, ±133, ±67, および0 ms; 負の時差は聴覚刺激の先行呈示を示す）を用いた。これらの時差は，2つの視覚刺激が重なるフレームのオンセットに対する聴覚刺激呈示タイミングを示す。実験プログラムはMac OS X上で動作するMATLAB（MathWorks, USA）およびPsychtoolbox 3 (Brainard, 1997) により作成・操作し，すべての聴覚刺激はUSBオーディオインターフ

ェイス（Fireface UCX, RME）を介して呈示された。被験者はPCキーボードを用いて反応を行った。

2.3. 手続き

実験は事前テストフェイズ，順応フェイズ，再順応フェイズおよび事後テストフェイズで構成され，後者3フェイズでは刺激観察中の注意課題に応じて3つの実験条件（順序注意条件，同時性注意条件，交差／反発条件）が設定された。練習試行として，事前テストの開始前には3つの判断課題（TOJ，SJおよびSB課題）を5試行ずつ，各条件による順応・再順応・事後テストフェイズの前には順応フェイズ10試行，再順応3試行および事後テスト5試行を3セット実施した。実験条件の実施順序は被験者間でカウンターバランスをとった。

事前テストでは，3つの判断課題のうちいずれかの課題教示画面が表示され，被験者がキーを押すと画面中央に注視点（白色の正円；0.42 deg^2）が500-750 ms間呈示された後，注視点とともに9種類のうちいずれかの時差によるSB刺激が呈示された。被験者は刺激呈示中に視覚刺激を目で追わずに注視点を凝視するよう教示された。刺激呈示後の反応教示画面で被験者が反応を行うと，再び注視点およびSB刺激が呈示され，一度の課題教示につき5試行を連続して行い，5試行が終わると再び3課題のうちいずれかの課題教示および5試行を実施した。各課題および各時差につき20試行を実施したため，被験者は5試行のブロックを108回ずつ，計540試行を行った。

順応フェイズから事後テストフェイズは，時間順序条件，同時性条件および交差／反発条件のうちいずれかの注意条件下で実施された。順応フェイズの各試行では，画面中央に注視点（白色の十字；0.42 deg^2）が500-750 ms間呈示された後，3種類の時差のうちいずれかによるSB刺激が呈示された。各時差につき40回の刺激呈示（計120試行）が行われたが，そのうち2試行ずつの刺激呈示後に注意条件に応じた反応を課したため，被験者は常に時間順序，同時性もしくは交差／反発判断に注意を向けるよう求められた。

再順応フェイズでは，順応フェイズと同様の注意条件下で，各時差につき1回ずつの刺激呈示（計3試行）を行った。順応フェイズと同様に注視点として白色の十字形を呈示した。

事後テストフェイズでは，事前テストと同様に，初めに課題教示を行った後，正円形の注視点を用いた刺激呈示および教示に応じた判断課題を5試行実施した。5試行が終わると再び再順応フェイズに戻り，再順応フェイズ3試行と事後テストフェイズ5試行を計108回繰り返した。全540試行の事後テスト試行が完了すると，被験者は休憩をとった後異なる注意条件下で順応フェイズから事後テストフェイズを繰り返した。

2.4. データの処理法

事前テストフェイズおよび事後テストフェイズにおけるTOJ課題について，被験者および実験条件ごとに各試行における呈示時差を独立変数，「視覚刺激先行」判断率を従属変数

として最尤法を用いたロジスティック回帰による一般化線形モデルへの当てはめを行い，判断率 50 %点における時差の値を PSS_T として算出した。SJ 課題および SB 課題については，呈示時差を独立変数，それぞれ「同時」判断率および「反発」判断率を従属変数として最尤法を用いたロジスティック回帰によるガウス分布への当てはめを行い，分布曲線において判断率が最大となる時差をそれぞれ PSS_S および pBounce として算出した。各値について事前テスト・事後テスト間の差を再較正量として算出した。

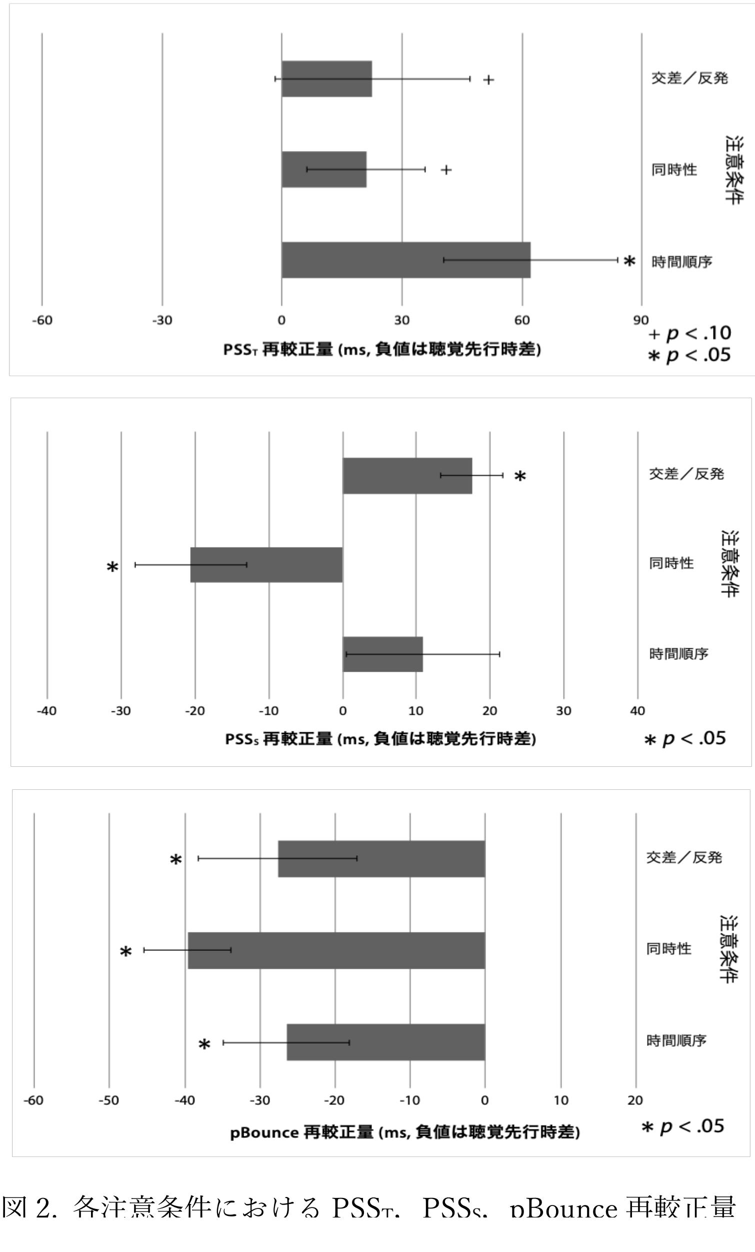

図 2. 各注意条件における PSS_T，PSS_S，pBounce 再較正量

3. 結果

各値の再較正量について，条件ごとに一標本 t 検定を行った。

全条件において PSS_T 再較正量は正値であり，一標本 t 検定の結果，時間順序条件における PSS_T 再較正量に，$t = 0$ と比較して有意な差が認められた（$t(6) = 4.94$, $p < .05$；図1)。一方で同時性条件および交差／反発条件においては，PSS_T 再較正量に $t = 0$ との有意な差は認められなかった（$p > .05$)。

PSS_S 再較正量についての一標本 t 検定の結果，交差／反発条件において PSS_S は呈示時差の方向へ有意にシフトし（$t(6) = 3.56$, $p < .05$；図 1)，同時性条件では呈示時差の反対方向へシフトした（$t(6) = 2.94$, $p < .05$)。時間順序条件では有意なシフトは認められなかった。

pBounce 再較正量は全条件において負値であり，一標本 t 検定の結果，全条件において $t = 0$ との間に有意な差が認められた（$ps < .05$；図 1)。したがって，SB 刺激の継続呈示中に，刺激間の時間情報および交差／反発の生起に注意を向けると，交差／反発判断分布は順応時差の反対方向へ推移することが明らかになった。

4. 考察

時差順応中に時間順序を向けた条件では時間順序判断分布は順応時差方向へシフトする一方で，同時性や交差／反発判断へ注意を向けた条件では同分布の有意な推移は見られなかった。このことは時間順序以外への注意条件においても再較正の生起を示した Heron et al. (2010)の報告とは一致しないものの，順応中にどのような情報へ注意を向けるかによって時間的再較正の現れ方が左右されることを示す結果であるといえる。特に，TOJ と共に主観的同時性の測定法として用いられる SJ を順応中課題として用いた条件では PSS_T のシフトが見られなかったことは，TOJ と SJ の機能的差異が時差への適応過程においても現れることを示している。

本研究において驚くべき結果は，SJ および SB 課題における判断分布の推移であろう。SJ に関しては，実験 1 ではこれまでに報告されてきた SJ の時間的再較正がどの条件でもみられず，実験 2 においては同時性注意条件において順応時差とは反対方向へ PSS_S がシフトする結果となった。SB に関しては，両実験共に順応中の注意条件にかかわらず，pBounce は順応時差とは反対方向へシフトした。このことは，SJ および SB 判断分布がともに順応時差方向へシフトすることを示した Fujisaki et al. (2004)の報告とは一致しない。

本研究と Fujisaki et al. (2004)の結果の相違については，順応刺激に用いた時差の違いに起因した可能性が考えられる。Fujisaki et al. (2004)では順応時差として同一方向の時差のみ用いられたが，本研究では平均して 150 ms の視覚先行となる 400, 150, -100 ms の 3 種類を等頻度で用いた。同時性条件における順応中課題は各時差についての同時か否かの判断であったが，このうち客観的に同時である 0 ms に最も近いものは平均時差とは反対の極性である-100 ms であった。したがって，実験 2 の同時性条件における PSS_S シフトは，より客観的に同時に近い時差を同時と見なすことで，「同時」判断をその時間順序の

時差に対して上昇させることで生じたものと解釈されうる。一方の SB 判断分布についても，感覚間相互作用の時間情報処理過程は客観的同時点により近い時差を同時性の窓として，その時差極性に依存的な適応特性を有する可能性がある。

一方で，多感覚統合における時差への適応特性が順応時差とは反対方向への応答を示すものであり，SJ における主観的同時性はその影響を反映したものである可能性も考えられる。既に TOJ と多感覚統合に関してはその判断分布は反対方向の時間的特性をもつことが示されており (Freeman et al., 2013)，SJ と多感覚統合については Fujisaki et al. (2004)によって同一方向の適応特性を示すことが明らかにされている。したがって，もし多感覚統合処理が前段で述べたような時差への応答特性を有する，もしくは TOJ とは異なりベイズ較正的な時間特性を有するとするならば，本研究における順応時差とは反対方向への SJ および SB 判断分布の推移は， SB 判断の変化に応じて SJ 判断分布が変化したものと捉えることも可能である。すなわち本研究の結果は，SJ における主観的同時性と多感覚統合の時間窓が相関的な関連を示すものであると捉えることも可能であろう。

本研究では視聴覚刺激の時間情報の統制を容易にするため，交差／反発錯覚刺激を用いた。一方で，遠隔コミュニケーション事態において最も頻繁に通信される情報は顔などの映像と話声である。そのため，本研究で得られた基礎的知見が遠隔コミュニケーション事態においても妥当なものであるかを明らかにするためには，口の動きと話声の統合的知覚事態について検討する必要がある。その代表例としては，口の動きによる話声知覚の干渉事態である McGurk 効果が挙げられる。したがって今後の研究では，McGurk 刺激などのより曖昧で情報量の多い刺激における時差情報を操作することで，より日常場面に即した事態における感覚処理メカニズムの解明が求められる。

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（3） 研究概要報告書に述べた研究内容の詳細と補足資料

４． 効果的なコミュニケーション活動を目指すツールについての研究

４-1. 子どもと高齢者にも装着しやすい脳波電極の開発

４-2. 発話困難者の会話補助ツール「マイボイス」の研究

４-3. 子どもの対人相互作用を促進するためのデバイスの検証

４-4. 弱視者のためのタブレット教材や閲覧アプリの開発

【概要４-1】子どもと高齢者にも装着しやすい脳波電極の開発

微小針電極を用いて計測された脳波による
言語音に対する認知指標の抽出

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１．研究の背景と目的

計測前処理なく簡便に有毛部での脳波計測を可能とする微小針電極は、従来の脳波計測で広く使用されている皿電極と同等の信号を計測可能であること、また計測された脳波から自発電位と ERP の脳波指標を検出可能であることが示されている。さらに、日常生活での実装を目指し、この電極を含めたウェアラブルな脳波計測システムの開発が進められている。しかし、誰でも脳波を簡便に計測できるシステムを開発しただけでは、体重や体温などと同様に日常生活でこのシステムを使用する人はいない。子どもや高齢者も対象にした社会実装には、当システムを用いた脳波計測によって「どのような場面で」、「何を知ることができるのか」を示す必要がある。そこで、本研究では、微小針電極を用いて計測された脳波から、心理指標の抽出に取り組んだ。
指標は、言語音に対する認知指標である。言語処理による脳活動の計測は、言語学習や聴覚情報処理障害の診断と治療などに応用できる。本実験では、3 つの言語(/itta/, /itte/, /itta?/)を用いて、脳の音韻処理と抑揚処理による認知指標の抽出を試みる。先行研究では、MEG や NIRS により、これらの言語を用いた言語処理機能の研究がされている。そこで、微小針電極による脳波計測と NIRS との同時計測により実験を行うことで、他の脳活動計測手法との比較を目的とする。

２．方法

本実験では、音韻と抑揚の異なる 3 つの音声言語(/itta/, /itte/, /itta?/)を用いたオドボール課題を被験者に負荷した。これまでに、MEG や NIRS を用いた、この 3 つの言語に対する認知指標の研究が多く取り組まれている[1-3]。NIRS を用いた研究では、音韻の違いの認識により左聴覚野近傍で脳内血液中の酸素化ヘモグロビン(Oxy-Hb)濃度が上昇、抑揚の違いの認識により右聴覚野近傍で Oxy-Hb 濃度が上昇することが示されている。本実験では、左右聴覚野近傍において脳波計測と NIRS 計測を同時に行い、音韻と抑揚の違いにより誘発される認知指標を比較する。

2-1．実験参加者

本実験は、右利きの成人男女 10 人(うち男子 7 人、女子 3 人)を対象とした(年齢 21-

25、平均 22.9 歳)。本研究で行われた実験はすべて、慶應義塾大学の倫理審査委員会の審査を通っているものであった。また、被験者には事前に書面に、実験内容について説明し、同意を得た。

2-2. オドボール課題

本実験では、音韻と抑揚の異なる 3 つの音声言語(/itta/, /itte/, /itta?/)を用いて刺激課題を作成した。これらの音声は分析再合成法により作成され、音韻・抑揚のみが異なり、音声の長さや強さは共通である[1]。第 1 音節の音声は、80ms の/i/であり、3 つの音声共通である。200ms の無音区間後、第 2 音節が開始する。第 2 音節の長さは有声開始時間の 12 ms を含め 92ms である。刺激に対し、脳波はミリ秒単位での瞬発的な反応、Oxy-Hb 濃度は秒単位での緩速な反応である。したがって、両反応を検出するために、逸脱刺激の呈示間隔が十分である必要がある。本課題では、刺激呈示間隔を 1000ms とし、標準刺激として/itta/を 22-24 回繰り返し呈示した後、逸脱刺激として/itte/もしくは/itta?/をランダムに 1 回呈示するブロックを 36 回繰り返した.刺激呈示プログラムは心理学実験ソフト PsychoPy (Peirce, JW(2007) PsychoPy-Psychophysics software in Python)にて実行し、被験者に装着したイヤーフォンから呈示した。音量は約 67dB に設定し、各被験者に不快なく聞き取れる大きさまで調整させた。また、被験者の注意を保つためにボタン押し課題を課した。

2-３. 生体信号およびトリガ計測

本実験では、左右聴覚上において微小針電極を用いた脳波計測と NIRS 計測の同時計測を行った。

2-３-1. 脳波計測

誘導法
脳波は異なる 2 部位における電位差を記録することで導出される。本研究では、単極導出法により脳波計測を行った。単極導出法とは、脳波計測箇所に設置した電極から、耳朶に設置した電極を基準電位(リファレンス電極)として 2 極間の電位差を導出する方法である[4]。一般的に、左半球に活性電極を配置する場合は国際 10-20 法により定義される A1 を、右半球に活性電極を配置する場合は A2 をリファレンス電極とする。本研究では、ERP 検出の基準電極として推奨されている両耳朶連結をリファレンス電極とした[5]。両耳朶連結とは、A1 と A2 に設置した電極を物理的に連結させ、基準電位とする方法である。また、差動増幅器で脳波信号を増幅させるために、ニュートラル電極が必要である。ニュートラル電極は増幅回路の電気的な基準となる電位として使用される。一般的に、ニュートラル電極は前額部に設置するが、基準電極とニュートラル電極を同一にする場合もある。本研究では、より簡便に脳波計測を行うため、ニュートラル電極と基準電極を同一とした。

計測機器
本研究では、計測機器として日本光電のポリグラフシステム RMT-1000 を用いて、1kHz のサンプリング周波数で脳波計測した。ポリグラフシステムとは、脳波や心電図、筋電図などの生体信号を計測および処理ができる機器である。また、フィルタ処理はデータ取得・解析ソフト(Labchart, ADinstruments)を用いて行い、0.05-30Hz の帯域フィルタを使用した。

計測電極

脳波の計測箇所は国際 10-20 法により定義される T3(左側頭部)、T4(右側頭部)とし、ゴムバンドを用いて微小針電極を頭部に保持した。微小針電極は厚さ 0.1mm の銀板で製作したホルダで固定し、ミノムシクリップのついたリード線(BE-403B、日本光電)を用いてポリグラフシステムに接続した。リファレンスおよびニュートラルは両耳朶連結で、A1 と A2 に皿電極(NE-113A、日本光電)を配置した。皿電極は、皮膚処理剤(スキンピュア、日本光電)による角質層の除去後、電解質ペースト(エレフィックス、日本光電)を塗布し、耳クリップ(NE-301B、日本光電)を用いて耳朶に保持した。

2-３-2. NIRS 計測

計測機器

本研究では、計測機器として日立の光トポグラフィ装置 OT-R40 を用いて、100Hz のサンプリング周波数で Oxy-Hb の濃度変化を計測した。また、フィルタ処理は信号解析ソフト(Platform for Optical Topography Analysis Tools(以下 POTATo)、日立製作所)を用いて行い、0.01-0.8Hz の帯域フィルタを使用した。

計測プローブ

NIRS による計測は、左右側頭部にそれぞれ照射・検知プローブを 3×5 の格子状に 3cm 間隔で配置し、44 チャンネルにより行った。

2-３-3. トリガ計測

刺激に対する認知活動を記録するには、脳機能計測システムに刺激が呈示されたタイミング(トリガ)を記録する必要がある。本実験では、ポリグラフシステムに音声波形を直接入力し、第 2 音節の開始時間をトリガとして使用した。また、光トポグラフィ装置には刺 激開始とともにシリアル信号を送り、トリガとして使用した。シリアル信号の送信は、心理学実験ソフト PsychoPy(Peirce, JW(2007)PsychoPy-Psychophysics software in Python)で作成した刺激呈示プログラムに加え、実行した。

2-4. 解析方法

本実験では、加算平均法により刺激に対する脳波反応および NIRS 反応を得た。また、反応の左右差を定量評価するため、各被験者の側化指数(Laterality Index)を算出した。すべての解析は数値計算ソフト(MATLAB, MathWorks)を用いた。

2-4-1. 加算平均

脳波はトリガ 100ms 前から 1000ms までの生波形を抽出し、試行とした。試行に対し、それぞれ線型的に基線動揺を除去した。また、ベースラインをトリガ前 100ms 間とし、各試行の電位からベースライン間の電位の平均値を引いた。アーチファクトが含まれる試行を除去するため、±50μV を超える電位が生じた試行を解析対象から除外した。以上の処理後、被験者毎の加算平均波形を求めた。そして、全被験者の加算平均波形をさらに加算平均した波形(総加算平均波形)を求めた。

NIRS は 5 秒の移動平均でデータを平滑化した。データはトリガの 5s 前から 15s 後までを抽出し、試行とした。アーチファクトが含まれる試行を除去するため、Oxy-Hb 濃度が 3mM・mm を超えた試行を解析対象から除外した。残った試行に対し、それぞれ線型的に基線動揺を除去した。また、ベースラインをトリガ前 5s 間とし、各試行の Oxy-Hb 濃度からベースライン間の Oxy-Hb 濃度の平均値を引いた。以上の処理後、被験者毎の加算平均波形を求め

た。左右側頭部の聴覚領域上の 3 つのチャネルの逸脱刺激に対する加算平均波形のうち、各領域で最大の変化を示した反応を抽出し、総加算平均波形を求めた。

2-4-2. 側性化

側性化を定量的に評価するために、各被験者の側化指数 LI(Laterality Index)を求めた。左側頭部上の反応の値を L、右側頭部上の反応の値を R とすると側化指数 LI は以下の式で求められる。

$LI = (L - R) / (L + R)$

側化指数 LI は値が大きいほど左有意の反応であることを示す。EEG の L および R は、総加算平均波形に出現した ERP の頂点潜時前後 5ms 間における、T3 と T4 の平均振幅とした。NIRS の L および R は、総加算平均波形で得られた Oxy-Hb 濃度のピーク潜時前後 2s 間における、Oxy-Hb 濃度の平均変化量とした。

3. 結果および考察

3-1. 加算平均

NIRS

本実験で得られた NIRS の総加算平均波形を図 1 に示した。(a)と(b)はそれぞれ左聴覚野、右聴覚野で計測された NIRS の反応である。図 1 より、左右聴覚野近傍において逸脱刺激呈示後、3-7s にかけて Oxy-Hb 濃度が上昇したことがわかる。脳内神経細胞の活動により Oxy-hb の増加が起こるため、この反応は、逸脱刺激の認知によって起こったものであると考えられる。この現象は先行研究でも確認されており、本実験で作成したオドボー ル課題によって、被験者が音韻と抑揚の違いを認知できることが確認できた。

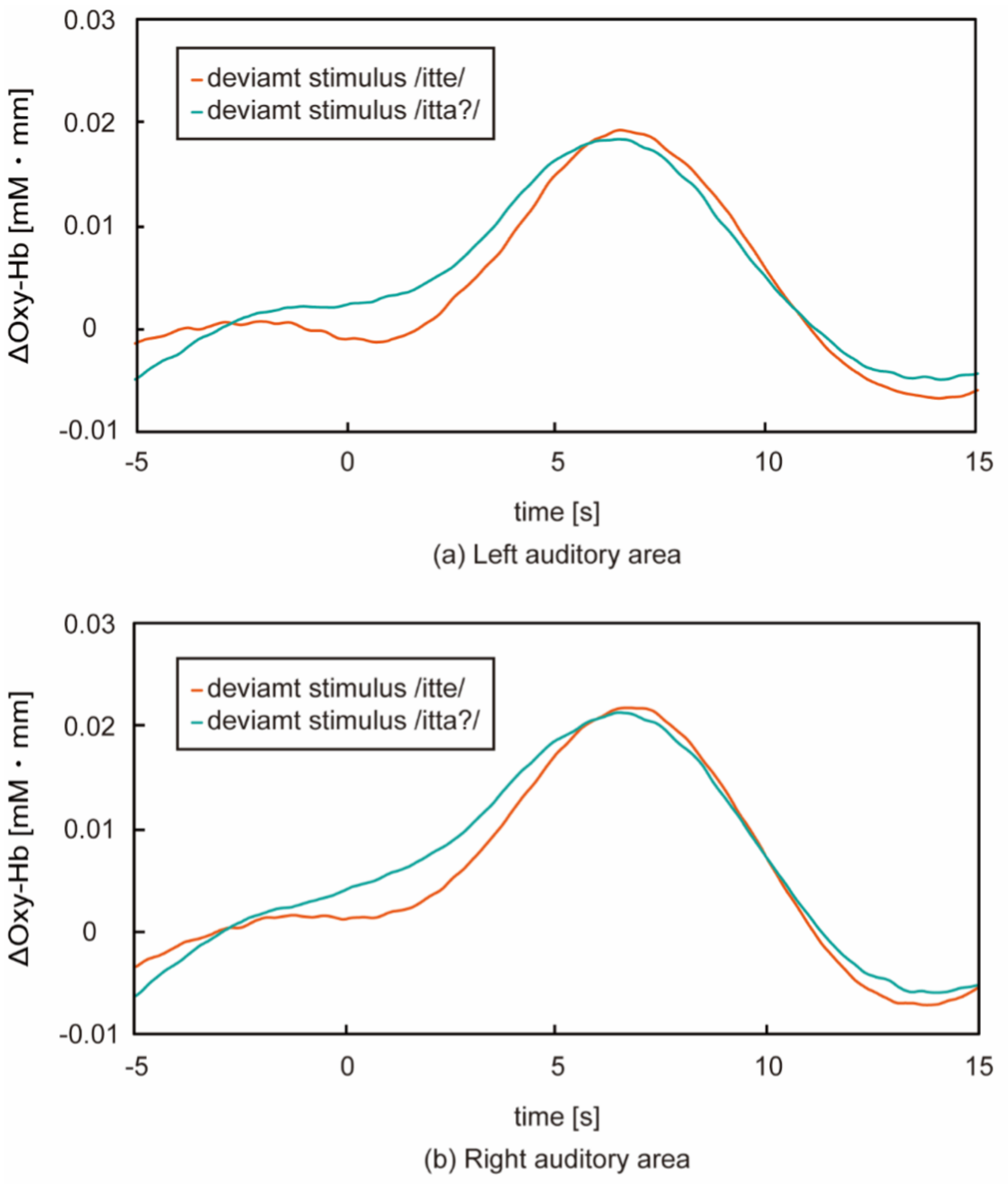
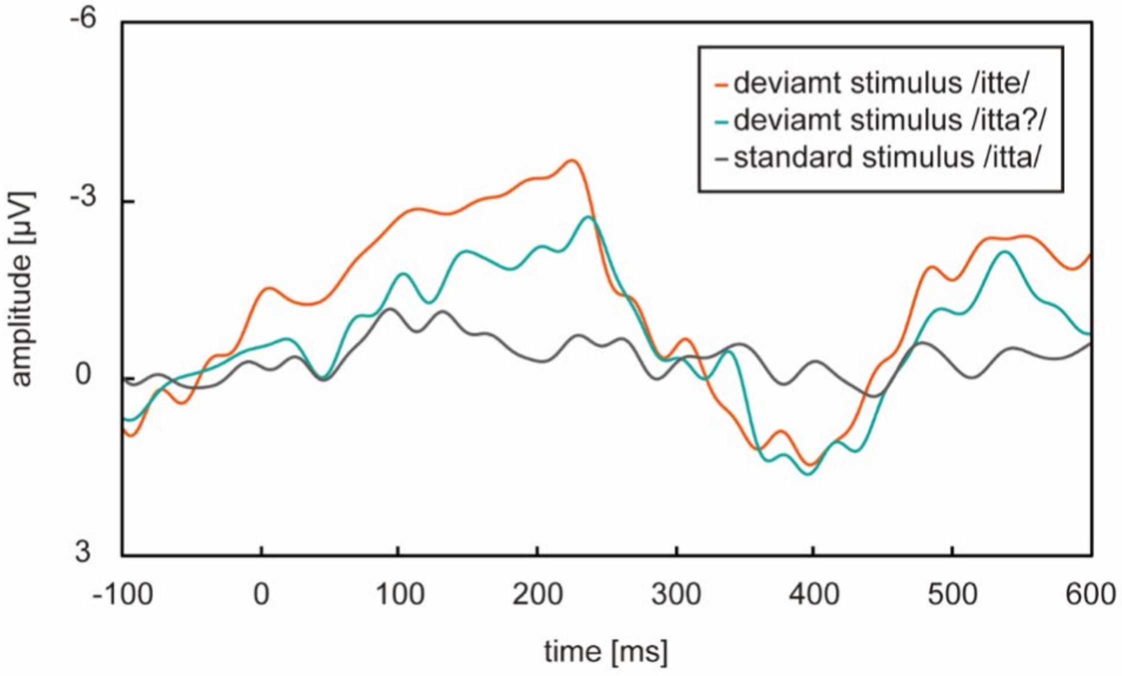


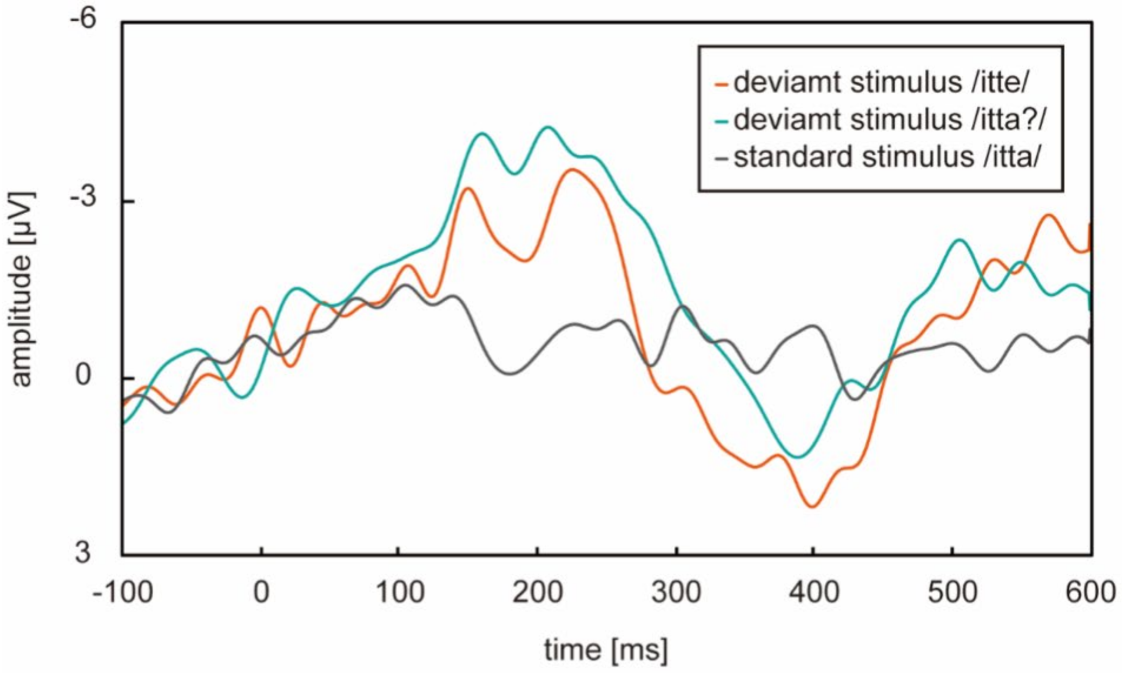
図 1　NIRS 計測により得られた総加算平均波形

脳波

本実験で得られた脳波の総加算平均波形を図 2 に示した。(a)と(b)はそれぞれ T3、T4 で計測された脳波である。図 2 により、標準刺激/itta/に対する総加算平均波形と比較して、逸脱刺激/itte/, /itta?/に対する総加算平均波形において、潜時 200ms 付近の陰性の成分と潜時 400ms 付近の陽性の成分が出現したことが確認できる。よって、これらの成分は逸脱刺激の認知によって生じた ERP であるといえる。さらに、これらの極性と潜時、形状から、陰性の成分はミスマッチ陰性電位(mismatch negativity: MMN)、陽性の成分は P300 であると考えられる。MMN と P300 の振幅と潜時を表 1 に示した。



(a) T3



(b) T4

図 2　微小針電極を用いて計測された脳波から得られた総加算平均波形

表 1　総加算平均波形における MMN と P300 の振幅と潜時

		T3		T4	
		/itte/	/itta?/	/itte/	/itta?/
MMN	Amplitude (μV)	−3.69	−2.74	−3.51	−4.25
	Latency (ms)	225	237	225	207
P300	Amplitude (μV)	1.48	1.63	2.16	1.36
	Latency (ms)	397	395	399	388

MMN は、聴覚事象の変化に対して潜時 100-200ms 付近に生じる ERP であり、前頭から中心部では陰性、後頭部では陽性の成分である。MMN は、先行して与えられた音(標準刺激)に基づいて入力された音の特徴を認識し、その認識した特徴と脳内に作られている記憶(標準刺激)を比較照合する過程により誘発される。MMN は、被験者が刺激に注意を向けていない条件でも出現するため、自動的なミスマッチの検出過程(入力された音が記憶と異なることを物理的に認知する自動的な脳機能)を反映する脳波指標とされている[6]。本実験で呈示した 3 つの刺激はそれぞれ第 2 音節目(/a/, /e/, /a?/)が異なるため、第 2 音節が入力された際、標準刺激との音韻、抑揚の違いを物理的に認知する脳内処理が行われる。したがって、本実験で呈示したオドボール課題により MMN が出現したといえる。また、MMN の振幅は、左側頭部(T3)では/itte/に対して出現したものが/itta?/に対して出現したものよりも大きく、逆に右側頭部(T4)では/itta?/に対して出現したものが/itte/に対して出現したものよりも大きくなった。これは、音韻の違い(/e/, /a/)は左聴覚野、抑揚の違い(/a?/, /a/)は右聴覚野有意に処理していることが反映されているのではないかと考えられる。
P300 は、刺激の変化に対して潜時 300ms 付近に生じる陽性の ERP である[7]。MMN と同様に、入力された刺激を脳内の記憶と比較照合する過程で誘発される。しかし、MMN と異なり、P300 は、被験者が刺激に注意を向けている条件のみ出現する。したがって、P300 は、意識的なミスマッチの検出過程に関連すると解釈されている[6]。被験者が刺激に注意を向けている場合、刺激に対する脳の自動的な認知が意識化することで P300 が誘発されるため、P300 は MMN に後続して出現する[8]。本実験では、被験者の注意を保つため、ボタン押し課題を追加した。そのため、被験者は刺激に注意を向けており、刺激の第 2 音節が入力された際、音韻、抑揚の違いを意識的に認知する脳内処理が行われる。したがって、本実験で呈示したオドボール課題により P300 が出現したといえる。また、P300 は、被験者の刺激に対する関与度や逸脱刺激と標準刺激の違いの大きさによって潜時や振幅が変化することは明らかになっている[6]。したがって、陽性の成分は、潜時は 100ms 遅れているが極性と形状から P300 であると考えられる。また、P300 の振幅は、左側頭部(T3)では/itta?/に対して出現したものが/itte/に対して出現したものよりも大きく、右側頭部(T4)では/itte/に対して出現したものが/itta?/に対して出現したものよりも大きくなり、MMN の振幅と逆の傾向を示した。
以上の結果から、微小針電極により計測された脳波から、音韻と抑揚の違いにより誘発される認知指標を自動的な認知(MMN)と意識化された認知(P300)に分けて検出することができたといえる。さらに、脳波が NIRS よりも早く認知指標を検出できることが確認できたといえる。

3-3. 側性化

本実験で得られた各被験者の *LI* を図 3 に示した。(a)は Oxy-Hb 濃度変化量、(b)は MMN の振幅、(c)は P300 の振幅から得られた *LI* である。一般的に *LI* が大きいほど左聴覚野有意の反応であるため、先行研究よりΔLI(*LI* for/itte/ − *LI* for/itta?/)は正となると考えられる[2,9]。

図 3(a)より、10 人の参加者のうち 6 人(sub.2、sub.3、sub.4、sub.6、sub.7、sub.8)の NIRS の *LI* は/itte/が/itta?/より大きかったことがわかる。先行研究では、右利きの参加者の 85%が正のΔLIを示し、右利きでない参加者の 50%が負のΔLIを示している[9]。本実験の被験者は全員右利きであるため、負のΔLIを示した 4 人の被験者は右利き参加者の 15%に属す ると考えられる。

図 3(b)より、MMN の *LI* の傾向は、NIRS の反応が正のΔLIを示した 6 人の参加者のうち 4 人(sub.2、sub.6、sub.7、sub.8)と一致した。一方、図 3(c)より、P300 の *LI* の傾向は 3 人(sub.2、sub.6、sub.7)と一致した。MMN は聴覚野から生成され、聴覚刺激の変化に対する反応である[10]。したがって本実験では、聴覚刺激の母音と抑揚の違い(/a/, /e/, /a?/)を認識することで MMN が出現し、NIRS と同じ傾向を示したといえる。P300 は聴覚刺激の変化に対する反応ではなく、予期しない刺激に対する反応である[11]。また、頭頂部 Cz において P300 が最大振幅で出現することが報告されており、P300 は聴覚野で起こる反応ではない[12]。したがって、P300 は逸脱刺激の違い(/e/, /a?/)を聴覚野で認識して発生するものではないと考えられる。以上の理由により、P300 は出現したが NIRS と同じ傾向を示さなかったと考えられる。

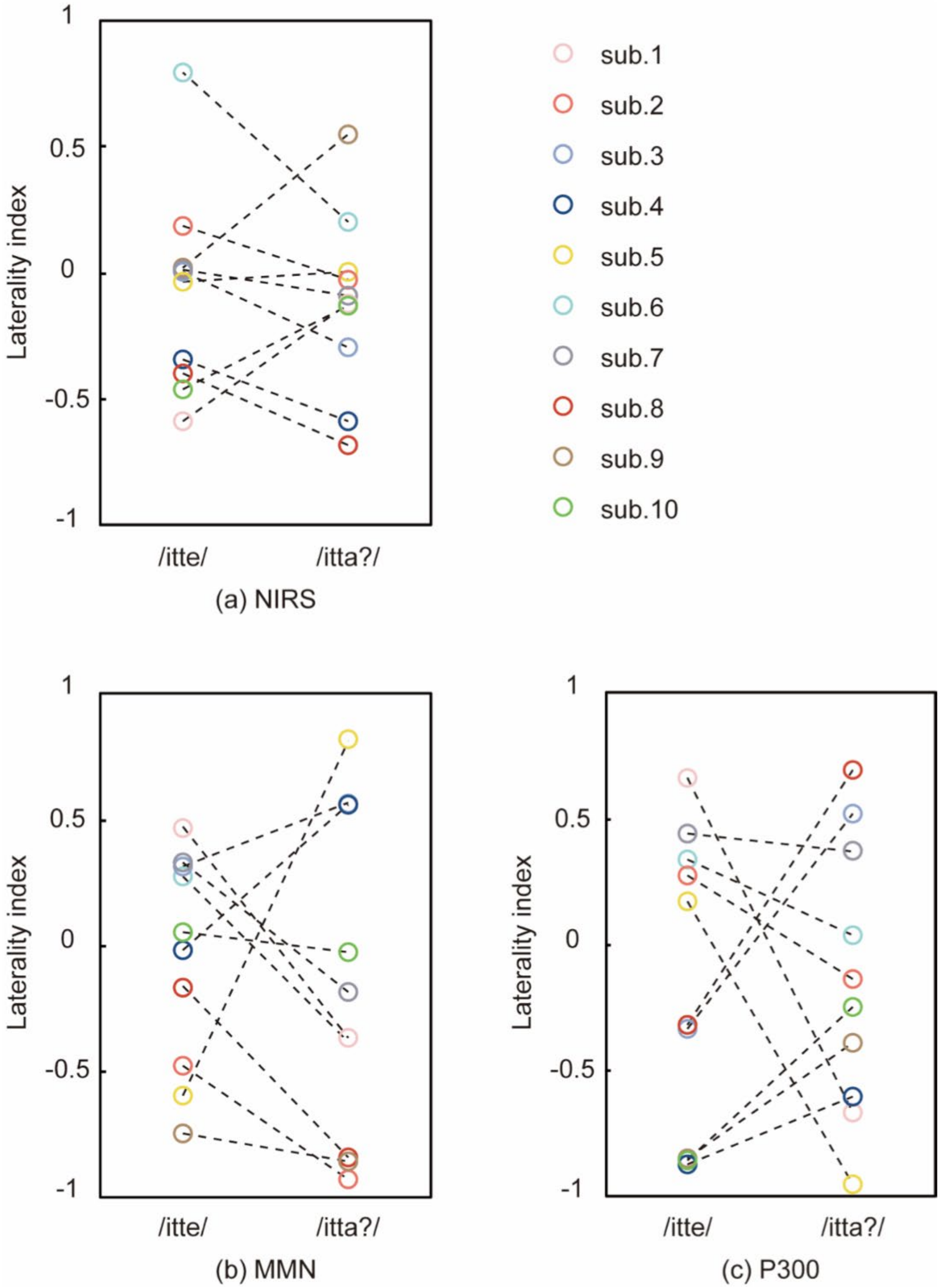


図３　側性化指数

上述の考察により、MMN は P300 よりも言語処理機能による側性化を検出できる可能性が高いことがいえる。また、脳波の総加算平均波形で現れた各 ERP の振幅の大きさを比較しても、MMN の振幅は、左側頭部では音韻の違い(/e/, /a/)に対して出現したものが抑揚の違

い(/a?/, /a/)に対して出現したものよりも大きく、右側頭部では抑揚の違い(/a?/, /a/)に対して出現したものが音韻の違い(/e/, /a/)に対して出現したものよりも大きくなったが、P300 にはその傾向が見られなかったことからも、MMN は P300 よりも言語処理機能による側性化を検出できる可能性が高いといえる。

まとめ
微小針電極を用いた脳波計測と NIRS を用いた oxy-Hb 濃度変化の計測の同時計測により、音韻と抑揚の異なる音声言語の認知処理による脳反応を観察した。本実験の結果から、微小 針電極を用いた脳波計測では NIRS 計測と比較して、高い時間分解能により、自動的な認知 処理(MMN)と意識的な認知処理(P300)を区別することができたことを示した。また、MMN は P300 よりも言語処理機能による側性化を検出できる可能性があることがわかった。

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Languages and us: Insights from MyVoice

The ultimate goal of generative linguistics is to study how our mind works, using language as a “mirror of mind” (Chomsky 1975). Given this, the general questions that should be addressed are those that address the relationship between human beings and languages. However, at least as we see it, arguments made in current linguistic debates are either extremely abstract, or too detail-oriented, so much as that they have no apparent connection to the general question of what it means for us to have language. In addition, linguists often face the problem of having difficulty in explaining what linguistics is to the “general” public. We consider these situations to be problematic.

Against this background, in this talk, we present “the MyVoice project”. In this project, we collaborate with occupational therapists and computational engineers to develop and promote the software “MyVoice”, with which ALS patients can keep communicating with their caretakers using their own voices, even after they lose the ability to speak (Kawahara et al. 2016). The most important principle that drives this activity is the importance of *individual voice*. For example, through this project, we met a young ALS mother with two small children; she is now trying her best to record those words and phrases that she will want to use with her children for years to come.

We grew up as generative linguists, and still conduct research in this framework. However, engaging in this activity has forced us to rethink what it means for human beings to communicate with friends and family through language; i.e. what it means for us to have language. This project also helps us relate our linguistic research to “real-life” activities. It also turns out that this project is extremely inspiring and could be even life-changing when used in undergraduate education.

マイボイスと大学言語学教育*

桃生朋子・川原繁人

1．はじめに

大学における言語学（または音声学）の講義に対して「とっつきにくい」「理解しにくい」などというイメージを抱いている学生は少なくない。この問題には様々な理由があると思われる。第一に言語学で使われる分析の中には、抽象度が高く、直感的な理解が難しいものが少なくない。入門の授業では時間が限られているため、言語学・音声学で使われるような概念を「なぜ」学ぶ必要があるのか、深く説明することが難しい場合もある。しかし、学生にとって、「なぜ」を理解せずに暗記させられるほど苦痛なことはない。

さらに、言語学がとっつきにくい理由のもう一つに「言語学が、どのように社会に関わっているのかが不透明である」ことが挙げられる。特に理論言語学内では社会への貢献を考える機会が少ないので、「言語学を専攻したものの、社会に全く役に立たないこの学問を勉強していいのか」と悩む学生すらいる。[1]「そんなこと（＝言語学）研究して何になるの？」と聞かれた経

* 本稿の内容は2017年に言語科学会（@京都女子大学）で発表された内容を基にしている。また本研究は、戦略的研究基盤形成支援事業「コミュニケーション行動の生涯発達研究拠点（PI: 皆川泰代）」及び第一著者への科学研究費（#26770198）の支援を受けている。マイボイスの開発に携わっている吉村隆樹氏、本間武蔵氏の両名、マイボイスを使用なさっている全ての患者様方々、マイボイスに関して素直な感想を共有してくれた学生たちに感謝いたします。

1 「学問が社会の役に立つべきか否か」という問題は、それ自体で議論しなけれ

験がある言語学者も少なくないはずである。[2]

これらの問題を受けて、本論文では、まず「マイボイス」と呼ばれる音声再生ソフトを通じて、言語学者が行なっている社会貢献を学生に明確に提示する試みを紹介する。次に、この試みによって、学生の学ぶ意欲一般を高められる可能性があることを実証的に示す。

2．マイボイスとは

マイボイスとは、神経性難病（例：ALS（Amyotrophic Lateral Sclerosis: 筋萎縮性側索硬化症））の進行などにより、自分の声を失うことになる患者様の日本語の基本モーラを、声が失われる前に録音しておき、声を失った後も自分の声で介護者様たちとコミュニケーションがとり続けられる音声再生ソ

ばならない重要な問いであり、「社会の役に立たない」＝「大学で扱う必要のない学問」ではない。しかし、現代日本では、大学は社会と密接に関わりながら機能しており、研究結果を社会に還元できるに越したことはない。特に文系科目への風当たりが強い昨今、言語学も「机上の学問」だけにとどまっていられない時代が来るかもしれない。ただし、「社会に貢献する学問」の中でも、例えば軍事産業への貢献は、最低でもしかるべき注意を持って行うべきであるし（村上 1994）、話は単純ではない。ただし、本稿で扱うマイボイスは、純粋に「社会福祉への貢献」である。また、理論言語学は、特に外部の人間から「何をやっているか分からない」と思われることが多い。文系廃止論すらある現代において、文系廃止論にただ感情的に反対するだけでなく、「言語学という学問がどういう学問であるか」を分かりやすくに発信し、身内の中での発表だけでなく、「言語学の成果をどのように社会に還元する方法があるのか」を建設的に社会に発言していくことが、これからの言語学の継続と発展に不可欠だと思われる（村上 1994, 1999）。本稿で扱うマイボイスに他に、「音声学の社会貢献」という観点から見本となるべき取り組みとしては、東京大学峯松信明教授の Online Japanese Accent Dictionary（OJAD: http://www.gavo.t.u-tokyo.ac.jp/ojad/）が挙げられる。その他の「音声学がどのように社会に貢献できるか」の議論は、川原（2015, 2017）を参照。

2　言語学の最終的な使命として「言語の分析を通して、人間の心の働きを探り (“languages as a mirror of mind”: Chomsky 1975)」、「人間とは何か」という問いを追求するという大きな目標が掲げられることがあるが、現状の理論言語学で、この目標が実証可能な形で探求されているかというと、残念ながらそれは疑わしいと感じられる。

フトである（川原他 2015, 2016a; 本間・長尾 2013; 萩原 2013; Kawahara et al. 2016、他）。このプロジェクトは、主にパソボラというボランティア団体の吉村隆樹氏と、東京都立神経病院の作業療法士である本間武蔵氏によって開発され、現在進行形で運用・改良されている。神経性の難病の患者様は、病気の後期には「意識ははっきりしているものの、体は動かず、自分の声で喋ることができない」という辛い状況に置かれる。そんな辛い状況の中で、自分の声で家族や介護者様とコミュニケーションを取り続けられるマイボイスは、多くの患者様の助けになっている。2017年現在の最新バージョンのマイボイスでは、よく使うフレーズや口癖なども簡単に登録でき、その管理も容易に出来るようになっている。この「短文再生機能」の充実により、マイボイスの有用性はますます向上している。また、開発理念として全てのソフトをフリーで公開しており、ただでさえ金銭的負担が厳しい難病患者様の助けになっている。[3]

我々は、2013年から、このマイボイス・プロジェクトに対して、様々な側面から研究協力を行なってきた。第一に、音声学・音韻論の観点から、マイボイスから再生される音声の音質改善に取り組んだ。また、言語学の学会や講演などで積極的にマイボイスの紹介を行い、言語学者からの協力を広く呼びかけている。さらに、定期的にワークショップを開き、マイボイスを使う患者様や介護者様、学生、言語学者や心理学者、作業療法士など様々な分野の人が集まってマイボイスに関する意見交換を行う場を設けている。[4] このワークショップは、ALS の患者様の間の情報交換の場にもなっている。これらの活動は学界でも認められ、2016年度には日本音声学会学術奨励賞を受賞した。

2016年3月に行われたワークショップでは、二人の幼い娘さんを持つ ALS の女性が参加してくれた。彼女は「自分の声で話すことができなくなった後も、自分の声で自分の子どもとコミュニケーションを取り続けたい」という

3　マイボイスに関する全てのソフトウェアは http://heartyladder.net/xoops から無料でダウンロードできる（Windows のみ）。

4　http://user.keio.ac.jp/~kawahara/MyVoiceMeetings.html

想いからワークショップに参加し、マイボイスでの録音を決意した。彼女は自分の声の基本モーラだけでなく、「娘さんたちへの呼びかけ」や「絵本の朗読」など多くの声を残す努力を行なっている。[5] この患者様は、ALS の進行によって、声が出しにくくなってきてしまって、「自分の言った言葉に対して、娘たちに『分からない』と言われる機会が増え、そのことが一番辛い」と述べている。しかし、そんな中でマイボイスによって再生された声を聞いた娘さんが「これで（お母さんが）疲れることなく、おしゃべりできるね」と発言したシーンは非常に印象的である。娘さんたちは母親が ALS によって発声するのも辛いことを知っている。しかし、マイボイスによって、娘さんたちがそのような気遣いをすることなく、お母さんと話し続けることができるのである。このように ALS の患者様にマイボイスの存在を周知する活動を大学で行うことには、言語研究の社会への還元という点で大きな意味を持つ。

我々は言語学入門や音声学入門の授業で、このような事例を通してマイボイスを紹介することにより、若い学生にこの「マイボイスを言語学的に補助する試み」を紹介している。医学系や看護系の学生を除けば、学生時代に医療の現場と（間接的にとは言え）接することは大きな刺激になる。実際にマイボイスを授業で紹介すると「言語学が社会に役立つことが分かった」「自分なりに社会に貢献できる道を考えてみたい」など、普段の言語学の授業では聞かれないような感想が得られる。また、「自分なりに家族の大切さ」を再確認する学生や、「大学で学ぶことの意義一般について」考え直す学生もいる（詳しくは川原他 2016b を参照）。マイボイスを題材として、卒業論文や修士論文に取り組む学生も少なくない。

川原他（2016b）では、「マイボイスが日本の言語学教育に貢献しうる」ということを、具体的な事例を引用しながら議論したが、量的な実験は行なっ

5　彼女のマイボイスとの出会い、録音の過程、家族との絆などは、長崎文化放送（NCC）の特集「自分の声を残したい」で取り上げられている（http://vod.ncctv.co.jp/2016/12/01/ 自分の声を残したい）。この患者様は学生達とも年が近く、この特集を学生たちに紹介すると、「自分の声の大事さ」「家族との絆の大切さ」が特によく伝わるようである。

ていない。よって、本稿では、「マイボイスが大学の言語学教育に有効である」であるかを吟味した予備的な実験を報告する。

３．実験

3.1. 方法

被験者である都内の大学生に対し、ドキュメンタリー番組を用いてマイボイスを紹介した後、言語学一般及び音声学・音韻論に関する講義を行い、その後実験を行った。ドキュメンタリー番組では、マイボイスによる再生音声がより自然な発音になるように奮闘する患者様や介護者様、及び「マイボイス・プロジェクト」に協力する言語学者の様子が紹介されている。講義では、日本語音声の特徴などをマイボイスに関連付けながら三週に渡って学んだ。

実験では、実験群である受講生32名に、以下の項目について５段階評価（「全くそう思わなかった」から「とてもそう思った」）を行ってもらった。質問項目は以下の通りである。

1. 「マイボイス」の授業を聞くことで、言語学や音声学を身近に感じることができた。
2. 言語学は実社会に役に立つ学問だと思った。
3. 言語学をより詳しく学びたいと思った。
4. マイボイスの講義は、日本語の音声の特徴を理解するのに役に立った。
5. 自分の声は大切だと思った。
6. 大学で学ぶことに関し、何らかの気持ちの変化があった。
7. 6. で「そう思った」または「とてもそう思った」と回答した場合、その気持ちの変化を具体的に、自由に記述してください。
8. 機会があればマイボイス・プロジェクトを手伝ってみたいと思った。

受講生にはドキュメンタリー番組の内容に関する簡単な問題も解いてもらい、不正解だった受講生のデータは、真面目に受講してなかったと判断し、

結果から除いた。統制群として、マイボイスについては知らないが、言語学概論の講義を受講したことのある同大学の学生8名に対して、同じく質問紙を使用した5段階評価を行ってもらった。統制群の学生はマイボイスに関しての紹介は行なっていないので、1-3の質問のみ回答してもらい、1の質問は「音声学をどのくらい身近に感じるか」で回答してもらった。

3.2. 結果

まず、実験群の学生のアンケート結果の平均スコアを図1に示す。

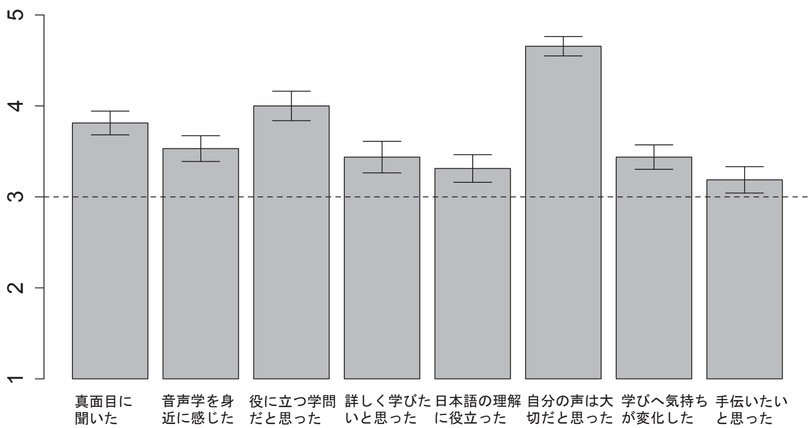

図1：マイボイスに関するアンケート結果。エラーバーは95％信頼区間。

縦軸は5段階評価の値、横軸は質問項目である。全ての質問項目において、平均値が「3：どちらでもない」を上回っており、エラーバーの下限も全ての項目で3を超えている。これは「マイボイス・プロジェクト」が学生に好意的に受け取られ、また「音声学が社会の役に立つ学問であり、身近な学問である」と感じられる題材であることを示している。また、「自分の声は大切だと思った」という質問に対しては、かなり高い値を示しており、マイボイスが学生たちに「自分の声の大切さ」を考えてもらういい機会になっていることがわかる。

また、7の質問に対する自由記述の回答例を下にあげる：

- 高校のときは数学・英語・国語などの基本的な事しかやらなかったが、前回の「マイボイス」の映像を見て改めて大学の授業は幅広くてすばらしいなと思った。
- 自分が今こうして大学で授業を受けて、発音することができるのは当たり前じゃないんだと思い直すことができました。
- 今まで声がなくなるなんて考えたことがなかったので、改めて考えるきっかけになりました。
- 概論の授業などは聞いているだけで、問題を解いたりしないでぼーっとしていることが多かったけど、マイボイスの講義を聞いて、言語学という学問に少し興味がわいたし、概論の授業もちゃんとうけなきゃと思いました。

最後の回答にあるように、マイボイスの紹介は学生の「大学の学びへの姿勢一般」にも良い影響を与えることがある。図1の「学びへの気持ちに変化があった」に対してポジティブな回答が寄せられたことも、この事実を物語っている。

次にアンケート項目1-3における実験群と統制群の比較を図2に示す。図2のすべての項目において、実験群（■ Myvoice）の方が統制群（□ Control）よりも高い値を示した。最初の二項目は統計的に有意な差が見られた（ノンパラメトリック Wilcoxon テストによる）。統制群の数が少ないため、最後の項目に関しては統計的有意差が検知されなかった。しかし、エラーバーの分布を見ると、被験者数が増えれば、統計的な有意差が期待できる効果量である。総じて、この結果は「マイボイスを学ぶことで、音声学と社会のつながりを理解し、実用的な学問であることを認識できる」ということを示している。[6]

6　今回の実験は被験者間比較であり、「二つのグループの他の要因の統制ができていなかったかもしれない」という批判があるかもしれない。現在、被験者間比較

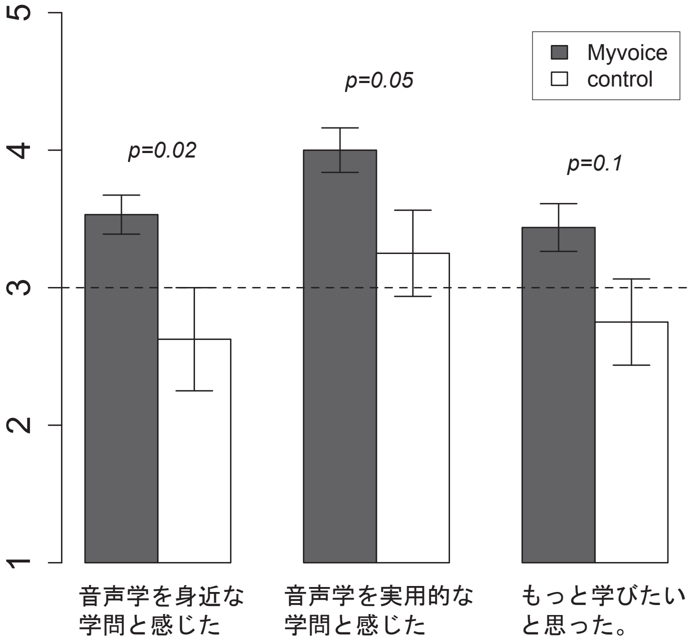

図2：実験群と統制群の比較。

4. 結辞

以上の結果から、マイボイスの紹介を通して行う言語学の講義は、受講生が持つ言語学に対する学びの動機付けに、影響すると言える。最後に、川原（2016b）で紹介しきれなかった、ある学生のマイボイスに関する声を紹介する。彼女はある大学の集中講義で、マイボイスに出会った。彼女は、「言語学に興味はなくはないものの、このような（社会の役に立たなそうな）学問を学んでいていいのか」と悩み続けながら、あまり学問に興味を持てずにいた。実際に集中講義の前半では、お世辞にもやる気のある学生とは言えなかった。しかし、マイボイスの紹介を見て、彼女の顔色は変わった。課題と

による実験も進めている。

して出した「マイボイスに取り組んでいる本間先生や吉村さんへ手紙を書く」というものの中で彼女はこう述べている：

> （今の大学に入ったのも、今の専攻を選んだのも、本意からではありませんでした。そんなわけで今まで大学の授業に関してやる気が出ませんでした。しかし…）学んでいる学問が実際に役立っている光景を目にして自分が学ぶ上でのモチベーションが変わる予感がしています。何となく興味を持てなくもないと思いながらも拒絶をしたい気持ちがありましたが、もっと意欲的に取り組んでいこうと思えました。

また、彼女は「自分の声の大切さ」に関して以下のように述べている：

> 「（母親の声は）聞けるだけで安心するし、彼氏の声を聴くだけで嬉しくなることもあるし、声は人になくてはならないものだと実感するシーンは（略）いくつも思いつきます。」

マイボイスの講義を聞いてから、彼女は音声学の授業に積極的に参加し、授業中に質問するまでになった。そして、彼女は次の年の集中講義にまた参加した。改めてマイボイスに関する映像を見て、彼女は以下のように言う：

> （去年の集中講義）から後期の授業にちゃんと出るようになって言語学と真面目に向き合うようになって、そうするとあれだけ「嫌だ、興味がない」と思っていたのに、面白くなってきたんです…私の気持ちを変えたのはマイボイスです。
>
> …
>
> 「面白そう！」と前向きに言語学、そして大学生活に取り組めているとは 1 年前マイボイスを知るまでは思いませんでした。全く関わりはないし、マイボイスを使うわけでもないのに、マイボイスの存在がある意味、私を救ってくれたと思います。（強調は筆者）

彼女は「マイボイスの話を聞いて、大学生活に対してやる気が出て、そのやる気が一年後も継続していることを伝えるために、同じ集中講義に出席した」という。

また理論言語学で大学院進学を目指す別の学生は以下のように言う：

> 今の自分の勉強が実際の生活にどう結びついているのか、またはどのようにすれば社会で役に立つのか疑問を抱く機会はこれまで何度もありました。しかし、その度に「自分の勉強している分野が社会の接点が薄いのは仕方がない」と自分に言い聞かせていました。今回マイボイスの活動を知って、何よりもそんな自分の姿勢を正されたように思います。言い訳、甘えは捨てて、自分の意志で貪欲に努力していなければ、自分が社会とどう関わっていくことになるのかも見えてこないと思います。

このような学生達の声を聞くと、「言語学者がマイボイスの手伝いをする」のではなく、「マイボイスこそが、言語学者に自分たちの研究成果を社会に還元するチャンスを与えてくれている」のだと痛感させられる。世の中の役に立つものだけが学問ではない。しかし、言語学が世の中の役に立てる機会をしっかり見つけだし、積極的にその成果を発信することは、言語学という分野の将来にとってマイナスになることではないであろう。

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乳児の社会的相互作用における随伴性に関与する脳反応

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背景・目的　乳児期の発達において他者との社会的相互作用は重要な役割を果たす。養育者は子どもに対してアイコンタクト、体を撫でる、対乳児音声（IDS）、子どもの行動に随伴した反応（随伴性反応）など、多様な社会的信号を用いた働きかけを自然に行っていることが知られており、とりわけ随伴性反応はアイコンタクトと同様に非常に強力な社会的信号であるとされている (Csibra, 2010; Hiraki, 2006)。成人と同様に乳児においても社会的刺激の処理には上側頭溝（STS）や側頭頭頂接合部（TPJ）領域が関わることが報告されているが (Lloyd-Fox et al., 2009)、実際の相互作用場面おける社会的信号に対する乳児の脳反応はまだほとんど明らかにされていない (Lloyd-Fox et al., 2015)。そこで本実験では、(1) 社会的に意味のあるポジティブな随伴性反応（Social-positive 条件）、(2) 社会的に意味のあるネガティブな随伴性反応（Social-negative 条件）、(3) 社会的に意味のない随伴性反応（Non-social 条件）に対する左右の STS-TPJ 領域の反応を、近赤外線分光法（fNIRS）を用いて計測した。

方法　18 名の 6−8 ヶ月児が実験に参加した。実験者である成人女性が乳児の前で IDS による話しかけを行いながら人形または絵本を呈示した。3 つの条件ごとに独立に計測を行ったため、各参加児につき最大で 3 セッションの計測を行った。各実験はブロックデザインを用い、1 種類のターゲット条件（Social-positive 条件/ Social-negative 条件/ Non-social 条件）がベースライン条件と交互に複数回呈示された。ターゲット条件の時間は 20 秒とし、ベースライン条件の時間は、20 秒または 25 秒であった。ターゲット条件では実験者は乳児と目があったら即座に条件別の特定の反応（Social-positive 条件：笑いかけ、Social-negative 条件：顔をそらす、Non-social 条件：実験者の頭につけたデバイスを白く点灯）を行った。ベースライン条件では、実験者は同様に乳児の顔を見ながら IDS による話しかけと視覚刺激の呈示を行ったが、乳児と目が合った場合は約 3 秒後に反応した。つまり、ベースライン条件において実験者は即時的な随伴性反応は行わなかった。fNIRS 計測では□3×5 の 22 チャンネルのプローブを左右の側頭部に 1 つずつ配置し、プローブ間隔は 2 cm とした。

結果・考察　実験の結果、Social-positive 条件において rTPJ 領域（pSTS または角回）でベースラインからの有意な oxy-Hb の増加が認められた（図 1）（注、本実験はまだ進行中であり、結果は予備的なものであることから、多重比較の補正は行っていない）。さらに、母親との自由遊び場面において母親の顔を見る頻度がより高い乳児は、Social-positive 条件における rTPJ 領域の活動の増加量がより大きい傾向にあることが示され、乳児においても、他者の心的状態に対する敏感さと右の TPJ 領域の活動には関連があることが示唆された。Social-negative 条件では、両側頭部においてベースラインからの有意な oxy-Hb の増加は認められなかった。Non-social 条件においては、左右の TPJ 領域でベースラインからの有意な活動の増加が認められた（図 2）。しかし、Non-social 条件において oxy-Hb の増加が見られたチャンネルは、Social-positive 条件とは位置が若干異なっており、TPJ 領域の前方（pSTS または縁上回）に位置していた。成人を対象とした先行研究より、同じ TPJ 領域内でも場所によって機能が分化している可能性が指摘されており (Carter & Huettel, 2013; Kubit & Jack, 2013)、本実験の結果は、TPJ 領域における機能分化が、6-8 ヶ月乳児において既に成人と同様に発達していることを示唆するものとなった。

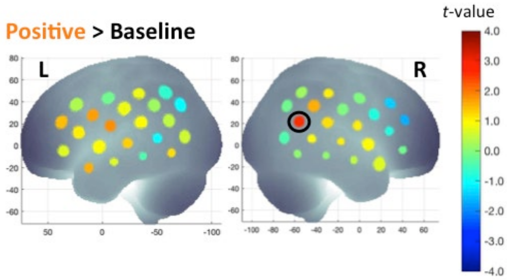

図 1. Social-positive 条件におけるベースライン条件からの oxy-Hb 濃度の変化量を表した *t*-map。丸印は有意な活動の増加が見られたチャンネルを表す。

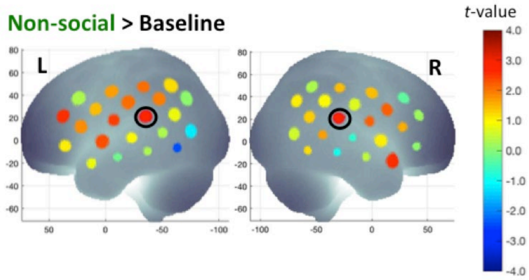

図 2. Non-social 条件におけるベースライン条件からの oxy-Hb 濃度の変化量を表した *t*-map。丸印は特に活動の増加が大きかったチャンネルを表す。

Which is a better digital textbook format for students with low vision for daily learning situations: reflowable or fixed?

Session C Oral Presentations ”Reading” - Oral

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Background

According to previous studies, a reflowable format like the web page is easier to use than a fixed format like PDF. They used text-only materials to conduct experiments in these studies. But ordinary textbooks consist not only of texts but also tables, figures, and structural explanations. If the layouts of these structures were also given importance in the textbooks, the students would also use the fixed format. Considering these reasons, we conducted comparative research on both data formats used for daily learning situations.

Methods

To compare the usage of both formats, a new browser application was developed which could easily switch between the reflowable and the fixed format depending on the user’s needs. 167 high school students with low vision participated in this research. They were provided with the application along with 210 digital textbooks. They were instructed to use these digital textbooks for daily learning at classroom and home during the 11 months of trial. Each and every item of operational data by each student was automatically recorded by the application. The operational data was analyzed to determine which format is more suitable for participants.

Results

105 valid responses were gathered from 167 students. The usage rate of the fixed format was 52.4% whereas, the reflowable format was only 8.6%. 55,383 valid operational data from 56 students were collected. The rate of operational data of the fixed format was 89.8% whereas, the reflowable format was only 10.2%. The fixed format was used more often in daily learning.

Significance

Although previous research suggested that the reflowable format was effective for people with low vision, the fixed format was used more often in daily learning from this research. The advantage of data format might depend on the content and structure of the books.

日本ロービジョン学会誌　18：106–120，2018.

ロービジョンの生徒のための教科書閲覧アプリの開発（2）

―閲覧アプリ iBooks と UD ブラウザがデジタル教科書の利用実態に及ぼす影響―

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Journal of Japanese Society for Low-vision Research and Rehabilitation

ロービジョンの生徒のための教科書閲覧アプリの開発（2）

－閲覧アプリ iBooks と UD ブラウザがデジタル教科書の利用実態に及ぼす影響－

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Development of a Textbook Browser Application for Students with Low Vision (2)

– Comparison between Actual Usage of iBooks or UD Browser Apps to Read a Digital Textbook –

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緒言：本研究の目的は，閲覧アプリがデジタル教科書の利用実態に及ぼす影響を検討することであった。紙媒体の教科書と盲学校でよく利用されている二つの閲覧アプリ（iBooks と UD ブラウザ（B））を比較した。

方法：最初に全国の盲学校から協力校を募集した。その結果，15 校の協力校と 75 人のロービジョン（LV）生徒の協力が得られた。次に，希望に基づいて閲覧アプリとデジタル教科書を提供した。7 カ月間の試用の後，アンケート調査を実施した。

結果：iBooks と UDB の二つの閲覧アプリを比較した結果，UDB を利用する方が，デジタル教科書の利用率が向上し，学習意欲などの学習効率も向上させることが明らかになった。UDB が iBooks と比較してデジタル教科書の閲覧に適しているのは，LV 生徒の視認性や操作性が高かったためだと考えられる。

結論：デジタル教科書の利用実態は閲覧アプリによって異なることがわかった。

（日本ロービジョン学会誌　18：106―120，2018）

キーワード：ロービジョン，拡大教科書，デジタル教科書，タブレット端末，iPad

Purpose：To compare actual usage by students in schools for the blind of 2 popular browser applications (apps), iBooks and UD Browser.

Methods：We recruited participants from designated schools for the blind from all over Japan to participate in our study. A total of 75 students from 15 designated schools consented to participate in the research. We then asked each student's teacher about the student's digital textbook needs and provided the participating students and their teachers with both digital reading apps (iBooks and UD Browser) and the digital textbooks the teachers had specified. We asked the students to use either browser to read the digital textbooks. After 7 months, we surveyed students via questionnaire to determine if using a digital app helped motivate them to read textbooks, which app they preferred, and why they preferred one app over the other.

Results：The answers to survey questions showed that students were more often motivated to read digital textbooks using UD Browser vs iBooks. We determined that this was due to the digital textbooks being easier to see using UD Browser and that the students found UD Browser to be more user-friendly than iBooks.

Conclusions：We found that actual usage of digital textbooks was affected by the features of the browser application used for digital reading.

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Key Words：Low Vision, Large-Print Textbook, Digital Textbook, Tablet Personal Computer, iPad

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緒　言

教育における情報化が進展するなかで，児童生徒の学びを質・量両面から向上させるため，学びの手段や学習環境としてのInformation and Communication Technology（以下 ICT）の将来性・可能性を見据えて，教科書へのICTの活用の在り方について検討が求められている[1]。ICTの活用のなかで，とくに注目されているのはデジタル教科書であり，2015年5月の教育再生実行会議第七次提言において，「教科書のデジタル化の推進に向けて，教科書制度の在り方や，それに応じた著作権の在り方などの課題についての専門的な検討を行う」とされた。また，2015年6月に閣議決定された日本再興戦略においても，「いわゆる「デジタル教科書」の位置付けおよびこれに関連する教科書制度の在り方について専門的な検討を行い，来年中に結論を得る」とされた。

デジタル教科書に関しては様々な定義があるが，大別すると，指導者用デジタル教科書と学習者用デジタル教科書の2種類に分けられる[2]。指導者用デジタル教科書とは，指導者である教員が電子黒板などにより子どもたちに提示して指導する集団学習用のデジタル教科書である。これに対して，学習者用デジタル教科書は，学習者である児童生徒が個別に利用するデジタル教科書である。「学びのイノベーション事業」[2]においては，学習者用デジタル教科書を，単に紙媒体の教科書の内容がそのままあらわされるだけではなく，音声の再生，動画，拡大などの機能に加え，インターネットの活用，教員と子どもたちまたは子どもたち同士の間の双方向性のある授業，ネットワークを介した書き込みの共有，教員による子どもたちの学習履歴の把握，子どもたちの理解度に応じた演習や家庭・地域における自学自習などに資するものだと定義していた。しかし，文部科学省初等中等教育局教科書課による『「デジタル教科書」の位置付けに関する検討会議の最終まとめ』（以下「文部科学省の最終まとめ」）では，学習者用デジタル教科書は，紙媒体の教科書と学習内容が同一であることが必要であると再定義された[1]。

中野ら[3]は，紙媒体の教科書と内容が同じデジタル教科書を作成し，視覚障害特別支援学校の高等部に在籍するロービジョン生徒（以下 LV生徒）を対象に，紙媒体の拡大教科書の比較を行った。その結果，LV生徒にとって「見る対象に応じて拡大率を変更できること，かさばらないので持ち運びや机上作業が楽であること，辞書検索や読み上げ機能があること，持ち帰りが楽なこと，目が疲れないこと，ページがめくりやすくて使いやすいこと，細かい図も拡大できること，図を見やすく拡大してもきれいに表示されること，拡大教科書よりも図が見やすいこと，白黒反転ができること」がデジタル教科書のメリットであったと述べている。一方で，デジタル教科書のデメリットの一つとして，「目が疲れる，書き込みができない，見たい場所を探すのが難しい」ことを挙げ，その原因としてデジタル教科書を閲覧（ブラウザ）するアプリ（以下 閲覧アプリ）として用いたアップル社製の「iBooks」（iPad上でPDFデータを閲覧するための標準アプリ）の視認性や操作性に問題があった可能性を指摘した。そして，中野ら[4]は，iBooksの問題点を解決するために，新しい閲覧アプリ「UD（ユニバーサルデザイン）ブラウザ」（以下 UDB）を開発し，iBooksと機能の比較を行った結果，UDBの方が視認性・操作性の観点で優れていることを確認した。しかし，UDB版のデジタル教科書の利用率は，紙媒体の教科書よりも低かったことを報告している。また，UDB版デジタル教科書の利用率が高くなかった理由として「アプリが異常終了したり，表示が乱れたりなど，動作が不安定になる割合が高かったことや速度が遅いこと」が原因だったのではないかと考察している。更に，LV生徒のニーズ調査の結果に基づき，デジタル教科書には書き込み機能と文章の読み上げ機能が必要であることを指摘している。

中野ら[4]の指摘が正しければ，デジタル教科書が授業において利用されるかどうかは，閲覧アプリの安定性や機能などによって決まると考えられる。そこで本研究では，紙媒体の教科書と内容が同一である学習者用デジタル教科書を用い，7カ月という比較的長期間の試用を通して，閲覧アプリの安定性や機能などがデジタル教科書の利用実態などに及ぼす影響を検討した。また，UDBの利用率を向上させるために必要な機能などについて調査を実施した。

方　法

1．概　要

「文部科学省の最終まとめ」[1]に基づく学習者用デジタル教科書は，紙媒体と教科書の内容が同一でなければならない。現在，障害のある児童生徒に利用可能な学習者用デジタル教材には，（公財）日本障害者リハビリテーション協会の「マルチメディアデイジー教科書」[5,6]（http://www.dinf.ne.jp/doc/daisy/book/server_download.html），東京大学先端科学技術研究センターの「AccessReading（アクセス・リーディング）」（https://accessreading.org），認定NPO法人EDGE（エッジ）の「音声教材BEAM」，慶應義塾大学の「PDF（Portable Document Format）版拡大図書（教科書）（以下 PDF版拡大教科書）」[3,4]があるが，紙媒体と教科書の内容が同一なのは，「PDF版拡大教科書」のみであった。そこで，デジタル教科書のデータ形式は「PDF版拡大教科書」にした。「PDF版拡大教科書」が利用できる閲覧アプリは，アップル社製の「iBooks」と慶應義塾大学中野泰志研究室製の「UDB」のみであったため，本研究では，この二つの閲覧アプリを比較した。

被験者の選定にあたっては，最初に，本研究の趣旨を理解し，学校全体で本研究に協力可能な視覚障害特別支援学校（以下　協力校）を募集した。次に，応募のあった協力校に対して，上述の2種類の閲覧アプリを紹介した上で，利用を希望する閲覧アプリを選択させた。そして，高等部に在籍し高等学校の教科書を利用して学年相当の教科学習を行っているLV生徒およびその保護者に対して書面でインフォームドコンセントを行った上で，被験者の募集を行った。協力校には，被験者が希望する教科のPDF版拡大教科書をタブレット型情報端末（以下　タブレット端末）にインストールして提供した。タブレット端末は，生徒1人に2台提供し，1台は生徒自身が，もう1台は当該生徒を指導する教員が利用できるようにした。PDF版拡大教科書は2015年6月に提供し，7カ月間，授業や家庭学習で自由に活用させた。その後，2016年2月に，閲覧アプリとPDF版拡大教科書の利用状況や視認性・操作性などについて郵送方式のアンケート調査を実施した。なお，本研究は，慶應義塾大学研究倫理委員会の審査を受けた上で計画・実施し，学校長，担当教員，生徒，保護者の合意を得た上で実施した。

2．提供したデジタル教科書システム

1）タブレット端末

タブレット端末には，視覚障害特別支援学校（以下　盲学校）で最も利用されているiPad（Apple社製のiPad Air WiFi 32GBモデルMD786J/A，OSはiOS8）を用いた。

2）iBooks

iBooksは，アップル社が無償で提供している電子書籍閲覧アプリである。iBooksには，電子書籍に効果的にアクセスするために，ピンチ操作による画面の拡大，ブックマーク，ラインマーク，手書き文字の書き込みなどの機能がある。またiBooksは，「固定型レイアウト（フィックス型レイアウト）」であるPDFにも，「リフロー型レイアウト」であるEPUB（国際電子出版フォーラムが策定したオープンフォーマットの電子書籍ファイルフォーマット規格）にも対応している。EPUBデータを用いれば，書体，配色，文字サイズなどを変更して表示させることが可能であるが，デジタル教科書のEPUBデータは存在しないため，本研究ではPDF版のデジタル教科書を用いた。なお，本研究で利用したiBooksは，バージョン3であった。

iBooks用のデジタル教科書は，教科書発行者から提供を受けた教科書デジタルデータ[3]を編集・加工して作成した透明テキスト付きPDFファイルであった。作成した教科書は，国語10種類，地理歴史12種類，公民3種類，数学7種類，理科7種類，保健体育2種類，芸術9種類，外国語12種類，家庭4種類，情報2種類の合計68種類で，総ページ数は14,457ページであった。なお，iBooksでは横書きの文章を想定しているため，ページをめくる際には，右から左にスワイプする仕様になっている。しかし，国語のような縦書きの教科書の場合，左から右にスワイプする動作の方が自然である。そこで，縦書きの教科書の場合には，ページの順番を逆転させ，左から右にスワイプする動作でページめくりができるようにした。また，検索性を向上させるために，目次をタッチするだけで，当該単元にジャンプできるようにハイパーリンクの設定を行った。

3）UDB

UDBは，LV生徒のニーズに基づいて開発された教科書や教材などを閲覧するためのアプリである[4]。LV生徒の利用を想定し，メインメニューやポップアップメニューの視認性，ページジャンプ機能やスクロール補助機能による操作性が考慮されている。また，デジタル教科書の条件である紙の教科書と同じレイアウトを保持しつつ，リフロー表示も可能なハイブリッド表示機能を有している。なお，本研究で利用したUDBのバージョンは，中野ら[4]が指摘した「アプリが異常終了したり，表示が乱れたりなど，動作が不安定になる割合が高かったことや速度が遅い」という問題点を修正し，書き込み機能と読み上げ機能を搭載したバージョン1.0.1であった。

UDB用のデジタル教科書には，iBooks用に作成したアクセシブルPDFファイルに加え，教科書の本文をリフロー型レイアウトで表示するためのHTMLファイルも用意した。

3．調　査

1）被験者

全国盲学校長会を通して全国の盲学校に研究協力を呼びかけた結果，15校の盲学校から承諾が得られた。デジタル教科書を閲覧するアプリは，各協力校の希望に基づいて決定した。その結果，iBooksを選択した学校が7校（以下　iBooks利用者群），UDBを選択した学校が5校（以下　UDB利用者群），両方を選択した学校（以下　iBooks・UDBの両方の利用者群）が3校であった。学校長を通して，研究の趣旨などを説明した上で協力校の高等部普通科に在籍するLV生徒に協力を依頼した結果，LV生徒75人（iBooks利用者25人，UDB利用者20人，iBooksとUDBの両方の利用者30人）およびその生徒達の授業を担当している教員181人（iBooksを利用している生徒の担当73人，UDBを利用している生徒の担当81人，iBooksとUDBの両方を利用している生徒の担当27人）の協力を得た。

2）デジタル教科書の試用

閲覧アプリにiBooksを選択した協力校にはiBooks用のデジタル教科書1種類を，UDBを選択した協力校にはUDB用のデジタル教科書1種類を，そして，両方を選択した協力校にはiBooks用のデジタル教科書とUDB用のデジタル教科書の2種類を提供した。デジタル教科書は，各生徒が履修しているすべての教科であった。なお，デジタル教科書を閲覧するためのiPadはLV生徒には一人一台提供した。また，授業を担当する教員にも生徒と同じデジタル教科書をインストールしたiPadを提供した。

LV 生徒の課題は，紙媒体の教科書と同様にデジタル教科書を授業や家庭学習で必要に応じて利用し，使いやすさを比較することであった。対象生徒の担当教員の課題は，生徒が希望する場合にはデジタル教科書を活用した授業を実施し，生徒の活用状況を把握することであった。なお，必要に応じてデジタル教科書やタブレット端末の利用方法に関する研修会を実施した。試用期間は，2015 年 6 月～2016 年 2 月までであった。

3）アンケート調査

試用期間終了後，当該生徒と学校に対してアンケート調査を実施した。LV 生徒に対するアンケートは，担当教員が生徒にヒアリングをして回答する方式をとった。主な質問項目は，視力などの見え方，iPad の利用方法，使用している教科書ごとの紙媒体やデジタル教科書（iBooks，UDB）の利用状況，UDB の視認性・操作性や改良点などであった。なお，アンケート調査は 2016 年 2 月 6 日～3 月 4 日に実施した。

結　　果

1．回収率

1）iBooks のみを利用した生徒

25 人中 18 人から有効回答が得られた（回収率 72.0%）。性別は男子が 11 人，女子が 7 人で，学年は 1 年生が 7 人，2 年生が 4 人，3 年生が 7 人であった。

2）UDB 利用のみを利用した生徒

20 人中 17 人から有効回答が得られた（回収率 85.0%）。性別は男子が 12 人，女子が 5 人で，学年は 1 年生が 6 人，2 年生が 5 人，3 年生が 6 人であった。

3）iBooks と UDB の両方を利用した生徒

30 人中 24 人から有効回答が得られた（回収率 80.0%）。性別は男子が 12 人，女子が 12 人で，学年は 1 年生が 5 人，2 年生が 12 人，3 年生が 7 人であった。

4）協力校

15 校中 15 校から有効回答が得られた（回収率 100.0%）。iBooks を利用した協力校は 7 校，UDB を利用した協力校は 5 校，iBooks と UDB の両方を利用した協力校は 3 校であった。

2．利用者の視機能

1）iBooks 利用者群

表 1 に被験者ごとの眼疾患，主な視機能（両眼もしくは良い方の目の小数視力，羞明，夜盲，視野狭窄，中心暗点，暗点，色覚異常，眼球振盪の有無），利用している主なアクセシビリティ機能を示した。小数視力を対数変換して平均を求め，逆変換した平均小数視力は 0.08 であった。

2）UDB 利用者群

表 1 に被験者ごとの眼疾患，主な視機能（両眼もしくは良い方の目の小数視力，羞明，夜盲，視野狭窄，中心暗点，暗点，色覚異常，眼球振盪の有無），利用している主なアクセシビリティ機能を示した。小数視力を対数変換して平均を求め，逆変換した平均小数視力は 0.10 であった。

3）iBooks・UDB の両方の利用者群

表 1 に被験者ごとの眼疾患，主な視機能（両眼もしくは良い方の目の小数視力，羞明，夜盲，視野狭窄，中心暗点，暗点，色覚異常，眼球振盪の有無），利用している主なアクセシビリティ機能を示した。小数視力を対数変換して平均を求め，逆変換した平均小数視力は 0.09 であった。

4）利用者群による視機能の差

iBooks 利用者群，UDB 利用者群，iBooks・UDB の両方の利用者群で視力に偏りがなかったかどうかを検討するために，小数視力を対数に変換し一元配置分散分析を行った。その結果，F (2,56)＝0.35，p＝0.705 であり，利用者群間に有意差はみられなかった。利用者群間で，視力以外の見えにくさに差があるかどうかをフィッシャーの正確確率検定で検討した結果，羞明（p＝0.571），夜盲（p＝0.688），視野狭窄（p＝0.081），中心暗点（p＝0.916），中心以外の暗点（p＝0.053），色覚異常（p＝0.906），眼球振盪（p＝0.620）のいずれも有意差はみられなかった。

3．教科別の教科書利用状況とデジタル教科書を利用しない理由

表 2 に利用者群ごとの教科別教科書利用状況とデジタル教科書を利用しなかった理由を示した。

利用者群別，教科別にメディアの利用状況を分析した結果，デジタル教科書の利用率は，iBooks 利用者群で 60 冊（43.2%），UDB 利用者群で 87 冊（60.4%），iBooks・UDB の両方の利用者群で 145 冊（71.8%）であった。紙媒体の利用率の方が高かった教科は iBooks 利用者群の国語と数学のみで，それ以外の条件・教科では，デジタル教科書の利用率の方が高いことがわかった。

デジタル教科書を利用せず紙媒体を利用した教科で，その理由を調べた。iBooks 利用者群では「アプリの使い勝手が悪い」が 13 人（23.6%），「使いたくない」が 1 人（1.8%），「先生らの方針」が 24 人（43.6%），「その他」（「書き込みができないから」「紙の方が見開きで表示できるので見やすい」など）が 14 人（25.5%）であった。UDB 利用者群では「アプリの使い勝手が悪い」が 8 人（16.0%），「使いたくない」が 0 人（0.0%），「先生らの方針」が 3 人（6.0%），「その他」（「授業で教科書を利用しなかった」など）が 37 人（74.0%）であった。iBooks・UDB の両方の利用者群では「アプリの使い勝手が悪い」が 10 人（9.0%），「使いたくない」が 5 人（4.5%），「先生らの方針」が 52 人（46.8%），「その他」（「紙に慣れている」「授業で教科書を使うことが少ない」「問題の位置がわかりにくい」など）が 31 人（27.9%）であった。iBooks 利用者群と iBooks・UDB の両方の利用者群では，「先生らの方針」で利用しなかったというケースが最も多く，UDB 利用者群では「その他」が

表１　利用者群別の被験者の主な視機能，アクセシビリティ機能の使用状況

利用者群	No	眼疾患	主な視機能：良い眼の小数視力	羞明	夜盲	視野狭窄	中心暗点	暗点	色覚異常	眼球振盪	利用している主なアクセシビリティ機能：白黒反転	より大きな文字	文字を太くする	コントラストを上げる	明るさの調整
iBooks利用者群	1	未熟児網膜症	0.1												使用
	2	レーベル病	0.05	あり			あり	あり				使用	使用		
	3	滲出性硝子体網膜症	0.3			あり									使用
	4	視神経萎縮	0.1			あり					使用				使用
	5	コロボーマ	0.04	あり		あり		あり	あり		使用	使用			
	6	視神経萎縮	0.08												
	7	小角膜，前眼部ぶどう膜欠損，瞳孔偏位，脈絡膜欠損	0.05											使用	使用
	8	小眼球，両角膜新生血管，両眼内反症	0.1	あり							使用			使用	使用
	9	心因性	0.04	あり							使用	使用	使用		使用
	10	多発性硬化症	0.08											使用	使用
	11	不明	0.08	あり		あり		あり			使用	使用	使用	使用	使用
	12	無虹彩症，白内障	0.1	あり	あり			あり		あり	使用	使用	使用	使用	
	13	視神経萎縮	0.1				あり	あり	あり		使用	使用			使用
	14	未熟児網膜症	0.1	あり	あり	あり		あり				使用	使用		
	15	視神経萎縮，先天眼振	0.1				あり					使用	使用		使用
	16	網膜色素変性症，眼球振盪症	0.07	あり	あり	あり	あり	あり	あり	あり	使用		使用	使用	使用
	17	視床下部星細胞腫（中枢神経性）	0.1									使用	使用		
	18	網膜剥離，緑内障	0.03												
		小計		8	3	6	4	7	3	2	8	9	8	6	11
UDB利用者群	1	白内障	0.06	あり		あり									
	2	白子眼	0.2	あり	あり						使用		使用		使用
	3	眼球振盪症，内斜視，近視性乱視，弱視，両眼視機能障害	0.4	あり						あり		使用			使用
	4	網膜色素変性症	0.8	あり	あり	あり						使用			使用
	5	両黄斑低形成，先天性眼振	0.1	あり	あり										使用
	6	両無水晶体眼，両外斜視	1.2		あり	あり						使用			
	7	水晶体混濁	0.04		あり	あり								使用	使用
	8	先天性による視力障害	0.07	あり			あり		あり						
	9	白内障	0.15	あり		あり		あり							
	10	緑内障	0.2			あり		あり			使用				使用
	11	レーベル病	0.01	あり			あり	あり							使用
	12	無虹彩症	0.1	あり											
	13	白内障，黄斑変性症，ぶどう膜炎，飛蚊症	0.1	あり				あり			使用				使用
	14	未熟児網膜症	0.01			あり			あり		使用				
	15	網膜色素変性症	0.09												
	16	黄斑部低形成症	0.06												
	17	レーベル病	0.03				あり		あり			使用	使用		使用
		小計		10	5	7	3	4	3	1	4	4	2	1	9
iBooks・UDBの両方の利用者群	1	視神経萎縮	0.04							あり		使用			使用
	2	白皮症関連	0.1	あり								使用			使用
	3	レーベル病	0.04	あり	あり	あり	あり	あり	あり			使用	使用		使用
	4	眼球振盪症	0.1												使用
	5	網膜色素変性症	0.06				あり					使用	使用	使用	使用
	6	無虹彩症	0.04	あり						あり					
	7	網膜剥離，家族性滲出性硝子体網膜症，網脈絡膜萎縮	0.1									使用	使用		使用
	8	未熟児網膜症	0.1	あり	あり	あり					使用	使用	使用	使用	使用
	9	視野欠損	0.3					あり							使用
	10	スティーブンスジョンソン症候群	0.15							あり		使用	使用	使用	使用
	11	未熟児網膜症	0.3	あり	あり										使用
	12	眼球振盪症，先天性内斜視	0.1						あり						
	13	精神性	0.3	あり											使用
	14	緑内障，虹彩炎	0.1									使用			
	15	レーベル病	0.02				あり								使用
	16	眼球振盪症，小角膜，虹彩コロボーマ，強度近視性乱視，強度混合乱視	0.06	あり											使用
	17	無虹彩症，白内障，黄斑変性症，眼球振盪症	0.1												使用
	18	無虹彩症，白内障	0.25												
	19	網膜脈絡膜脳回転性異常症，網脈絡膜萎縮	0.08												
	20	緑内障，未熟児網膜症	0.15		あり	あり									
	21	視神経低形成	0.15							あり					使用
	22	眼球振盪症，遠視性乱視，弱視	0.15	あり					あり						使用
	23	未熟児網膜症，	0.2	あり	あり										使用
	24	視神経萎縮	0.02	あり	あり		あり				使用	使用	使用		
		小計		10	6	3	4	2	3	4	2	9	6	3	17
		合計		28	14	16	11	13	9	7	14	22	16	10	37

表には，各被験者の主な視機能（両眼もしくは良い方の目の小数視力，羞明，夜盲，視野狭窄，中心暗点，暗点，色覚異常，眼球振盪の有無），利用している主なアクセシビリティ機能（白黒反転，より大きな文字，文字を太くする，コントラストを上げる，明るさの調整）を，利用者群別に示した。なお，視機能は学校が把握している資料に基づいて調査した。なお，利用している主なアクセシビリティ機能は，ピンチアウトでの拡大以外に利用している機能であった

表 2　利用者群別の教科別教科書利用状況とデジタル教科書を利用しなかった理由

利用者群	教科	利用した教科書の種類 紙媒体	デジタル	紙・デジタル両方	無回答	計	デジタル教科書を利用しない理由 使い勝手が悪いから	使いたくないから	先生らの方針だから	その他
iBooks利用者群	国語	10	6	8	0	24	3	0	5	4
	地理歴史	1	10	3	2	16	0	0	2	2
	公民	2	4	3	0	9	0	0	1	1
	数学	14	6	2	0	22	4	1	5	2
	理科	1	10	6	0	17	0	0	0	1
	保健体育	3	6	0	0	9	1	0	1	0
	芸術	2	2	2	0	6	2	0	2	0
	外国語	6	10	4	1	21	2	0	4	3
	家庭	4	6	1	0	11	1	0	4	1
	情報	0	0	4	0	4	0	0	0	0
	小計	43	60	33	3	139	13	1	24	14
	割合（%）	30.9	43.2	23.7	2.2	100.0	23.6	1.8	43.6	25.5
UDB利用者群	国語	8	12	2	0	22	1	0	0	7
	地理歴史	6	11	2	0	19	2	0	0	6
	公民	0	6	0	0	6	0	0	0	0
	数学	7	9	2	0	18	2	0	1	4
	理科	7	10	3	0	20	2	0	0	6
	保健体育	4	7	1	0	12	0	0	0	3
	芸術	0	8	0	0	8	0	0	1	0
	外国語	9	13	2	0	24	1	0	1	7
	家庭	3	5	0	0	8	0	0	0	3
	情報	1	6	0	0	7	0	0	0	1
	小計	45	87	12	0	144	8	0	3	37
	割合（%）	31.3	60.4	8.3	0.0	100.0	16.0	0.0	6.0	74.0
iBooks・UDBの両方の利用者群	国語	8	24	7	0	39	3	1	3	5
	地理歴史	2	12	1	0	15	0	0	16	7
	公民	1	7	2	0	10	0	0	2	0
	数学	10	20	1	0	31	1	3	2	4
	理科	3	19	2	0	24	0	1	3	2
	保健体育	3	15	2	0	20	1	0	2	2
	芸術	0	1	0	0	1	0	0	18	0
	外国語	7	28	2	0	37	5	0	0	2
	家庭	3	10	1	0	14	0	0	0	8
	情報	0	9	2	0	11	0	0	6	1
	小計	37	145	20	0	202	10	5	52	31
	割合（%）	18.3	71.8	9.9	0.0	100.0	9.0	4.5	46.8	27.9

表には，授業で主として利用した教科書を教科別，利用者群別に示した。また，デジタル教科書を利用しなかった場合の理由（複数回答あり）を示した。
iBooks 利用者群では，数学と国語は，紙媒体の利用している割合が高かったが，他の教科ではデジタル教科書を利用しているケースの方が多かった。デジタル教科書を利用しなかった理由としては，「先生らの方針だから」という回答が多く，「使い勝手がわるいから」，「使いたくないから」というデジタル教科書の機能などの問題が原因であるケースは多くなかった。
UDB 利用者群では，すべての教科でデジタル教科書を利用しているケースの方が多かった。デジタル教科書を利用しなかった理由としては，「その他」（「授業で教科書を利用しなかった」など）という回答が多く，「使い勝手がわるいから」，「使いたくないから」というデジタル教科書の機能などの問題が原因であるケースは多くなかった。
iBooks・UDB の両方の利用群では，UDB 利用者群と同様すべての教科でデジタル教科書を利用しているケースの方が多かった。デジタル教科書を利用しなかった理由としては，「先生らの方針だから」という回答が多く，「使い勝手がわるいから」，「使いたくないから」というデジタル教科書の機能等の問題が原因であるケースは多くなかった

最も多いことがわかった。

表 3 に，iBooks・UDB の両方の利用者群において，iBooks と UDB のどちらをより多く利用していたかを調べた結果を示した。iBooks は 26 人（10.8%），UDB は 214 人（89.2%）で，圧倒的に UDB の利用率の方が高かった。教科別に比較しても，すべての教科で UDB の利用率は 8 割以上であった。

4．デジタル教科書を利用し始めて起こった行動の変化

表 4 にデジタル教科書を利用し始めて起こった行動の変化を利用者群別に示した。利用者群による差を検討するために，「非常に増えた（上がった）」に 2 点，「やや増えた（上がった）」に 1 点，「変わらない」に 0 点，「やや減った（下がった）」に−1 点，「非常に減った（下がった）」に−2

表 3　iBooks・UDB の両方の利用者群における教科別閲覧アプリの利用状況

教科	iBooks 人数(人)	iBooks 割合(%)	UDB 人数(人)	UDB 割合(%)	計 人数(人)
国語	4	9.5	38	90.5	42
地理歴史	2	7.1	26	92.9	28
公民	2	18.2	9	81.8	11
数学	3	9.4	29	90.6	32
理科	3	10.3	26	89.7	29
保健体育	2	9.5	19	90.5	21
芸術	1	14.3	6	85.7	7
外国語	6	15.4	33	84.6	39
家庭	1	6.7	14	93.3	15
情報	2	12.5	14	87.5	16
計	26	10.8	214	89.2	240

表には，iBooks と UDB の両方の閲覧アプリを利用した各被験者が，iBooks と UDB のどちらの閲覧アプリを多く利用したのかを教科別に示した。すべての教科で UDB を利用した被験者の方が多かった

表4　利用群別のデジタル教科書を利用し始めて起こった学習行動などの変化

		iBooks 利用者群 (n=18)		UDB 利用者群 (n=17)		iBooks・UDB の両方の利用者群 (n=24)		平均 (増減率)
		人数(人)	比率(%)	人数(人)	比率(%)	人数(人)	比率(%)	
勉強時間	非常に増えた	0	0.0	1	5.9	1	4.2	0.32
	やや増えた	1	5.6	8	47.1	7	29.2	
	変わらない	17	94.4	7	41.2	16	66.7	
	やや減った	0	0.0	1	5.9	0	0.0	
	非常に減った	0	0.0	0	0.0	0	0.0	
	増減率	0.06		0.53		0.38		
成績	非常に上がった	0	0.0	0	0.0	0	0.0	0.18
	やや上がった	3	16.7	3	17.6	6	25.0	
	変わらない	14	77.8	14	82.4	18	75.0	
	やや下がった	1	5.6	0	0.0	0	0.0	
	非常に下がった	0	0.0	0	0.0	0	0.0	
	増減率	0.11		0.18		0.25		
学習意欲	非常に増えた	2	11.1	1	5.9	1	4.2	0.63
	やや増えた	6	33.3	11	64.7	12	50.0	
	変わらない	10	55.6	5	29.4	11	45.8	
	やや減った	0	0.0	0	0.0	0	0.0	
	非常に減った	0	0.0	0	0.0	0	0.0	
	増減率	0.56		0.76		0.58		
視覚補助具の利用頻度	非常に増えた	0	0.0	0	0.0	0	0.0	−0.47
	やや増えた	0	0.0	1	5.9	0	0.0	
	変わらない	9	50.0	8	47.1	18	75.0	
	やや減った	6	33.3	4	23.5	4	16.7	
	非常に減った	2	11.1	3	17.6	2	8.3	
	増減率	−0.56		−0.53		−0.33		
拡大教科書の利用頻度	非常に増えた	0	0.0	0	0.0	1	4.2	−0.90
	やや増えた	1	5.6	0	0.0	0	0.0	
	変わらない	7	38.9	7	41.2	4	16.7	
	やや減った	6	33.3	4	23.5	5	20.8	
	非常に減った	4	22.2	6	35.3	11	45.8	
	平均増減率	−0.72		−0.94		−1.04		
平均（増減率）		−0.11		0.00		−0.03		

表には，デジタル教科書を利用し始めて起こった学習行動など（勉強時間，成績，学習意欲，視覚補助具の利用頻度，拡大教科書の利用頻度）の変化を利用者群別に示した。各学習行動などの増減を比較するために，「非常に増えた（上がった）」に2点，「やや増えた（上がった）」に1点，「変わらない」に0点，「やや減った（下がった）」に−1点，「非常に減った（下がった）」に−2点で得点化し，平均得点を求め増減率とした。増減率はプラスの値だと行動などが増加したことを，マイナスの値だと減少したことを示す。「勉強時間」，「成績」，「学習意欲」は利用者群にかかわらずすべて増加しており，「視覚補助具の利用頻度」と「拡大教科書の利用頻度」はすべて減少していた

点で得点化し，平均得点を求めて増減率とした（増減率はプラスの値だと増加したことを，マイナスの値だと減少したことを示す）。

「勉強時間」，「成績」，「学習意欲」は，利用者群にかかわらずすべて増加していることが明らかになった。一方，「視覚補助具の利用頻度」と「拡大教科書の利用頻度」は，すべて減少したことが明らかになった。

活動別に増減率を比較すると，「学習意欲」(0.63)，「勉強時間」(0.32)，「成績」(0.18)，「視覚補助具の利用頻度」(−0.47)，「拡大教科書の利用頻度」(−0.90）の順であった。

利用者群別に増減率を比較すると，「勉強時間」と「成績」と「学習意欲」の平均はUDB利用者群（0.49)，iBooks・UDBの両方の利用者群（0.40)，iBooks利用者群（0.24）の順で，「視覚補助具の利用頻度」と「拡大教科書の利用頻度」の平均はiBooks利用者群（−0.64)，iBooks・UDBの両方の利用者群（−0.69)，UDB利用者群（−0.74）の順であった。UDB利用者群では「勉強時間」・「成績」・「学習意欲」が最も増加し，「視覚補助具」や「拡大教科書」の利用頻度が最も減少することがわかった。利用者群間の増減率の差を分散分析で検定した結果，有意な差があったのは「勉強時間」($F(2,56)=3.46$, $p=0.038$）のみであった。TukeyHSDで多重比較を行った結果，UDB利用者群とiBooks利用者群の間のみに有意差（$p=0.035$）が認められた。

5．デジタル教科書の継続利用希望

デジタル教科書に関する継続利用希望の必要度を調べるために，「今後も（在学中)，iPadを使い続けたいと思いますか？」「卒業した後もiPadで読書をし続けたいと思いますか？」「ブラウザを今後も使い続けたいと思いますか？」という質問をした結果を図1に示した。利用者群による差を検討するために，「非常に思う」に2点，「やや思う」に1点，「あまり思わない」に−1点，「全く思わない」に−2点で得点化し，平均得点を求め必要度とした（必要度は，−2〜+2の値をとり，値が大きいほど継続利用の必要性が高いことを示す)。

「今後も（在学中)，iPadを使い続けたいと思いますか？」という質問に対する利用者群ごとの継続利用の必要度を比較した結果，iBooks利用者群が1.44，UDB利用者群が1.41，iBooks・UDBの両方の利用者群が1.88で，いずれ

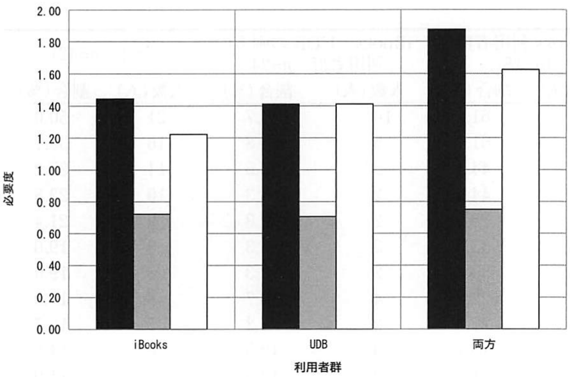

図１　利用者群別のデジタル教科書等の継続利用の必要度
図には，「iPad やデジタル教科書を今後（在学中）も使い続けたいか」，「iPad やデジタル教科書を卒業後も使い続けたいか」，「当該閲覧アプリを使い続けたいか」という質問に対する回答を利用者群別に示した。継続利用の必要性を比較するために，「非常に思う」に２点，「やや思う」に１点，「あまり思わない」に−１点，「全く思わない」に−２点で得点化し，平均得点を求め必要度とした。必要度は，−２〜＋２までの値をとり，値が大きいほど継続利用の必要性が強いことを，値が小さいほど継続利用の必要性が弱いことを示す。在学中の継続利用の必要度は高かった。また，閲覧アプリの継続希望に関しては，iBooks よりもユニバーサルデザインブラウザ（UDB）の利用者群の方が高かった。
■：在学中，使い続けたい，▩：卒業後も使い続けたい，□：当該閲覧アプリを使い続けたい

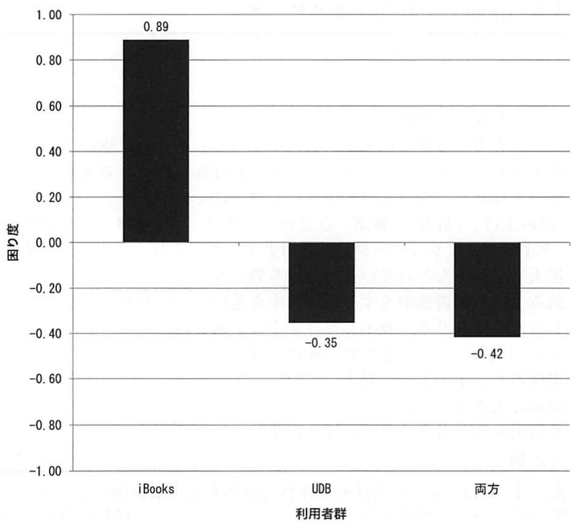

図２　紙媒体の教科書がなくなり，デジタル教科書だけになった際の困り具合
図には，紙媒体の教科書がなくなり，デジタル教科書だけになった際の困り具合を利用者群別に示した。困り具合を比較するために，「非常に困る」に２点，「やや困る」に１点，「あまり困らない」に−１点，「全く困らない」に−２点で得点化し，平均得点を求め困り度とした。困り度は−２〜＋２の値をとり，値が大きいほど紙媒体がなくなると困ることを，値が小さいほど紙媒体がなくなっても困らないことを示す。iBooks 利用者は紙媒体がなくなると困る割合が多かったが，UDB 利用者は紙媒体がなくなると困ると回答した割合が少なかった。

も比較的高い値であった。

「卒業した後も iPad で読書をし続けたいと思いますか？」という質問に対する利用者群ごとの継続利用の必要度を比較した結果，iBooks 利用者群が 0.72，UDB 利用者群が 0.71，iBooks・UDB の両方の利用者群が 0.75 とほぼ同程度であり，在学中の継続よりは必要度が低いことがわかった。

「ブラウザを今後も使い続けたいと思いますか？」という質問に対する利用者群ごとの継続利用の必要度を比較した結果，iBooks 利用者群が 1.22，UDB 利用者群が 1.41，iBooks・UDB の両方の利用者群が 1.63 といずれも継続の必要度が高いことがわかった。iBooks よりも UDB の利用者の方が継続の必要度が高い傾向があったが，分散分析の結果（$F(2,54)=0.56$，$p=0.577$），有意な差は認められなかった。

６．紙媒体の教科書との併用の必要性

デジタル教科書と紙媒体の教科書を併用する必要性について調べた結果を，利用者群ごとに整理し図２に示した。利用者群による差を検討するために，「非常に困る」に２点，「やや困る」に１点，「あまり困らない」に−１点，「全く困らない」に−２点で得点化し，平均得点を求め困り度とした（困り度は−２〜＋２の値をとり，値が大きいほど，紙媒体がなくなると困ることを，値が小さいほど，紙媒体がなくなっても困らないことを示す）。

iBooks 利用者群は 0.89 と紙媒体の必要性が高かったのに対して，UDB 利用者群では−0.35，iBooks・UDB の両方の利用者群では−0.42 で紙媒体との併用の必要性が低くなっていることがわかった。利用者群間の困難度の差を分散分析で検定した結果，$F(2,51)=5.45$，$p=0.007$ であった。TukeyHSD で多重比較を行った結果，iBooks 利用者群と UDB 利用者群（$p=0.029$），iBooks 利用者群と iBooks・UDB の両方の利用者群（$p=0.01$）に有意な差が認められた。

７．iBooks と UDB の使いやすさの比較

UDB と iBooks の両方のブラウザ・アプリを利用した経験のある UDB 利用者群と iBooks・UDB の両方の利用者群に iBooks と UDB の使いやすさを比較させた結果を分析した。利用者群による差を検討するために，「UDB の方が使いやすいととても思う」に２点，「UDB の方が使いやすいとまあまあ思う」に１点，「UDB の方が使いやすいとあまり思わない」に−１点，「UDB の方が使いやすいと全く思わない」に−２点で得点化し，平均得点を求め UDB の使いやすさ度とした（UDB の使いやすさ度は値が高いほど，UDB の方が使いやすいと思っていることを示す）。

UDB の使いやすさ度は，UDB 利用者群が 1.29，iBooks・UDB の両方の利用者群が 1.63 で，分散分析では有意な差は認められなかった（$F(1,38)=2.27$，$p=0.14$）が，iBooks・UDB の両方を利用している利用者の方が高い値を示した。iBooks・UDB の両方の利用者群では，常時，二つの閲覧アプリを比較しているため，その差が明確になったのではな

表 5　iBooks の視認性・操作性の課題

	iBooks 利用者群 (n=18)		iBooks・UDB の両方の利用者群 (n=24)		合計 (n=42)	
	人数(人)	割合(%)	人数(人)	割合(%)	人数(人)	割合(%)
ページを探すのが難しい	11	61.1	10	41.7	21	50.0
ページをめくる度に拡大率がもとに戻ってしまうので使いにくい	11	61.1	5	20.8	16	38.1
拡大すると，左右にスクロールしなければならないので大変	8	44.4	3	12.5	11	26.2
辞書を検索した際の文字が小さくて見えにくい	8	44.4	2	8.3	10	23.8
「読み上げ」「辞書」「検索」などのポップアップするメニューが見えにくい	7	38.9	2	8.3	9	21.4
「ライブラリ」や「ページ」などの上下に表示されるメニューが見えにくい	6	33.3	2	8.3	8	19.0
拡大して行をたどっていると気持ち悪くなる	6	33.3	2	8.3	8	19.0
読み上げや辞書検索をする際に文字を選択するのが難しい	4	22.2	4	16.7	8	19.0
しおりを挟んだり，表示したりするのが難しい	5	27.8	2	8.3	7	16.7
音声で読み上げさせるための操作が難しい	3	16.7	3	12.5	6	14.3
書棚の表示が小さくて見えにくい	2	11.1	3	12.5	5	11.9
画面の大きさが小さい	4	22.2	0	0.0	4	9.5
教科書を切り替えるための操作が難しい	0	0.0	1	4.2	1	2.4
その他	3	16.7	7	29.2	10	23.8

表には，iBooks の視認性や操作性の課題を利用者群別に示した。「ページを探すのが難しい」，「ページをめくる度に拡大率がもとに戻ってしまうので使いにくい」，「拡大すると，左右にスクロールしなければならないので大変」，「辞書を検索した際の文字が小さくて見えにくい」，「「読み上げ」「辞書」「検索」などのポップアップするメニューが見えにくい」などを課題として選択した利用者が多かった

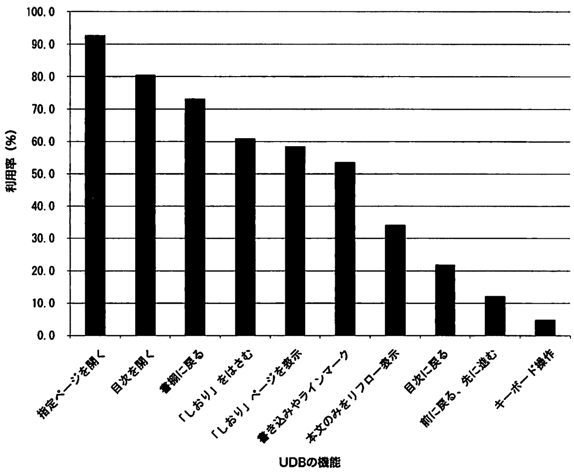

図 3　UDB で利用している機能
図には，生徒が利用している UDB の機能を利用者群別に示した。「指定したページを開く」，「目次を開く」，「書棚に戻る」，「「しおり」をはさむ」，「「しおり」をはさんだページを表示する」，「教科書に書き込みやラインマークができる」の利用率が高かった。

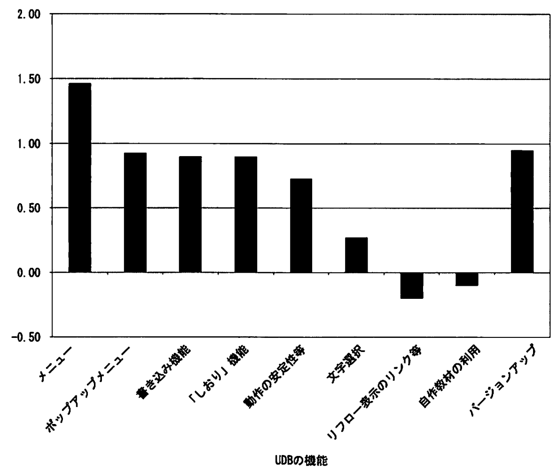

図 4　UDB の各機能に対する満足度
図には，UDB の各機能に対する満足度を利用者群別に示した（「とても思う」に 2 点，「まあまあ思う」に 1 点，「あまり思わない」に−1 点，「全く思わない」に−2 点で得点化し，平均得点を求めて満足度とした）。「メニューの見やすさ」，「バージョンアップの効果」，「ポップアップメニューの見やすさ」，「書き込み機能」の満足度は高かった。一方，「リフロー表示のハイパーリンクや白黒反転表示など」，「自作教材の利用」に関しては満足度が低かった。

いかと考えられる。

8．iBooks の視認性・操作性の課題

iBooks 利用者群と iBooks・UDB の両方の利用者群に対して，iBooks の視認性や操作性に関する課題を質問した結果を表 5 に示した。指摘が多かった順に列挙すると「ページを探すのが難しい」(50.0%)，「ページをめくる度に拡大率がもとに戻ってしまうので使いにくい」(38.1%)，「拡大すると，左右にスクロールしなければならないので大変」(26.2%)，「辞書を検索した際の文字が小さくて見えにくい」(23.8%)，「「読み上げ」「辞書」「検索」などのポップアップするメニューが見えにくい」(21.4%) などであった。

9．UDB で利用されている機能と課題

UDB 利用者群と iBooks・UDB の両方の利用者群に対して，UDB の主要な機能の利用状況を質問した結果を図 3 に示した。利用率が高かった機能は，「指定したページを開く」(92.7%)，「目次を開く」(80.5%)，「書棚に戻る」(73.2%)，「「しおり」をはさむ」(61.0%)，「「しおり」をはさんだページを表示する」(58.5%)，「教科書に書き込みやラインマークができる」(53.7%) であった。

UDB の主要な機能に対する満足度を質問した結果を図 4 に示した（「とても思う」に 2 点，「まあまあ思う」に 1 点，「あまり思わない」に−1 点，「全く思わない」に−2 点で得点化し，平均得点を求めて満足度とした）。「メニューの見

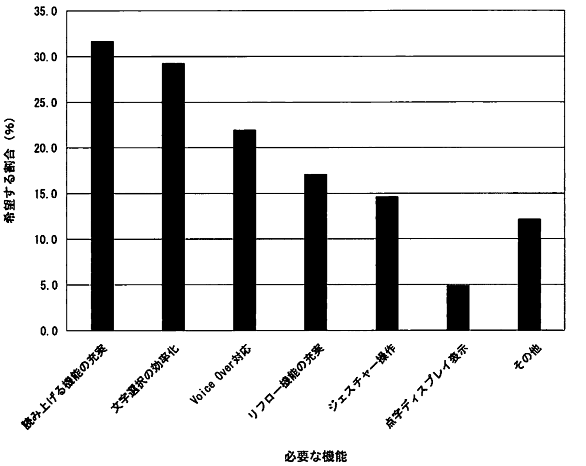

図5　UDBのバージョンアップに期待する機能
図には，UDBにバージョンアップに期待する機能を利用者群別に示した。「本文を音声で読み上げる機能を充実して欲しい」，「辞書検索等のための文字選択が楽になるようにして欲しい」，「Voice Overに対応して欲しい」，「リフロー拡大の機能を充実して欲しい」という要望が高かった。

やすさ」(1.46)，「バージョンアップの効果」(0.95)，「ポップアップメニューの見やすさ」(0.93)，「書き込み機能」(0.90)，「しおり機能」(0.90) の満足度は高かった。一方，「リフロー表示のハイパーリンクや白黒反転表示など」(−0.20)，「自作教材の利用」(−0.10) に関しては満足度が低いことがわかった。

UDBの今後のバージョンアップに期待する機能を質問した結果を図5に示した。「本文を音声で読み上げる機能を充実して欲しい」(31.7%)，「辞書検索などのための文字選択が楽になるようにして欲しい」(29.3%)，「VoiceOverに対応して欲しい」(22.0%)，「リフロー拡大の機能を充実して欲しい」(17.1%) という要望が高いことがわかった。また，その他として，書き込み機能の充実や音声の読み上げ速度調節などの要望があった。

10. 協力校における全体としての評価と課題

協力校の教員に対して，協力校におけるデジタル教科書に対する評価（生徒にとっての有用性，教材としての有用性），管理上の課題，普及・啓発の効果（校内の理解，保護者の理解）について質問した結果を表6に示した（「とても思う（たくさんあった）」に2点，「まあまあ思う（少しあっ

表6　協力校におけるデジタル教科書に対する評価，管理上の課題，普及・啓発の効果

		iBooks 利用協力 (n=7)		UDB 利用協力校 (n=5)		iBooks・UDBの両方の利用協力校 (n=3)		合計 (n=15)	
		学校数	割合(%)	学校数	割合(%)	学校数	割合(%)	学校数	割合(%)
生徒にとって有用だったか？	とても思う	5	71.4	4	80.0	2	66.7	11	73.3
	まあまあ思う	2	28.6	1	20.0	1	33.3	4	26.7
	あまり思わない	0	0.0	0	0.0	0	0.0	0	0.0
	全く思わない	0	0.0	0	0.0	0	0.0	0	0.0
	有用度	1.71		1.80		1.67		1.73	
教材として有用だったか？	とても思う	5	71.4	3	60.0	2	66.7	10	66.7
	まあまあ思う	2	28.6	2	40.0	1	33.3	5	33.3
	あまり思わない	0	0.0	0	0.0	0	0.0	0	0.0
	全く思わない	0	0.0	0	0.0	0	0.0	0	0.0
	有用度	1.71		1.60		1.67		1.67	
管理上の課題	たくさんあった	0	0.0	1	20.0	0	0.0	1	6.7
	少しあった	3	42.9	2	40.0	1	33.3	6	40.0
	あまりなかった	3	42.9	2	40.0	2	66.7	7	46.7
	全くなかった	1	14.3	0	0.0	0	0.0	1	6.7
	課題度	−0.29		0.40		−0.33		−0.07	
全国に広げるべきか？	とても思う	5	71.4	4	80.0	2	66.7	11	73.3
	まあまあ思う	2	28.6	1	20.0	1	33.3	4	26.7
	あまり思わない	0	0.0	0	0.0	0	0.0	0	0.0
	全く思わない	0	0.0	0	0.0	0	0.0	0	0.0
	普及必要度	1.71		1.80		1.67		1.73	
校内の理解は広がったか？	とても思う	1	14.3	0	0.0	1	33.3	2	13.3
	まあまあ思う	5	71.4	4	80.0	1	33.3	10	66.7
	あまり思わない	1	14.3	1	20.0	1	33.3	3	20.0
	全く思わない	0	0.0	0	0.0	0	0.0	0	0.0
	普及度	0.86		0.60		0.67		0.73	
保護者の理解は広がったか？	とても思う	0	0.0	0	0.0	1	33.3	1	6.7
	まあまあ思う	6	85.7	3	60.0	2	66.7	11	73.3
	あまり思わない	1	14.3	2	40.0	0	0.0	3	20.0
	全く思わない	0	0.0	0	0.0	0	0.0	0	0.0
	普及度	0.71		0.20		1.33		0.67	

表には，協力校におけるデジタル教科書に対する評価（生徒にとっての有用性，教材としての有用性），管理上の課題，普及・啓発の効果（校内の理解，保護者の理解）を利用者群別に示した（「とても思う（たくさんあった）」に2点，「まあまあ思う（少しあった）」に1点，「あまり思わない（あまりなかった）」に−1点，「全く思わない（全くなかった）」に−2点で得点化し，平均得点を求め，有用度，普及度，普及必要度，課題度とした）。生徒にとっての有用度，教材としての有用度は高かったが管理上の課題は低かった。また，全国に広げるべきという必要度は高かったが，校内全体や保護者への普及度は低かった

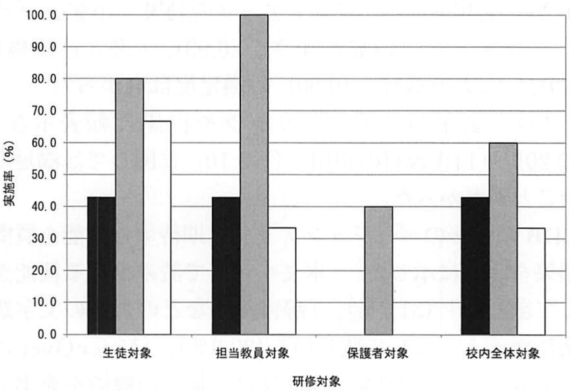

図6　協力校における研修実施状況
図には，協力校における研修（生徒対象，担当教員対象，保護者対象，校内全体対象）の実施状況を利用者群別に示した。生徒や教員を対象とした研修を実施している学校は比較的多かったが，校内全体や保護者を対象にした研修は少なかった。
■：iBooks，▒：UDB，□：両方

た)」に1点，「あまり思わない（あまりなかった）」に−1点，「全く思わない（全くなかった）」に−2点で得点化し，平均得点を求め，有用度，普及度，普及必要度，課題度とした)。生徒にとっての有用度（1.73），教材としての有用度（1.67）は高く，一方，管理上の課題（−0.07）は低かった。全国に広げるべきという必要度（1.73）は高かったが，校内全体（0.73）や保護者（0.67）への普及度は十分ではなかった。

協力校における研修（生徒対象，担当教員対象，保護者対象，校内全体対象）の実施状況について質問した結果を図6に示した。生徒対象（60.0%），教員対象（60.0%）を実施している学校は比較的多かった（生徒対象，担当教員対象の研修会を実施しなかった学校は前年度までに研修を実施済みであった）が，校内全体対象（46.7%）や保護者対象（13.3%）の研修は少なかった。デジタル教科書の普及度と研修の関係を分析したところ，研修を実施した学校の普及度が高いことがわかった。

デジタル教科書に対する自由記述では，「データ流出に対するセキュリティ対策が心配である」，「機器の故障などを考え，紙媒体と併用できるようにして欲しい」，「全盲の生徒も利用できるようにして欲しい」，「ピンディスプレイに対応して欲しい」，「VoiceOverで使用したい」，「生徒が所有している個人端末でも利用できるようにして欲しい」，「UDBの安定性を更に向上させて欲しい」，「リフローモードでゴシック体などの見やすいフォントが選択できるようにして欲しい」，「通常の高等学校でも使えるようにして欲しい」，「小学生や中学生にも使えるようにして欲しい」，「生徒が書き込んだデータをバックアップできるようにして欲しい」，「タブレット端末をゲームなどに利用されてしまうのではないかという懸念がある」，「すべての教員に普及できていない」，「デジタル教科書を使用することに抵抗がある教員がいた」などの意見があった。

考　按

本研究では，紙媒体の教科書と内容が同一である学習者用デジタル教科書を用い，閲覧アプリがデジタル教科書の利用実態に及ぼす影響を検討した。そのために，15校の協力校のLV生徒75人，担当教員181人を得て，7カ月間，異なる閲覧アプリ（iBooksとUDB）でデジタル教科書を試用させ，その間の利用実態などをアンケート調査で明らかにした。アンケートの回収率は78.7%と高く，視力などの視機能の差がない三つの利用者群から利用実態などのデータを集めることができた。iBooksとUDBを比較した結果，UDBを利用する方がデジタル教科書の利用率が向上し，学習意欲などの学習効率も向上させることが明らかになった。

以下，閲覧アプリがデジタル教科書の利用実態，学習行動，紙媒体との併用の必要性にどのような影響を及ぼしているかを考察した。その上で，デジタル教科書の利用を促進するための閲覧アプリの機能や今後の課題について考察した。

1．閲覧アプリによるデジタル教科書の利用率の違い

閲覧アプリの利用率を比較した結果，iBooksよりもUDBの利用率の方が高い傾向があることがわかった。この傾向は，iBooks・UDBの両方の利用者群において，iBooksとUDBのどちらをより多く利用していたかを調べた結果，圧倒的にUDBの利用率の方が高かったことからも支持された。なお，デジタル教科書の利用率が教科の特性と関係があるかどうかを調べたところ，紙媒体の利用率の方が高かった教科はiBooks利用者群の国語と数学のみで，それ以外の教科では，デジタル教科書の利用率の方が高いことがわかった。iBooksで国語と数学の利用率が低かった原因としては，教科書への書き込みができない点が考えられる。例えば，国語では段落の区切りに印をつけるという活動が行われたり，数学では図形に補助線を入れるという活動が行われたりすることが多い。これらの結果から，デジタル教科書には閲覧だけでなく，書き込みができる機能が必要であると考えられる。

閲覧アプリの安定性・機能などがデジタル教科書の利用率に与える影響を別の観点から比較するために，UDB ver.1.0を利用した中野ら[4]の研究の結果と安定性を向上させ，書き込み機能と音声読み上げ機能を追加したUDB ver.1.0.1を利用した本研究の結果を比較した。中野ら[4]の研究では，LV生徒38人が利用した合計447冊の教科書のうち，UDBを利用したケースは103冊（23.0%）にとどまっていた。これに対して，UDB ver.1.0.1を利用した本研究では，UDB利用者群で144冊中87冊（60.4%），iBooks・

UDBの両方の利用群で202冊中145冊（71.8%）がUDBを利用していた。そのため，アプリの安定性・機能などがデジタル教科書の利用率を向上させたと考えられる。

現在，障害のある児童生徒が利用できる閲覧アプリには，本研究で比較したiBooksやUDB以外にも，「いーリーダー」などのマルチメディアデイジー再生アプリ[5,6]，マイクロソフトワードに「読み上げアドオンソフトWordTalker」(https://www.est.co.jp/epub/word/help）や「読み上げソフト 和太鼓（Wordaico)」(http://www.geocities.jp/jalpsjp/wordaico/wordaico.html）をインストールして利用する方法などがある。本研究の結果，閲覧アプリによってデジタル教科書の利用率が異なることがわかったため，これらほかの閲覧アプリとの利用率を比較することが今後の課題であることがわかった。また，本研究の結果，同じ閲覧アプリでも教科によって利用率が異なることもわかった。教科による差が教科の特性なのか，それとも，その教科を教えている教員の特性なのかについて，今後更なる研究が必要だと考えられる。

2．閲覧アプリによる学習行動などの違い

デジタル教科書を利用し始めて起こった学習行動の変化を調べた結果，学習意欲，勉強時間，成績が向上し，視覚補助具や拡大教科書の必要性が低下することがわかった。また，閲覧アプリとの関係を分析した結果，UDB利用者群の方がiBooks利用者群よりも学習意欲，勉強時間，成績を向上させ，視覚補助具や拡大教科書の必要性を低下させる効果があることがわかった。つまり，閲覧アプリにかかわらずデジタル教科書を利用することで，利用者の学習意欲などの学習行動は変化するが，その効果は閲覧アプリによって異なっており，iBooksよりもUDBの方が大きい傾向があることが明らかになったのである。

デジタル教科書の効果は，今後も使い続けたいかどうかという継続利用行動にも影響することがわかった。デジタル教科書を継続して利用したいかどうかを調べた結果，在学中は使い続けたいという回答がどの利用者群でも多かった。また，在学中の継続利用希望よりも低かったが，卒業した後もタブレット端末で読書をし続けたいと思う生徒も多いことがわかった。継続利用に対する希望は閲覧アプリによって異なっており，iBooks利用者群よりも，UDB利用者群の方が継続して使いたいという傾向が強いことがわかった。UDBは高等学校を卒業した後，大学などに進学した後でも引き続き利用しているケースがあり，アプリの利用方法などに関する相談が寄せられている。相談では，様々な書籍をUDBで利用するための方法や自分自身で書籍などを私的複製する方法に関する質問が多い。現在，障害のある児童生徒に利用可能な学習者用デジタル教材には，「マルチメディアデイジー教科書」[5,6]，「AccessReading」，「音声教材BEAM」などがあるが，いずれも障害のある児童生徒が自分自身で教材を作成することは容易ではない。一方，UDBはPDFに対応しているため，データを入手しやすいし，スキャナーを利用して自分自身で作成することも容易である点に特徴がある。

3．利用率を向上させるために閲覧アプリに必要な機能

UDBと比較してiBooksの利用率が低かったり，学習行動などへの影響が小さかったり，紙媒体との併用の必要性が高かったりする理由を分析するために，iBooksの視認性や操作性に関する課題を調べた。書き込みができないという問題点に加え，「ページを探すのが難しい」，「ページをめくる度に拡大率がもとに戻ってしまうので使いにくい」，「拡大すると，左右にスクロールしなければならないので大変」，「辞書を検索した際の文字が小さくて見えにくい」，「「読み上げ」「辞書」「検索」などのポップアップするメニューが見えにくい」という課題があることが明らかになった。

UDBは，iBooksの主な課題を解決するために設計[4]されているため，iBooksよりも視認性や操作性が優れていると予想される。そこで，UDBの機能の利用状況と満足度を調べた。その結果，「指定したページを開く」，「目次を開く」，「書棚に戻る」，「「しおり」をはさむ」，「「しおり」をはさんだページを表示する」，「教科書に書き込みやラインマークができる」という機能の利用率が高かった。また，「メニューの見やすさ」，「バージョンアップの効果」，「ポップアップメニューの見やすさ」，「書き込み機能」の満足度が高かった。一方，「キーボード操作」や「リフロー表示」の利用率は低く，「リフロー表示のハイパーリンクや白黒反転表示など」，「自作教材の利用」に関しては満足度が低かった。今後，「キーボード」操作などの機能を充実させると同時に，これらの機能の必要性を再検討したり，効果的な利用方法に関する理解・啓発活動を行ったりする必要があると考えられる。

UDBの今後のバージョンアップに期待する機能としては，「本文を音声で読み上げる機能を充実して欲しい」，「辞書検索などのための文字選択が楽になるようにして欲しい」，「VoiceOverに対応して欲しい」，「リフロー拡大の機能を充実して欲しい」という要望が高かった。現在，本文の読み上げは，選択した範囲を読み上げる機能だけである。そのため今後は，文章単位，段落単位，ページ単位で読み上げるなどの機能が必要だと考えられる。また，辞書検索などを行う際には当該箇所を指で長押しする必要があるが，選択された範囲が適切でない場合には範囲を変更しなければならない。目と手の協応動作が苦手なLV生徒にとって，選択範囲変更は困難な課題だと考えられる。そのため今後は範囲選択や範囲変更が容易にできるようにする必要があると考えられる。VoiceOverは，iOSに標準装備されている音声読み上げ機能である。現在のUDBは，VoiceOverに部分的にしか対応できていない。そのため，今後はUDBのすべての機能をVoiceOverで利用できるようにする必要

がある。UDBのリフロー機能は本文の文章を読むための役割として設計されており，最低限の機能しか搭載されていない。そのため，今後はPDF表示モードと同様に辞書検索やページ・ジャンプができる機能などを搭載すると同時に，リフロー表示の特徴を活かすことができる機能（フォント・文字間・行間隔等の変更など）を付加していく必要があると考えられる。

その他，協力校に対するアンケートの自由記述には，「データ流出に対するセキュリティ対策が心配である」，「ピンディスプレイに対応して欲しい」，「生徒が所有している個人端末でも利用できるようにして欲しい」，「リフローモードでゴシック体などの見やすいフォントが選択できるようにして欲しい」，「生徒が書き込んだデータをバックアップできるようにして欲しい」，「タブレット端末をゲームなどに利用されてしまうのではないかという懸念がある」という意見があった。これらの要望や懸念に対応できる機能も必要だと考えられる。

4．デジタルよりも紙媒体の教科書が利用される理由

デジタル教科書の利用率を利用者群別に分析した結果，いずれの利用者群でも紙媒体よりも高い利用率を示していることがわかった。デジタル教科書を使わず紙媒体を利用したケースについて，その理由を調べた結果，閲覧アプリが使いにくかったり，紙媒体の方を好んだりするケースよりも，「先生らの方針」や「その他」の理由で紙媒体を選択せざるを得なかったケースの方が多いことがわかった。つまり，デジタル教科書が選択されなかったケースでも，デジタル教科書の機能そのものが原因だったケースは多くないことが明らかになった。なお，「先生らの方針」や「その他」の内容については詳細な理由が記載されていなかったが，「授業では教科書を利用していない」，「教科書ではなくプリントなどの自作教材を使っている」，「実技系の科目なので，教科書そのものを利用しない」などが挙げられていた。今回のアンケート調査は，担当教員がヒアリング形式でLV生徒に質問していることもあったためか，先生がタブレット端末の活用方法に詳しくないために，授業で積極的にデジタル教科書を利用していないという回答はなかった。しかし，協力校に対するアンケートの自由記述のなかに，「すべての教員に普及できていない」，「デジタル教科書を使用することに抵抗がある教員がいた」という意見があった。また，担当教員への研修は比較的実施されていたが，校内全体を対象とした研修を実施している学校は少なかった。更に，デジタル教科書に関する教員研修や相談で協力校を訪問した際に，教員がデジタル教科書の利用方法や指導方法などに熟知していないと授業で活用することが困難だという指摘があった。ユネスコのパリ行動計画では，メディア教育において教員が主導的な役割を果たすことを求めている[7,8]。しかし，日本ではICTに関する教員研修体制はいまだ確立されていない[9]。とくに，特別支援教育においては，生徒の障害特性に合わせたアクセシビリティ機能などの活用方法に関する知識・技術も必要になるため，研修体制の確立が急務の課題だと考えられる。

5．紙媒体との併用に対するニーズ

デジタル教科書と紙媒体の教科書を併用する必要性について調べた結果，iBooks利用者群は紙媒体の必要性が高かったのに対して，UDB利用者群やiBooks・UDBの両方の利用者群では紙媒体との併用の必要性が低くなっていることがわかった。現在，学校教育法第34条には，「文部科学大臣の検定を経た教科用図書又は文部科学省が著作の名義を有する教科用図書を使用しなければならない」（教科書の使用義務）と規定されている。そのため，現時点では，紙媒体の教科書を使用する義務があると考えられる。しかし，2018年に学校教育法の一部が改正され，「視覚障害，発達障害その他の文部科学大臣の定める事由により教科用図書を使用して学習することが困難な児童に対し，教科用図書に用いられた文字，図形などの拡大又は音声への変換その他の同項に規定する教材を電子計算機において用いることにより可能となる方法で指導することにより当該児童の学習上の困難の程度を低減させる必要があると認められるときは，文部科学大臣の定めるところにより，教育課程の全部又は一部において，教科用図書に代えて当該教材を使用することができる。」という項が追加される予定である。その結果，デジタル教科書を紙媒体の教科書に代えて使用する（紙媒体の教科書も給付されるため併用も可能）ことができるようになる。同じデジタル教科書のデータを用いても，閲覧アプリによって紙媒体との併用の必要性は異なるため，今後閲覧アプリの機能はより重要になると考えられる。なお，iBooksで紙媒体との併用の必要性が高い理由は，前述したとおり書き込みができないことに起因するところが大きいと考えられる。なお，協力校へのアンケートの自由記述に「機器の故障などを考え，紙媒体と併用できるようにして欲しい」という回答があったことから，紙媒体が不要になるわけではないと考えられる。

6．今後の課題

本研究では，閲覧アプリがデジタル教科書の利用実態，学習行動，紙媒体との併用の必要性にどのような影響を及ぼしているか明らかにした上で，デジタル教科書の利用を促進するための閲覧アプリの機能や環境整備の在り方について分析した。その結果，UDBがiBooksと比較してデジタル教科書の閲覧に適しているのは，LV生徒の視認性や操作性を考慮[3,4]して作成され，LV生徒らのニーズに基づいてバージョンアップが繰り返されているアプリだからだと考えられることがわかった。今回の調査研究で，UDBには更に充実させるべき機能（文字選択機能の利便性の向上，音声読み上げ機能の充実，リフロー表示画面におけるフォント・文字間・行間隔などの変更機能，データ流失に対するセキュリティ機能，書き込みデータのバックアップ，ほ

かのアプリの利用制限，全盲の生徒の利用を前提としたVoiceOverへの対応）があるという問題が明らかになったが，この課題は視覚障害のある児童生徒や担当する教員のニーズに基づき，今後更に充実させることが可能だと考えられる。一方，閲覧アプリの機能ではなく，「先生らの方針」，「その他」の理由でデジタル教科書を利用していないケースがあったという点については，今後，教員のICTリテラシーとの関係で考えていく必要のある課題だと考えられる。更に，閲覧アプリを考える際，教科書と同等に教員が作成したプリントなどの自作教材を取り扱えるようにするという視点，卒業後にも利用できるという生涯学習の視点，読みたい書籍などをLV生徒が自分自身で作成できるようにするという自立活動の視点も大切な検討課題であることがわかった。また，本研究では盲学校の高等部の生徒を対象としたが，「通常の高等学校でも使えるようにして欲しい」，「小学生や中学生にも使えるようにして欲しい」という意見があった。2018年に改正された学校教育法でも2019年度からすべての教育課程でデジタル教科書が利用できるようになることを考慮すると，今後，小中学校などでの実践的研究が必要になると考えられる。

従来から，デジタルディバイスを用いた読書では，HTML表示モードのようなリフロー表示が重要であることが指摘されてきた[10, 11, 12]。また，デジタルディバイスを用いた授業実践[13]，試験[14]，読書効率に関する実験研究[15, 16]でも，リフロー表示の方がPDF表示モードのような固定型レイアウト表示よりも読書効率が高いことが指摘されてきた。しかし，本研究で用いたUDBは，リフロー（HTML）表示と固定レイアウト（PDF）表示を切り替えて利用することが可能なように設計してあるが，リフロー（HTML）表示の利用率（34.1％）は必ずしも高くなかった（図3）。本研究と先行研究の結果に不一致があった理由は，従来の研究が長文を読む短時間の場面設定であったのに対して，本研究では授業での様々な教科書の利用場面を7カ月という長い期間でトータルに評価した点にあると考えられる。授業場面における教科書の役割は通常の読書とは異なり，文章を読むだけではない。本文の文章と図表を見比べて考えたり，漢字の読みや意味を脚注などで確認しながら読み進めたり，練習問題を解くために本文と設問を行き来したりする必要がある。長文を読む場合にも，前後の段落を意識しながら読む必要があり，多くの読書効率研究で使われてきた短時間の速読課題とは異なると考えられる。したがって，今後授業場面におけるデジタル教科書の効果を検討する際には，教員が教科書を授業場面でどのように活用しているのかを明らかにした上で，授業での教科書の活用方法と関係させて課題設定をし，各課題に適したデジタル教科書の機能などを分析するというアプローチも必要になると考えられる。

結　　論

本研究では，紙媒体の教科書と内容が同一であるデジタル教科書を用い，閲覧アプリがデジタル教科書の利用実態に及ぼす影響を検討した。iBooksとUDBの二つの閲覧アプリを比較した結果，UDBを利用する方がデジタル教科書の利用率が向上し，学習意欲などの学習効率も向上させることが明らかになった。UDBがiBooksと比較してデジタル教科書の閲覧に適しているのは，LV生徒の視認性や操作性を考慮して作成され，LV生徒などのニーズに基づいた機能を搭載し続けているためであると考えられる。今後，UDBの更なる機能充実が望まれると同時に，LV生徒や担当教員のメディアリテラシーを向上させるための研修や普及・啓発，利用対象者の拡大などが必要だと考えられる。また，デジタル教科書の効果を検証する際には，短時間での読書効率だけでなく，授業のなかでの多様な活用方法との関係で検討する必要があることが示唆された。

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（3） 研究概要報告書に述べた研究内容の詳細と補足資料

5． 発達障害スクリーニングを目指すシステムの研究

5-1. 嗅覚刺激に対する脳反応計測による
スクリーニング法の検証

5-2. 発達障害早期発見のための微細運動の
自動評価システムの開発

【概要 5-１】嗅覚刺激に対する脳反応計測によるスクリーニング法の検証

Prefrontal responses to odors in individuals with autism spectrum disorders: functional NIRS measurement combined with a fragrance pulse ejection system

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Abstract

Individuals with autism spectrum disorders (ASD) are impaired not only in social competencies but also in the sensory perception of various modalities, particularly olfaction. The olfactory ability in individuals with ASD has been examined in several psychophysical studies, but the results have vastly varied, which might be primarily due to methodological difficulties in the control of odor stimuli (e.g., the problem of lingering scents). In addition, the neural correlates of olfactory specificities in individuals with ASD remain largely unknown. Hitherto, only one study has tackled this question using neuroimaging with functional magnetic resonance imaging (fMRI). The present study utilized a sophisticated method—a pulse ejection system—to present well-controlled odor stimuli to participants with ASD using an ASD-friendly application. With this advantageous system, we examined their odor detection, identification, and evaluation abilities, and measured their brain activity evoked by odors using functional near-infrared spectroscopy (fNIRS). As the odor detection threshold (DT) of participants with ASD varied largely, they were divided into two groups according to their DT: an ASD-Low DT group and an ASD-High DT group. Behavioral results showed that the ASD-High DT group had a significantly higher DT than did the typical development (control) group and the ASD-Low DT group, indicating their insensitivity to the tested odors. In addition, while there was no significant difference in the odor identification ability between groups, there was some discrepancy between their evaluations of odor pleasantness. The brain data identifies, for the first time, that neural activity in the right dorsolateral prefrontal cortex (DLPFC) was significantly weaker in the ASD-High DT group compared to the control group. Moreover, the strength of activity in the right DLPFC was found to be negatively correlated with the DT. These findings suggest that participants with ASD have impairments in the higher-order function of olfactory processing, such as olfactory working memory and/or attention.

Introduction

Individuals with autism spectrum disorders (ASD) generally have unusual sensory awareness, showing either hyper- or hypo-responsiveness to various sensory modalities, including olfaction (Kientz and Dunn, 1997; Rogers et al., 2003; Rogers and Ozonoff, 2005; Schreck and Williams, 2006; Ben-Sasson et al., 2009; Wiggins et al., 2009). Accumulating evidence indicates that individuals with ASD suffer more sensory disturbances than those with typical development (TD) or other intellectual disabilities (Leekam et al., 2007; Tomchek and Dunn, 2007). Particularly, an aberrant response to smell has been reported repeatedly in the ASD population (Schecklmann et al., 2013; Martin and Daniel, 2014; Rozenkrantz et al., 2015; Endevelt-Shapira et al., 2018) and has been suggested to be a prominent criterion when distinguishing individuals with ASD from those with other developmental disorders (Rogers et al., 2003; Leekam et al., 2007; Schoen et al., 2009).

Sensory psychophysical studies on olfactory perception in ASD

Previous studies have found that over 50% of sampled ASD children had symptoms of unusual smell/taste sensitivity (Schoen et al., 2009; Lane et al., 2010). Moreover, olfactory problems have been suggested to be a good predictor of social deficiency in individuals with ASD (Liss et al., 2006; Bennetto et al., 2007; Hilton et al., 2007; Lane et al., 2010), and olfactory alterations may be an early marker for ASD (Brewer et al., 2006; Hrdlicka et al., 2011).

Odor is a very powerful sensory modality. It serves as a potent cue for both social and cognitive development in children with ASD (Parma et al., 2013; Woo et al., 2015). Despite its importance, relatively few studies have investigated the sense of smell in individuals with ASD and those studies have arrived at contradictory results across a variety of domains (Suzuki et al., 2003; Bennetto et al., 2007; Brewer et al., 2008; Dudova et al., 2011; May et al., 2011; Tavassoli and Baron-Cohen, 2012; Galle et al., 2013; Ashwin et al., 2014; Wicker et al., 2016; Kumazaki et al., 2016; Addo et al., 2017). This is in contrast to the well-described literature on abnormalities in vision (Simmons et al., 2009), audition (O'Connor, 2012), and touch (Puts et al., 2014) in individuals with ASD.

The discrepancies between studies might be due to many factors including participant rom children to adults), ASD subtype (e.g., high functioning ASD (HFA), Asperger’s syndrome (AP), and Pervasive Developmental Disorder (PDD)), tests used (e.g., Sniffin’ Sticks (Hummel et al., 1997), University of Pennsylvania Smell Identification Test (UPSIT) (Doty et al., 1984), alcohol sniff test (AST) (Davidson and Murphy, 1997), and custom-made) and/or odors (e.g., n-butanol, alcohol, custom-made), making direct comparison difficult.

Neuroimaging studies of olfaction in ASD

Studies investigating sensory differences in ASD have predominantly investigated auditory and visual differences in individuals with ASD. Olfaction is one of the least studied aspects of ASD (Martin and Daniel, 2014; Kumazaki et al., 2019), particularly at the neural level. Non-invasive neuroimaging modalities such as magnetic resonance imaging (MRI) have expanded the knowledge of olfactory dysfunction in humans (Han et al., 2019). Unfortunately, functional neuroimaging studies investigating the neural basis of olfactory processing in individuals with ASD are scarce. To the best of our knowledge, only one MRI (fMRI) study have probed the neural responses of individuals with ASD to odors (Koehler et al., 2018). The authors found impairment in both odor detection and odor identification in ASD participants and reported, for the first time, significantly attenuated odor-induced brain response in the piriform cortex as well as a trend for decreased activity in the OFC in ASD compared to TD controls.

With functional near-infrared spectroscopy (fNIRS), much knowledge has been accumulated for various sensory functions. Chemical senses such as olfactory processing have also been studied (Ishimaru et al., 2004a; Ishimaru et al., 2004b; Harada et al., 2006; Kobayashi et al., 2009; Takakura et al., 2011). Ishimaru et al. (2004a, b), Harada et al. (2006), and Kobayashi et al. (2009) reported activation (increased Oxy-Hb concentration) of the most anterior part of the prefrontal areas in response to olfactory stimuli and suggested that such hemodynamic responses might reflect activity in the OFC corresponding to the secondary olfactory cortex (Zatorre et al., 1992; Saive et al., 2014). Similar prefrontal activity was reported by Takakura et al. (2011), which primarily lay in the frontal pole (FP) and dorsolateral PFC (DLPFC), and, therefore, has been suggested to indicate attention and working memory related to the odor detection task. Nevertheless, an important knowledge gap remains, in that none of these fNIRS studies included individuals with ASD in spite of its amenability to the ASD population.

Considering the general abnormality of executive functions including attention and working memory in individuals with ASD (Russell, 1997; Travers et al., 2011; Hill, 2004; Kenworthy et al., 2008), it is possible that their brain activity in region responsible for these functions, i.e., the DLPFC (Duncan and Owen, 2000; Levy and Goldman-Rakic, 2000), to be different from that of the TD people in tasks requiring executive functions to some extent. This possibility might also partially account for the olfactory hyposensitivity in individuals with ASD. Interestingly, Larsson et al. (2017) has suggested that ASD in younger populations (> 30 years) tend to show olfactory hyposensitivity, whereas older individuals (> 35 years) with ASD do not. Since the development of prefrontal region continues until early adulthood (Diamond, 2002), the immatureness of this region in younger individuals with ASD may result in their olfactory hyposensitivity as well.

Heterogeneity of odor sensitivity in ASD and methodological obstacles for olfactory stimulation

ASD is characterized by a high degree of heterogeneity across individuals (Jeste and Geschwind, 2014). In addition to the large variability in an individual's intelligence and their sensory and attentional capacities, neuroimaging studies have demonstrated both structural and functional abnormalities of heterogeneity among individuals with ASD (Anagnostou and Taylor, 2011; Dichter, 2012). When assessing odor-evoked neural responsiveness in individuals with ASD, whether and to what degree the used odors can be actually perceived is fundamental. Thus, it is critical to examine the odor detection threshold of each participant to evaluate their olfactory system functionality. Koehler et al. (2018) tested odor detection abilities in ASD participants before scanning their brains but did not directly correlate these datasets.

As mentioned above, the investigation of olfactory perception in individuals with ASD has yielded inconsistent results and methodological obstacles might be one of the most significant reasons. Most of these studies have used UPSIT, AST, and Sniffin' Sticks, for which the control of odor granularity is challenging due to the problem of lingering scents (Fukasawa et al., 2013). As olfaction is a highly adaptable sensory modality, measurements of the olfactory ability can be compromised when the odor stimuli remain in the air (Kumazaki et al., 2016). To solve these problems, we developed the Fragrance Jet for Medical Checkup (FJMC; Keio University) that uses a pulse ejection system (Fukasawa et al., 2013) and has been reliably standardized and successfully used in our previous work (Kumazaki et al., 2016; Kumazaki et al., 2018a; Kumazaki et al., 2018b; Kumazaki et al., 2019). It employs an identical technique as a basic inkjet printer, using a very small quantity of odorant to emit tiny droplets of scent. This technique can be fine-tuned with respect to the amount and time of exposure to reduce lingering scents, allowing precise assessment of the olfactory function. More specifically, by modulating the number of simultaneous ejections (NSE), the ejection quantity per unit time (EQUT) can be adjusted, which, together with the ejection time (ET), determine the intensity of ejected odor (refer to Fukasawa et al., 2013 for details). Instead of preparing various concentrations of scent beforehand as conventional olfactory measurement techniques, our approach makes measurement possible by only changing the NSE. Using a very small quantity of an odor reduces lingering scents and avoids odor adaptation (Sato et al., 2008), which is an important confounding factor during the assessment of olfaction. This type of instrument cannot be used with fMRI scanning but can be combined with fNIRS because many parts of the instrument were made up of metal.

To address the aforementioned issues, the present study uses fNIRS to investigate cerebral activation in relation to olfactory processing in young adults with ASD and TD. The primary aim of this study was to examine the feasibility of combined usage of a fragrance pulse ejection system for presenting odor stimuli with fNIRS system. The secondary aim was to reveal differential functions of the prefrontal region between ASD and TD in odor processing by carefully examining the relationship between odor sensitivity in ASD participants and their neuronal responses. We predict that both odor perception and odor-induced neural function are impaired in ASD participants and that their brain activity is correlated with their odor sensitivity.

Methods and Materials

Participants

The present study was approved by the ethics committee of the Keio University, Faculty of Letters (No. 16028). The participants were young adults with ASD and TD. Twenty-five ASD participants (19 males, 18 to 24 years old, mean age: 20.50 years) and 16 TD participants (13 males, 19 to 24 years old, mean age: 21.33 years) volunteered for the study. The exclusion criteria for both ASD and TD participants included organic smell disturbance, nasal problems, diagnosed psychiatric conditions, and a history of head injury. After a complete explanation of the study, all volunteers and their parents agreed to participate in the study and provided written informed consent.

The ASD participants were diagnosed by psychiatrists using the criteria in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) (APA, 2013) and the standardized criteria taken from the Diagnostic Interview for Social and Communication Disorders (DISCO) (Leekam et al., 2002) at the time of enrollment in the study. The TD participants had no history or evidence of ASD, but they were tested for autism traits using autism spectrum quotient (AQ) (Baron-Cohen et al., 2001). The psychiatrists also categorized ASD into three types while referencing the result of DISCO: Asperger's syndrome (AP), autistic disorders (AD), and pervasive developmental disorder not otherwise specified (PDD-NOS) (see Table 1).

To assess autistic traits of individuals with ASD, the Childhood Autism Rating Scale-Tokyo Version (CARS-TV) was used. The CARS-TV is the Japanese version of the CARS (Schopler et al. 1980) – one of the most widely used scales to evaluate the degree and profiles of autism in children – and has been determined to have satisfactory reliability and validity (Kurita et al. 1989; Tachimori et al. 2003).

Intelligence testing in both ASD and TD participants was performed using the Wechsler Intelligence Scale for Children—Fourth Edition (WISC-IV) (Wechsler, 2003) or Wechsler Adult Intelligence Scale—Third Edition (WAIS-III) (Dumont and Willis, 2008). We missed to obtain IQ from one ASD participant due to his low motivation. In addition, both ASD and TD participants were tested for their perceptual traits using a sensory profile (Dunn et al., 1999). The above demographic information is shown in Table 1.

Procedure

First, both the ASD and the TD participants completed an olfactory measurement session that included odor detection threshold (DT), odor identification, and odor evaluation. They subsequently received an fNIRS assessment, after which they underwent odor identification and evaluation again. The details of procedure can be seen in Figure 1.

Table 1. Descriptive characteristics of the ASD and control (TD)groups

Characteristics	ASD-Low DT (n = 12) (ME, SD)	ASD- High DT (n = 13) (ME, SD)	Control (n = 13) (ME, SD)	Statistics
Age in years	19.8 (1.7)	19.9 (2.0)	20.6 (1.7)	F (2, 35) = 0.889, $p = 0.42$
Gender (M:F)	9:3	10:3	10:3	χ^2 (2) = 0.017, $p = 0.99$
Type of ASD	1 AD, 7 AP, 4 PDD-NOS	3AD, 1 AP, 9 PDD-NOS		
Full scale IQ	77.8 (10.8)	65.2 (12.7)	115.9 (7.6)	F (2, 35) = 79.83, $p < 0.001$ Control vs. ASD-Low DT: $p < 0.001$ Control vs. ASD-High DT: $p < 0.001$ ASD-Low DT vs. ASD-High DT: $p = 0.018$
AQ-J			17.5 (9.6)	
CARS-TV	32.7 (2.0)	31.8 (2.7)		t (23) = 0.945, $p = 0.36$
DT				See the Behavior results section
Rose	49.2 (7.0)	108.5 (6.7)	39.2 (6.7)	
Mint	27.5 (16.0)	82.3 (49.9)	28.5 (17.7)	
Mean	38.3 (9.4)	95.4 (20.4)	33.9 (15.8)	
				Two-way ANOVA: Main effect of odor: F (1, 35) = 6.51, $p = 0.02$ Rose > Mint Main effect of group: F (2, 35) = 59.24, $p < 0.001$ ASD-High DT > Control ($p < 0.001$) ASD High-DT > ASD Low-DT ($p < 0.001$) No interaction: F (2, 35) = 0.37, $p = 0.70$

ASD: autism spectrum disorders; TD: typical development; DT: odor detection threshold.

ME: mean, SD: standard deviation. Parentheses indicate SD. M: male, F: female.

AD: autistic disorder; AP: Asperger's syndrome; PDD-NOS: pervasive developmental disorder not otherwise specified

IQ: intelligence quotient. One individual with ASD cannot measure IQ because of low motivation.

AQ-J: autism spectrum quotient, Japanese version. Higher scores indicate a greater number of ASD-specific behaviors.

CARS-TV: Childhood Autism Rating Scale-Tokyo Version. Higher scores indicate high autistic symptoms.

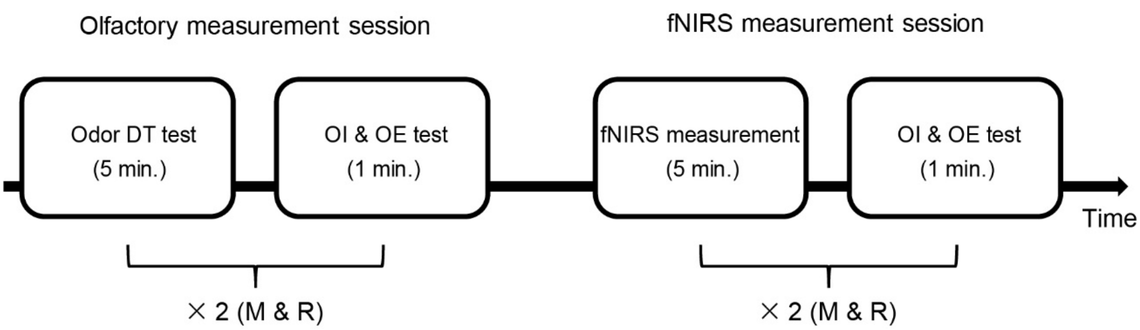

Figure 1. Time sequence of the whole experiment. There were two sessions: olfactory measurement session & fNIRS measurement session. The olfactory measurement session included both an odor detection threshold (DT) test and an odor identification (OI) & odor evaluation (OE) test. The odor DT test was performed for each odor (rose and mint, as shown with "×2"). Both odors were used for once in the OI & OE test. During the fNIRS measurement session, an OI & OE test was performed after the fNIRS measurement using each odor (two sets of fNIRS measurment). M: mint, R: rose.

Olfactory measurement

Odor presentation

Two types of odors were used for each of the olfactory measurement: a simple chemical β-phenylethyl alcohol that smells like rose and a natural fragrance of mint. Odorants were diluted to 5% using water and little ethanol to adjust their adhesiveness. The experiment room was well-ventilated to prevent lingering scents. Olfactory measurements were performed using an olfactory display (Figure 2A), which uses a pulse ejection system (Fukasawa et al., 2013) and can measure and quantify odor DT with high precision. It uses an ejection head to produce scent droplets from tiny holes. The device has one large tank and three small tanks. We used the large tank for DT measurement and the small tanks for odor identification and odor evaluation measurements. There are 255 tiny holes in the ejection head connected to the large tank and 127 tiny holes in the head connected to the small tanks. These tiny holes can emit scent simultaneously. The average ejection quantity from a single hole was referred to as the unit average ejection quantity, which is 7.3pL for the large tank and 4.7pL for the small tanks. The intensity of ejected odor is determined by two parameters: EQUT and ET. The EQUT can be adjusted by modulating the NSE (0 ~ 255 for the large tank, and 0 ~ 127 for the small tanks). Ejections can be controlled in pulses of 667μs, and ET determines the number of ejected pulses (ET/667) (refer to Fukasawa et al., 2013 for details). Our device makes measurement possible by only changing the NSE rather than preparing many intensities of odor stimuli beforehand as conventional olfactory testing did. Participants sat in front of the pulse ejection system with a distance of approximately 20cm (Figure 3B).

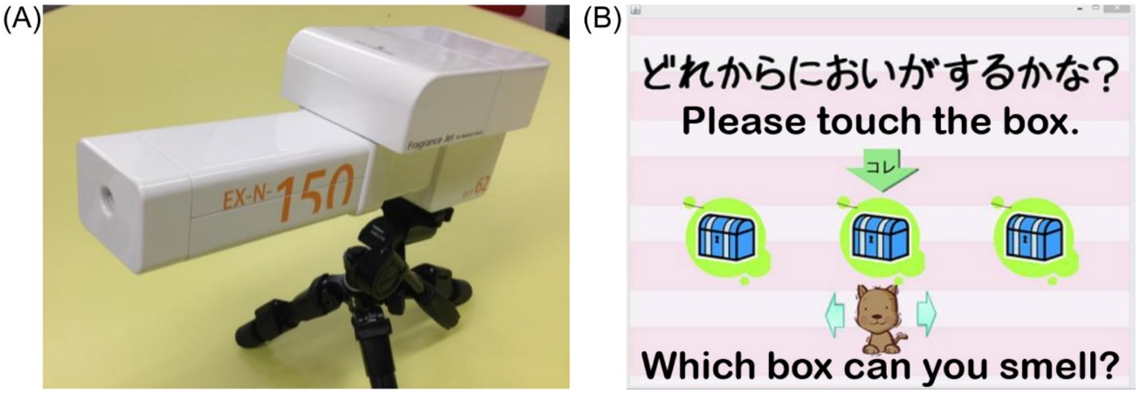

Figure 2. (A) The olfactory display using a pulse ejection system; (B) A screenshot of the application for odor detection threshold measurement designed for participants with ASD. (Matsuura et al., 2014).

Odor DT

The task was designed to be as simple as possible so that all ASD participants could concentrate and complete the measurement without making verbal responses. To this end, we used a game-like application developed in our previous work (Matsuura et al., 2014) to carry out the experiment using a touch panel (Figure 2B). In each trial, three boxes were shown on the display of the touch panel, each of which contained an odor stimulus. The three stimuli were arranged pseudo-randomly; one stimulus was scented while the other two were odorless. When the participants clicked one of the three boxes, an odor was given off 3.0 s later. They were allowed to click each box up to two times and were asked to identify the box that enclosed the odor stimulus (triple forced-choice). Before measurement, we confirmed that all participants understood the rules of the experiment. Based on the results of pre-experimental tests and our earlier studies (Fukasawa et al., 2013; Kumazaki et al., 2016), we began the measurement with an NSE of 60 and an ET of 200 ms. A specific measurement algorithm that employs a binary search (Fukasawa et al., 2013; Kumazaki et al., 2019) was used to determine the participant's DT. For the first trial, when a participant made a mistake (selecting a box that contained an odorless stimulus), the NSE increased by 50%; once two consecutive trials were successfully cleared, the NSE decreased by 50%. For the rest of the trials, the increment or decrement unit of the NSE was 10. The maximum and minimum of NSE was 120 and 10, which was also based on the results of pre-experimental tests and our earlier study on olfaction in individuals with ASD using the same odor presentation device (Kumazaki et al., 2019). All participants' measurements were completed in approximately 5 minutes. The DT was generated after the procedure was completed. This odor DT test was conducted once for both rose and mint odors.

Odor identification and odor evaluation

There were two sessions for measurement of odor identification and odor evaluation: the olfactory measurement session and the fNIRS session (see Figure 1). Both rose and mint odors were presented to the participants for once in each session, and the sequence of the two odors in each session was randomized among participants. In the olfactory measurement session, an odor stimulus at an intensity of 120 NSE was presented to a participant for an ET of 200 ms. Subsequently, the participant was asked to answer verbally what kind of odor he/she smelt (odor identification) and how pleasant they thought the smell was (odor evaluation) if he/she had perceived it. For odor identification test, we used a free identification paradigm that no descriptor was provided for the participants. The participants got 3 points if they explicitly named the odor, i.e., rose or mint. They got 2 points if they answered flower or herb. They got 1 point if they generalized the odor as sweet or cooling. Otherwise, they got 0 points. For odor evaluation, the participants were asked to verbally rate the pleasantness of the odor from 1 (very pleasant) to 5 (very unpleasant) for each trial. The details for odor identification and odor evaluation test in the fNIRS session are provided in the following subsection.

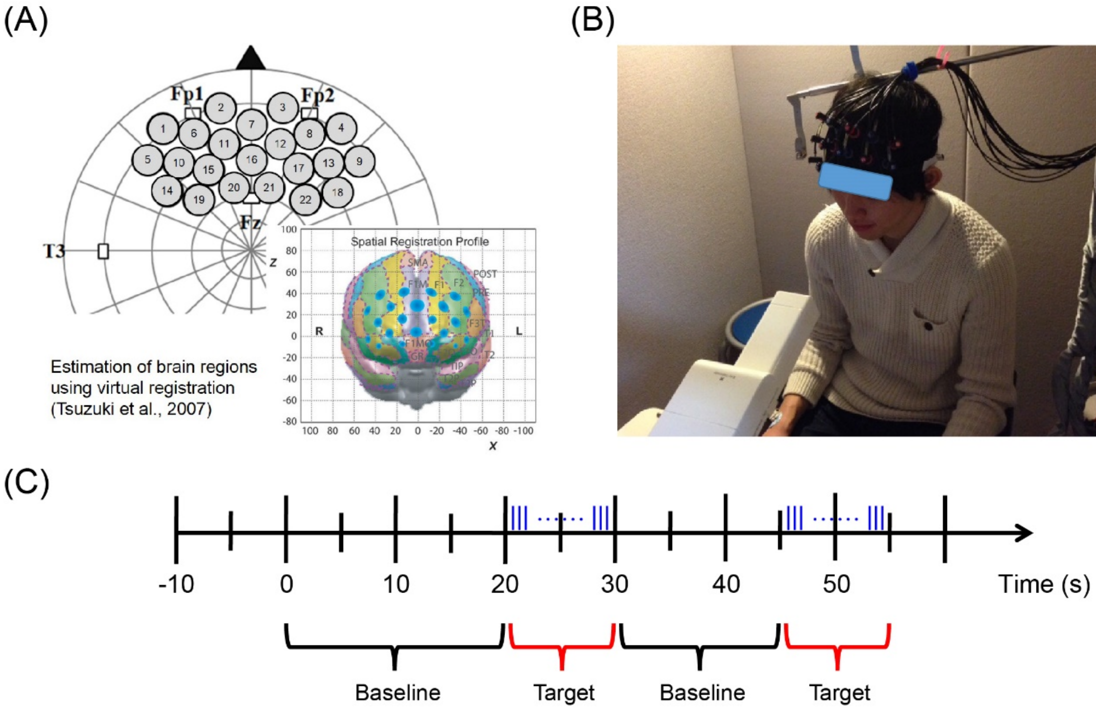

Figure 3. fNIRS measurement. (A) Probe set and position on the brain. (Xu et al., 2017); (B) fNIRS experimental environment (informed consent was obtained from the participant shown in the figure); (C) Block design of fNIRS measurement. Odor stimuli were emitted during the 10 s of the target period. The blue vertical lines represent the pulses of odor stimuli presented by the fragrance pulse ejection system. The odor stimuli were emitted for 200 ms (200/0.667 = 300 pulses) at a time, and the inter-stimulus interval was 80 ms.

fNIRS measurement

Hemodynamic responses in the prefrontal region were recorded using a multichannel NIRS system (ETG-7000, Hitachi Medical Co., Japan). The system emits continuous near-infrared lasers with fixed wavelengths of approximately 780 nm and 830 nm. Lasers are modulated at different frequencies depending on the wavelengths and the channels, and are detected using lock-in amplifiers (Watanabe et al., 1996). The device provides estimates of changes in hemoglobin (Hb) concentrations and oxygenation levels of the optical paths in the underlying brain regions between the nearest pairs of emitter and detector probes.

A silicon probe pad was used to arrange eight emitters and seven detector probes in a 3×5 rectangular lattice, forming 22 recording channels. Each pair of emitter and detector probes was separated by a distance of 30 mm. The 3×5 probe pad was placed on the participants' prefrontal region (Figure 3A) (Xu et al., 2017). Specifically, the bottom border of the probes was placed in a direction horizontal to the line connecting T3, Fp1, Fp2, and T4 on the international 10-20 system, and the center of the channels was positioned across the nasion–inion line (Klem et al., 1999). This probe arrangement enabled the spatial estimation of localized cerebral activity based on the virtual registration method (Tsuzuki et al., 2007). After probe placement, the experimenter verified that each probe was in adequate contact with the scalp. Only after this verification were fNIRS recordings initiated.

During the fNIRS measurement, the participants were shown a silent movie of various running trains to keep the position of their heads stable as much as possible while the odor was presented at a random time using a block design (Figure 3B). The length of the baseline period was randomized from 15 to 25 s, and the target period was 10 s, within which the odor stimuli were emitted for 200 ms (200/0.667 = 300 pulses) at a time, and the inter-stimulus interval was 80 ms (Figure 3C). The fNIRS measurement also used odors of mint and rose and executed eight blocks of odor stimulation for each odor. After the completion of the fNIRS session using each odor, the participants were required to identify and evaluate the odor.

Behavior data analysis

First, the ASD participants were divided into two groups using a median split according to their DT values. ASD participants with DT < 60 were labeled as the "ASD-Low DT" group and those with DT > = 60 were labeled as the "ASD-High DT" group. Next, their performance in odor identification and odor evaluation was also grouped. Two-way ANOVA with the groups used as between-subject factors (control, ASD-Low DT, ASD-High DT) and the odors used as within-subject factors (mint, rose) was applied to the DT using IBM SPSS Statistics 25. For odor identification and evaluation, two-way repeated ordinal regression with cumulative link mixed models (CLMM) (Christensen, 2015) was applied using R (R Core Team, 2018).

NIRS data analysis

The NIRS data were preprocessed using Platform for Optical Topography Analysis Tools (POTATo) developed by Research and Development Group, Hitachi, Ltd. in a Matlab 7.7 environment (The MathWorks, Inc., Natick, MA, USA). Changes in the concentration of oxygenated (oxy-) Hb and deoxygenated (deoxy-) Hb were calculated from absorbance changes of 780 nm and 830 nm laser beams sampled at 10 Hz. For each participant, the raw oxy- and deoxy-Hb data in each channel were high-pass filtered at 0.0167 Hz to remove components originating from systematic fluctuations (Naoi et al., 2012). Blocks with motion artifacts were excluded (signal variations larger than two standard deviations (SD) from the mean over 0.2 s). Any block containing oxy-Hb changes larger than 0.15 mM/mm within 0.2 s was discarded. The oxy-Hb and deoxy-Hb concentrations of the remaining baseline and target blocks were smoothened with a moving average of 5 s. To eliminate long-term signal trends due to systemic vascular factors, a first-degree baseline fit was estimated for each channel using the first 5 s and last 5 s of the analysis block.

For each group (control, ASD-Low DT, and ASD-High DT), the block analysis focused on a 25 s epoch composed of a 5 s pre-stimulus baseline period, a 10 s target period with odor stimulation, and a 10 s post-stimulus period. The Hb concentrations of all artifact-free trials were averaged. Subsequently, a time course of the mean change in oxy-Hb and deoxy-Hb concentration was compiled for each channel of each participant. These time courses for all the participants in each group were subsequently averaged to form time-dependent waveforms of the hemodynamic responses in each channel. Considering the slow characteristics of neural hemodynamic responses, a 10 s period starts from 5 s after stimulus onset was regarded as the analysis window (10 ~ 20 s of each block). A 5 s period immediately before stimulus onset was regarded as the time window for the baseline (0 ~ 5 s of each block). A two-way repeated measures ANOVA with the group as the between-subject factor and odor as the within-subject factor was analyzed for the oxy-Hb concentration changes (the mean of oxy-Hb during the analysis window *versus* the mean of oxy-Hb during the baseline) in each channel. A Bonferroni's post hoc test was used to further evaluate any significant main effects. In addition, the means of oxy-Hb during the analysis window and the baseline period in each channel were analyzed by a paired *t*-test to identify the activated regions in response to the olfactory stimuli for each group. The brain regions underlying each channel were estimated using the virtual registration method for NIRS channels (Tsuzuki et al., 2007). For those activated channels showing significant main effect of group, latency of the oxy-Hb peaks and mean amplitude of the deoxy-Hb and latency of the deoxy-Hb peaks within the analysis window were analyzed as well. Lastly, correlations between the oxy-Hb concentration changes and behavioral data (odor DT, odor identification, and odor evaluation), as well as the scores in the sensory profile, were assessed using Pearson's correlation.

Results

Demographic data

There were no significant differences between groups with regards to mean age ($F(2, 35) = 0.889$, $p = 0.42$) and gender proportion ($\chi^2(2) = 0.017$, $p = 0.99$). There were significant differences between groups with regard to IQ ($F(2, 35) = 79.83$, $p < 0.001$). Post-hoc analyses with Bonferroni's correction revealed that the IQ of the control group was significantly higher than the two ASD groups ($p < 0.001$), and the IQ of the ASD-Low DT group (77.8 ± 10.8) was significantly higher than the IQ of the ASD-High DT group (65.2 ± 12.7) ($p = 0.018$). There was no significant difference in scores of CARS-TV between the two ASD groups ($t(23) = 0.945$, $p = 0.36$). Details are presented in Table 1.

Behavior results

Due to the considerable variation in the odor DT of the ASD participants, they were divided into two groups according to their DT using a median split. ASD participants with DT < 60 (NSE) were defined as the "ASD-Low DT" group (N = 12) and those with DT > 60 were defined as the "ASD-High DT" group (N = 13). Three control participants were excluded from further data analysis because of technical problems in the odor stimulation device. Thus, the data from the remaining 13 control participants were used for analysis.

The results of DT (Figure 4A) showed higher DT for rose than for mint, and higher DT in the ASD-High DT group. This tendency was supported by two-way repeated ANOVA using odor (rose versus mint) as the within-subject factor and group (control versus ASD-Low DT versus ASD-High DT) as the between-subject factor. Specifically, it showed significant main effects of odor ($F(1, 35) = 6.51$, $p = 0.02$) and group ($F(2, 35) = 59.24$, p

< 0.001). There was no significant interaction effect between odor and group (F (2, 35) = 0.37, $p = 0.70$). For the significant main effect of odor, the DT (mean ± SD) for rose (66.05 ± 39.08) was significantly higher than that for mint (46.58 ± 40.82). A Bonferroni's post-hoc analysis for the significant main effect of group revealed that the DT was significantly higher in the ASD-High DT group (95.38 ± 42.35) than in the control group (33.85 ± 22.29) ($p < 0.001$) and the ASD-Low DT group (38.33 ± 18.10) ($p < 0.001$), indicating significantly lower odor sensitivity in the ASD-High DT group (Figure 4A).

Two-way repeated ordinal regression with CLMM was applied to the performance of odor identification and odor evaluation. For odor evaluation, a higher rate indicates unpleasantness while a lower rate indicates pleasantness. After comparisons of a series of models with different fixed and random effects, the most appropriate model evaluated by the likelihood ratio test was accepted. For odor identification, there were no significant main effects or interactions (Figure 4B). For odor evaluation (rating of pleasantness) (Figure 4C), the accepted most appropriate model included the odor (rose versus mint) and group (control versus ASD-Low DT versus ASD-High DT) as fixed effects and the intercepts for odor and NIRS (with or without NIRS measurement) and by-subject random slopes as random effects. Both odor ($\chi^2(1) = 6.03$, $p = 0.014$) and group ($\chi^2(2) = 7.02$, $p = 0.030$) significantly affected odor evaluation. Specifically, the odor of mint (2.14 ± 0.81) was rated as significantly more pleasant than that of rose (2.46 ± 0.83). Post-hoc analysis revealed that the odor evaluation was significantly different between the control group (2.73 ± 0.62) and the ASD-High DT group (2.04 ± 0.94) (coefficient estimate: 2.34, standard error (SE): 0.89, $p = 0.009$), and a tendency of significant difference between the control group and the ASD-Low DT group (2.13 ± 0.74) (coefficient estimate: 1.85, SE: 1.05, $p = 0.08$).

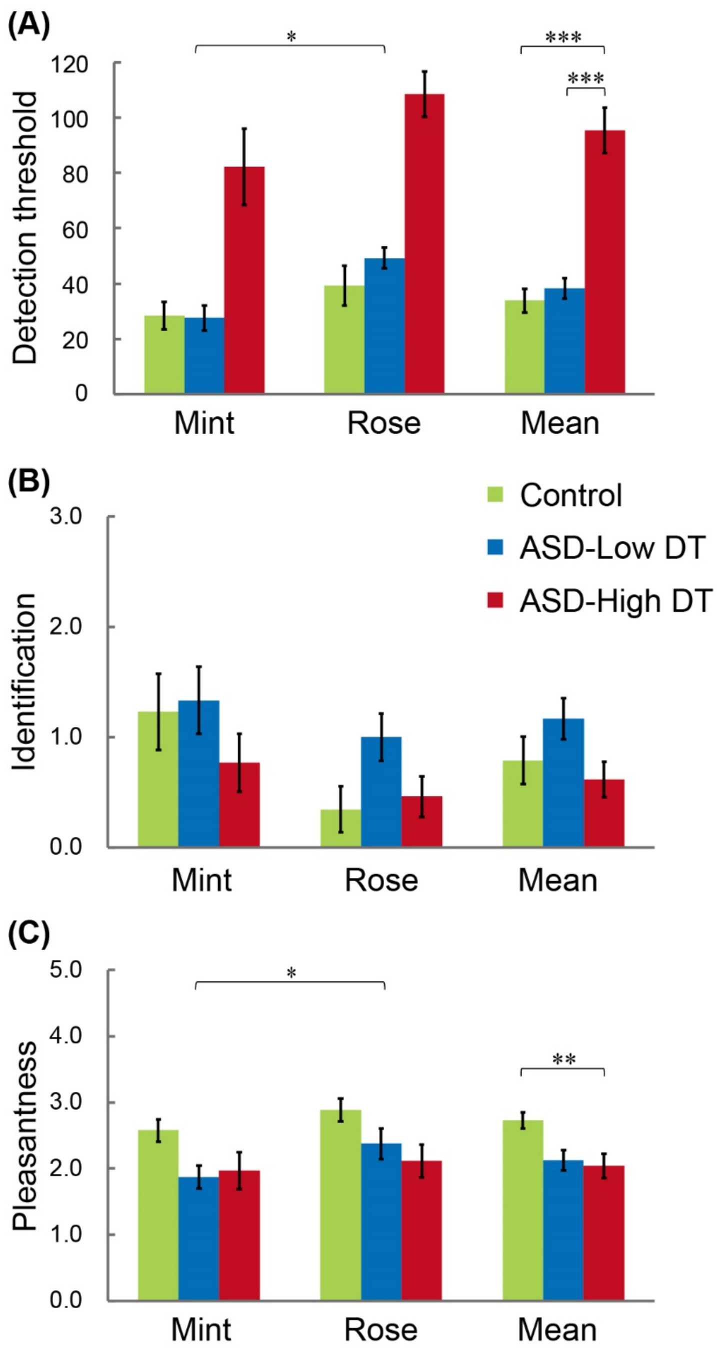

Figure 4. Performance of the control and ASD participants in the (A) odor detection threshold (DT), (B) odor identification, and (C) odor evaluation (pleasantness) tests. The ASD group was divided into "ASD-Low DT" (those DT < = 60, 12 participants) and "ASD-High DT" (those DT > 60, 13 participants) subgroups. Error bars represent 1 standard error. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

NIRS results

The concentration changes in oxy-Hb and deoxy-Hb were analyzed for the control, ASD-Low DT,

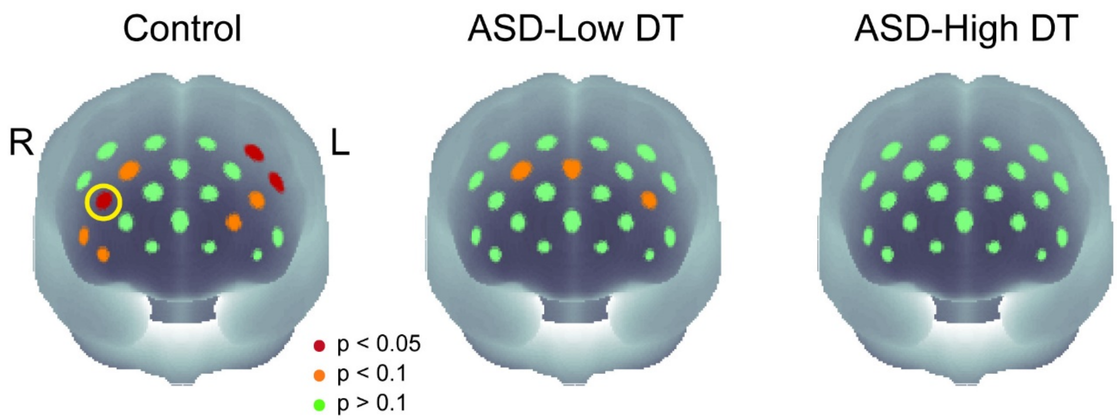

Figure 5. The *p*-maps of the averaged concentration changes in oxy-Hb for the three groups. CH13 that showed significant difference in response between the control group and the ASD-High DT group was marked using a yellow circle. The corresponding brain region of CH13 was estimated as right dorsolateral prefrontal cortex (DLPFC) using virtual spatial registration (Tsuzuki et al., 2007).

and ASD-High DT groups. Since two-way repeated measures ANOVA with group and odor as factors revealed almost no significant odor effect except for CH6 (F (1, 35) = 4.32, p <0.05) and no interaction for any channel, the trials in the mint and rose conditions were combined to identify the activated channels in each group (Figure 5) and to create the time course of Hb changes in all channels for each group. More channels were activated in the control group than in the ASD-Low DT group while there were no activated channels in the ASD-High DT group (Figure 5). In addition, similar regions were activated for both the control group and the ASD-Low DT group in CH10 and CH17. According to the virtual registration method (Tsuzuki et al., 2007), the corresponding brain regions of these activated channels are chiefly DLPFC: e.g., CH9, right DLPFC 100%; CH10, left DLPFC 91.7%, FP 8.3%; CH13, right DLPFC 78.9%, FP 21.1%; CH17, right DLPFC 50.5%, left DLPFC 39.8%. Among these DLPFC channels, CH9 (F (2, 35) = 3.49, p = 0.042) and CH13 (F (2, 35) = 3.39, p = 0.047) showed a significant main effect of group according to the results of two-way ANOVA with group and odor as factors. Particularly, activity of CH13 (right DLPFC) was significantly weaker in the ASD-High DT group than in the control group (p = 0.046, Bonferroni's correction) (Figure 6). The time series of Hb changes in CH13 (right DLPFC) with significant main effect of group (control > ASD-High DT) were shown in Figure 7. The pattern of brain activity of the ASD-High DT group was different from that of the other two groups. In addition, the level of brain activity was weaker than that of the control group. One-way ANOVA showed that there was no significant main effect of group for latency of the oxy-Hb peaks (F (2, 35) = 0.47, p = 0.63), mean amplitude of the deoxy-Hb (F (2, 34) = 2.41, p = 0.11), and latency of the deoxy-Hb peaks (F (2, 34) = 1.45, p = 0.25).

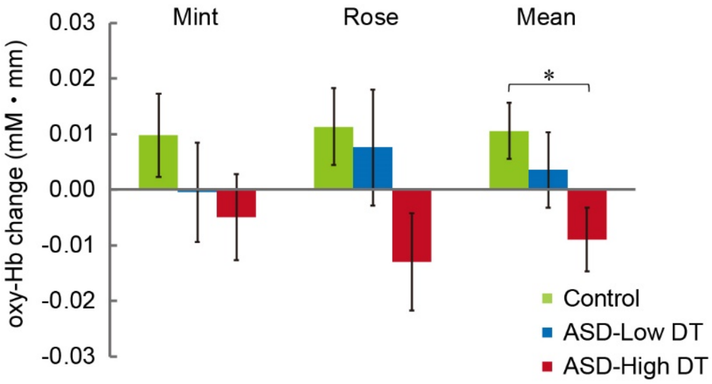

Figure 6. The results of two-way repeated measures ANOVA in CH13, which showed a significant main effect of group (Control > ASD-High DT), but no significant main effect of odor or interaction of group and odor. * $p < 0.05$.

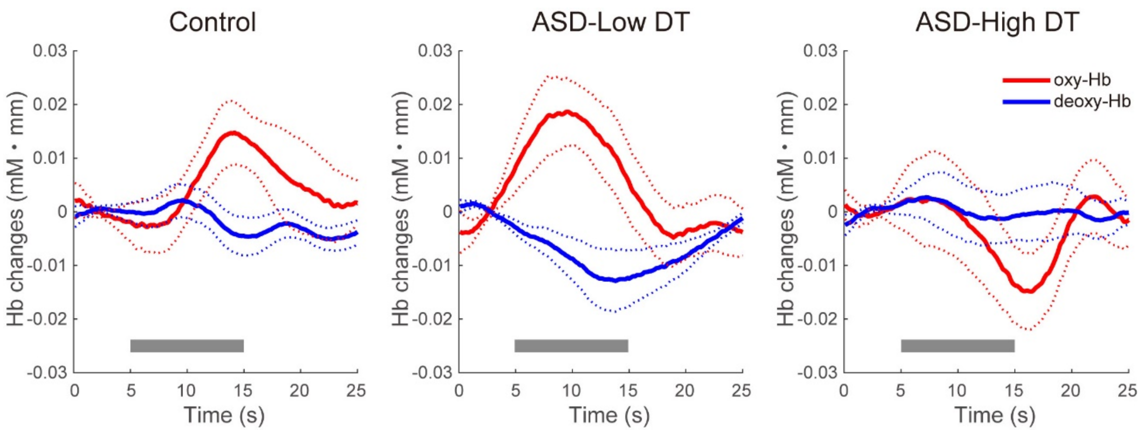

Figure 7. Time series of the averaged concentration changes in oxy-Hb and deoxy-Hb (mM・mm) in CH13 for the three groups. The gray bars represent the target period (5 ~ 15 s). The thick red and blue lines represent the mean concentration changes of oxy-Hb and deoxy-Hb, respectively. The thin dotted red and blue lines represent 1 standard error of concentration changes in oxy-Hb and deoxy-Hb, respectively.

The odor identification test after the fNIRS session indicated that almost all the participants recognized the odor except for three participants in the ASD-High DT group. To examine whether there was a relationship between odor detection sensitivity and the fNIRS data, the correlation between the oxy-Hb response to the odor in CH13 and the DT of all participants was assessed using Pearson's correlation. The result revealed a significant negative correlation ($r = -0.41$, $p = 0.012$) (Figure 8), indicating that participants with lower odor detection sensitivity might show reduced brain activity to a certain level of odor stimulation. The relationship between brain activity and other olfactory perception abilities, as well as other sensory characteristics observed from the sensory profile battery, was also evaluated, but no significant correlations were found.

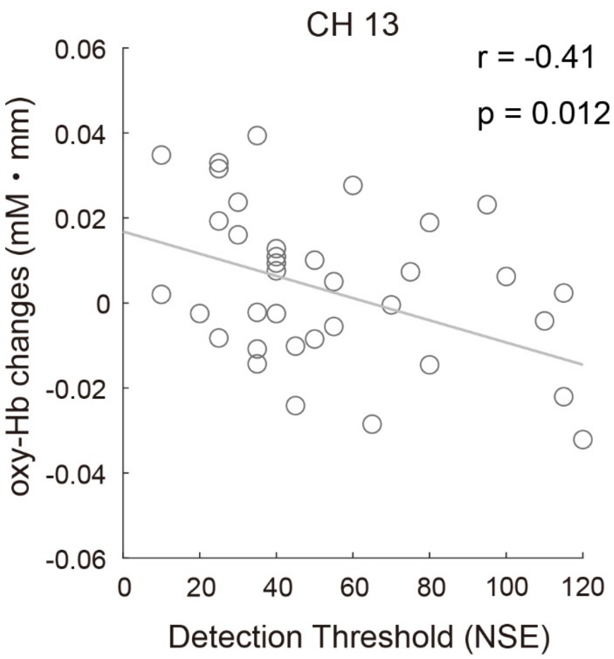

Figure 8. There was a significant correlation (r = -0.41, p = 0.012) between the mean concentration changes in oxy-Hb in CH13 and odor detection thresholds for all participants.

Discussion

The present study aimed to investigate the neural underpinnings of olfactory processing in individuals with ASD by combining a precise and ASD-friendly olfactory measurement system, which consists of a pulse ejection system, with fNIRS measurement. Significant differences were found between ASD and control groups not only at the behavioral level but also at the neural level. The ASD group with hyposensitivity (ASD-High DT group) to olfactory stimuli was found to be significantly different from the control group with respect to the olfactory DT and pleasant feelings to the used odors. The brain activity in the right DLPFC of the ASD-High DT group was significantly weaker than that of the control group. In addition, the strength of brain activity in the right DLPFC was found to be significantly correlated with the DT in all participants.

Combined use of a sophisticated system for olfactory examination and fNIRS

The present study successfully utilized a pulse ejection system in combination with fNIRS to examine neural dysfunction related to olfactory processing in individuals with ASD. The system is unique in that it can precisely control the interval of odor stimulation and, therefore, significantly reduce the potential confounding effect lingering scents have on olfactory perception. Together with an ASD-friendly game-like application for odor detection test, the system is feasible for gauging the olfactory ability of not only high functioning ASD but also ASD with intellectual impairment. While this system has been successfully used for olfactory assessment in children with ASD (Kumazaki et al., 2016; Kumazaki et al., 2018c; Kumazaki et al., 2019), the present study, for the first time tried a coregistration with fNIRS.

Since some parts of the pulse ejection system were made up of metal, it could not be used in fMRI scanning but could be used during fNIRS measurement. Our study verified the feasibility of the combination of this olfactory test system and a highly ecological valid neuroimaging method as fNIRS in order to localize the brain functions of olfactory processing in ASD. The system facilitated the examination of not only high functioning ASD but also individuals with ASD and a relatively low IQ, which has not previously been well established in the field. This olfactory neuroimaging experimental paradigm is friendly for mentally impaired individuals with olfactory symptoms, such as ASD and schizophrenia, and this method might be useful for the future diagnosis of these problems.

Olfactory sensitivity in individuals with ASD

Our findings showed that ASD participants with high DT were significantly impaired in their sensitivity and hedonic response to olfactory stimuli but there was no significant difference in their odor identification ability. Previous literature has suggested atypical olfactory function in ASD, but the pattern of findings shows much heterogeneity. This is particularly true for investigations of sensory-driven olfactory function, such as odor detection, while some studies reported either enhanced (Ashwin et al., 2014) or decreased odor sensitivity (Dudova et al., 2011; Kumazaki et al., 2016) in ASD; most studies reported no significant differences between individuals with ASD and controls in DT (Suzuki et al., 2003; Tavassoli and Baron-Cohen, 2012; Galle et al., 2013; Addo et al., 2017). The discrepancy in findings might come from a complex blend of variance in participants' demography (age and gender), subtype of ASD (AP, HFA, PDD, general ASD, etc.), sample size, and the study design/test method used.

Considering the similar sample size (over 20) and sampled population (ASD also including AP and HFA, 10 to 20 years old), our findings of impaired odor detection ability in young adults with ASD are consistent with the observations of Kumazaki et al. (2016) in children and teenagers with ASD. A potential explanation for the observed impaired odor sensitivity in these individuals with ASD might be that age matters. It is possible that young individuals with ASD might be compromised in their olfactory sensitivity, but the impairment may be relieved with maturation. This is an open question and warrants future research with longitudinal studies. However, the substantial heterogeneity across studies with respect to odor detection threshold in ASD is in accord with the idea that ASD may be associated with both hyposensitivity and hypersensitivity in olfaction. As such, it is necessary to treat individuals with ASD differently when investigating their relevant brain functions. Therefore, in the present study, we divided the ASD participants into two groups—ASD-Low DT and ASD-High DT—according to their DT and compared their brain responses elicited by odor stimuli with age-matched TD controls.

With respect to odor identification, our task did not provide written label alternatives (one target and several foils) as those used in UPSIT (Doty et al., 1984) and Sniffin' Sticks (Hummel et al., 1997). It was a little difficult for the participants to make the answer without any reference information. Even the control group had poor performance in this aspect. This might be the reason of non-significant difference between the groups. Although some previous studies have reported decreased odor identification ability in ASD (Suzuki et al., 2003; Bennetto et al., 2007; Galle et al., 2013; Wicker et al., 2016), there is also evidence that there is no significant impairment in ASD participants compared to control (Brewer et al., 2008; Dudova et al., 2011; Luisier et al., 2015; Addo et al., 2017).

With respect to the hedonic responses to odor stimuli, i.e., pleasantness, the ASD-High DT participants were found to be significantly different from healthy controls. This finding is consistent with a previous study on the estimation of odor pleasantness in children of around 10 years of age who had ASD (Hrdlicka et al., 2011). One possibility is that the ASD-High DT group could not process the odor stimuli at a metacognitive level to rate the pleasantness. Considering their impaired social capabilities including emotion (Legisa et al., 2013), another possibility could be that these ASD participants had a difficulty in emotionally rating an odor.

Weaker prefrontal activity in the individuals with ASD

With respect to the prefrontal fNIRS data, we found significantly weaker hemodynamic responses in the right DLPFC of ASD participants with lower olfactory sensitivity (ASD-High DT) as compared to the TD control group. Although there was no significant difference in neural activity between the ASD participants with relatively higher olfactory sensitivity (ASD-Low DT) and the control group, the ASD-Low DT group did not show significant right DLPFC activity compared to the control group. These results indicate that individuals with ASD generally have differential DLPFC neuronal basis in processing odor stimuli compared to TD individuals. Such discrepancies may relate to impaired olfactory processing in ASD. More specifically, considering the important role of the DLPFC in executive functions including attention (Duncan and Owen, 2000) and working memory (Levy and Goldman-Rakic, 2000), reduced activity in this region may reflect the general abnormality in attention and working memory in individuals with ASD (Russel, 1997; Travers et al., 2011) during olfactory processing.

In the fNIRS session, although the task requirement was passive perception/olfaction, the participants were instructed that there would be or not be an odor stimulus during the fNIRS measurement and they would be asked to report whether they had smelt something after the fNIRS measurement. Therefore, the participants might have attentively monitored their sense of smell, demanding some degree of attention and working memory. In addition, right DLPFC activation was found to be significantly related to odor sensitivity, which was assessed in the odor DT test, requiring attention and working memory as well. Thus, it is possible that odor sensitivity indirectly reflects the participants' ability of attention and working memory, and consequently correlates with the level of brain activity in the region responsible for these functions. In this perspective, the weaker response in the DLPFC of ASD participants with lower sensitivity (the ASD-High DT group) may be attributed to their deficits in attention and working memory. The neural correlates of olfactory attention and olfactory working memory have been suggested to be in the olfactory bulb or the piriform cortex (Keller, 2011) and in the primary olfactory cortex (Zelano et al., 2009), respectively. On the other hand, robust involvement of the DLPFC in olfactory working memory has been demonstrated in a positron emission tomography (PET) study (Dade et al., 2001). Another fNIRS study also reported the engagement of the bilateral DLPFC and FP in response to a olfactory task requiring attention and working memory (Takakura et al., 2011). Similarly, the significant channel (CH13, virtually covering DLPFC 78.9% and FP 21.1%) of our study also partially covered the FP, which is suggested to function as "gateway" biases of attention (Burgess, et al., 2005; Gilbert et al., 2006; Takakura et al., 2011).

The question remains as to how altered working memory processing and attention is associated with the olfactory anomaly in ASD. There are two possible explanations, one is at the perceptual level and the other is at the cognitive level. The perceptual explanation is that individuals with ASD basically may have impairments in sensory processors such as the olfactory bulb and/or olfactory cortex and these weakened perceptual signals may be reflected as impaired olfactory working memory. An alternative explanation posits the cause at the cognitive level. Specifically, the ASD participants' perceptual processing may not be problematic, but these perceptual signals may not be processed efficiently to be kept as explicit meta-cognitive signals in the DLPFC. Namely, even if individuals with ASD may have unconsciously processed the odors to a similar sensory degree with TD individuals, they themselves could not consciously process the odors due to the problem of attention and/or working memory. This imprecise operation may lead to compromised olfactory processing in ASD.

The cognitive explanation may, however, be the most likely. One reason is that the DLPFC may not activate as a function of the intensity of olfactory stimulation, instead it may primarily encode the presence or the type of olfactory stimuli at the conscious cognitive level. During the fNIRS measurement, we used an odor stimulus with an intensity of 120 NSE, which is higher than the DT of almost all participants and, therefore, should have been perceived. This is also validated by their performance in the post-experiment odor identification task: for the ASD-Low DT group, none of the 12 participants failed to recognize the odor; for the ASD-High DT group, three of the 13 participants failed to explicitly recognize the odor. Thus, the significant difference in neural responses between the ASD-High DT group and the control group is not likely caused by low-level sensory processing of odor stimuli but might possibly be due to higher-order olfactory processing, such as executive function, which has been shown to be impaired in ASD (Hill, 2004; Kenworthy et al., 2008). Moreover, while there was no statistically significant difference in brain activity between the ASD-Low DT group and the control, their brain activity showed a similar but weaker pattern compared to the control group (Figure 5). Considering that the two groups have almost equivalent olfactory sensitivity, the odor used should have stimulated their olfactory system to a comparable degree. However, the ASD-Low DT group showed weaker neural responses. This group may have a problem in odor processing in more complicated social situations that require a higher load of olfactory working memory and/or attention.

A precise definition of the DLPFC's contribution to olfactory working memory and attention is not established. On the one hand, the ASD participants might not be able to activate the DLPFC in response to olfactory stimuli as efficiently as the control group. On the other hand, they may recruit brain regions other than the DLPFC in situations requiring olfactory working memory. A future systematic examination of the relationship between working memory ability and DLPFC activity in individuals with ASD is necessary to investigate these possibilities. In any case, DLPFC deficit as a cause of olfactory processing plausibly explain age dependent olfactory sensitivity for ASD individuals as stated before. Prefrontal cortex develops rapidly during adolescent period and that facilitates matured DLPFC function resulted in unimpaired olfactory function in adults with ASD.

There are also some other issues about DLPFC worth considering. For instance, a recent genetic study reported decreased olfactory receptor expression in the DLPFC of individuals with chronic schizophrenia (Ansoleaga et al., 2015). They suggested that the deregulation of these receptors is associated with olfactory alterations in these patients. Whether there is a similar mechanism in individuals with ASD remains unclear and would be interesting to investigate in future studies. Additionally, while the present study discovered significant group difference in the DLPFC of the right hemisphere only, it does not necessarily indicate that the right DLPFC is predominantly involved in olfactory working memory, but it may contribute to the ongoing research on the lateralization of the working memory of various modalities in the DLPFC (Smith et al., 1996; Murphy et al., 1998) and the lateralization of olfactory-related processing (Zatorre et al., 1992; Brand et al., 2001; Ishimaru et al., 2004b).

Finally, differences in IQ among groups in relation to fNIRS results and DT should be discussed. As for fNIRS results, one may ask whether the weaker prefrontal activity in the ASD groups is due to their impaired ability, as reflected by IQ, to engage in the fNIRS experiment properly. Although the participants in the ASD groups have lower IQ than the TD control group (Table 1), they had no problem in participating the experiment at any stage as confirmed by their proper verbal responses to the odor identification and evaluation questions after each fNIRS session. In addition, they did not have a problem in performing the odor detection task which was more complicated than the fNIRS task. Another issue about IQ is that perceptual sensitivity of odor may directly relate to IQ as our ASD-Low DT group had higher IQ than ASD-high DT group. However, this is not likely, because no correlation between IQ and sensory processing has been reported (Hedner et al., 2010). On the other hand, since the performance of IQ test requires executive functions including attention, the lower IQ of the ASD groups may indirectly reflect their deficits in directing attention toward odor stimulus, which may have led to their impaired olfactory processing and weaker/absence of prefrontal activity.

Conclusion

The present study verified the feasibility of combining a precise and easy-to-use system—the pulse ejection system—for olfactory measurement with fNIRS. We successfully measured olfactory function in individuals with ASD including those with moderate to severe intellectual impairment using this ASD-friendly system. Compared to typically developing controls, ASD participants with lower odor sensitivity showed blunted activity in the right DLPFC in response to odor stimulation. Even in ASD participants with normal odor sensitivity, DLPFC activities were not as significant as the control group. In addition, the strength of olfaction-evoked neural activity in the right DLPFC was found to be correlated with DT. These findings indicate that differential DLPFC function for olfactory processing, particularly olfactory working memory/attention, is related to odor anomaly in ASD. The present study provides insight into the neural mechanisms for specific olfactory malfunctions associated with ASD by revealing deficit at the cognitive brain function as a possible cause. Future establishment of fNIRS-based biomarkers might facilitate as a non-invasive technique to better diagnose olfactory problems suffered by individuals with ASD.

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（４）講演会等の補足資料：

コミュニケーション行動の生涯発達研究拠点

(LSDCOM: Center for Life-Span Development of Communication Skills)では様々な学会，研究会，講演会やシンポジウムを主催，共催してきました。詳細は下記を参照下さい。

http://lsdcom.keio.ac.jp/event/index.html

（４）では一部の LSDCOM 講演会，セミナーシリーズ，シンポジウムのポスター案内等を補足資料として示します。

慶應義塾大学 戦略的研究基盤形成支援事業・コミュニケーション行動の生涯発達研究拠点

第1回　fNIRSセミナーシリーズ

コミュニケーション行動の生涯発達研究拠点ではコミュニケーション行動について心理学・理工学部・医学部による分野横断的研究を行います．その一環として本セミナーシリーズではfNIRS（functional Near-Infrared Spectroscopy)を使った研究手法を正しく理解し脳機能計測手法として有効に活用していくための連続教育講演ならびに研究交流を図るための研究発表を行います．

2016年3月30日（水）18:00～20:00

場所：慶應義塾大学信濃町キャンパス2号館11階中会議室

http://www.keio.ac.jp/ja/access/shinanomachi.html#prg2

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《教育講演》　18:00～

「近赤外分光法による脳機能計測の原理と留意点」

岡田英史（慶應義塾大学 理工学部電子工学科）

近赤外分光法（NIRS）に基づいた脳機能計測やイメージングは，被験者の拘束や測定を行う場所の制約が少ないことから，多様なタスクに対する脳機能計測に応用されている．一方，頭皮上に装着したプローブによって脳組織の血液量変化を検出する手法であることから，得られた信号や画像を解釈するためには正しい計測原理の理解が前提となる．本講演では，NIRSの原理および正確な測定を行うための留意点について解説する．

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《研究発表》　19:30～

「気分障害におけるNIRSの臨床応用」

平野仁一、堀田章悟、山縣文、山中佳保里、三村將

（慶應義塾大学 医学部精神・神経科学教室）

－－－－－－－－－－－－－－－－－－－－

問合せ先：慶應義塾大学日吉心理学研究室・コミュニケーション行動の生涯発達研究拠点・皆川minagawa@flet.keio.ac.jp

参加希望の方はお名前、ご所属を事務局の相吉までメールにてお知らせ下さい

参加受付：　tomomiaiyoshi@gmail.com

慶應義塾大学　戦略的研究基盤形成支援事業・
コミュニケーション行動の生涯発達研究拠点

第2回　fNIRSセミナーシリーズ

本研究拠点ではコミュニケーション行動について心理学・理工学部・医学部による分野横断的研究を行います。その一環として本セミナーシリーズではfNIRS(functional Near-Infrared Spectroscopy)を使った研究手法を正しく理解し，脳機能計測手法として有効に活用していくための連続教育講演ならびに研究交流を図るための研究発表を行います。

日時　2016年 9月8日(木) 18時～20時

場所：慶應義塾大学　三田キャンパス 東館6・7F　G-SEC Lab
https://www.keio.ac.jp/ja/maps/mita.html

教育講演

18:00～
「fNIRSは何を測っているのか？」
山田　亨　（国立研究開発法人 産業技術総合研究所 人間情報研究部門）

【要旨】昨今、応用研究への利用が広がっているfNIRS計測ですが、皮膚血流の影響などが時に深刻なデータ解釈の誤りをもたらすことも近年では知られるようになりました。今回はそのような轍を踏まないために必要なデータの眺め方についてお話します。

研究発表

19:30～19:45
「NIRS による嗅覚機能計測と発達障害との関連の検討」
直井　望[1]，安井愛可[2]，松浦絵理[3]，熊崎博一[4]，岡田謙一[5]，皆川泰代[6]
[1]国際基督教大学教養学部，[2]慶應義塾大学大学院社会学研究科，[3]慶應義塾大学大学院理工学研究科，[4]金沢大学・子どものこころの発達センター、[5]慶應義塾大学理工学部，[6]慶應義塾大学文学部

19:45～20:00
「社会的インタラクション時における乳児の視線と脳反応」
白野陽子[1]，皆川泰代[2]
[1]慶應義塾大学大学院社会学研究科，[2]慶應義塾大学文学部

お問合せ　慶應義塾大学 日吉心理学研究室 コミュニケーション行動の生涯発達研究拠点
参加希望申込　同研究拠点　事務局　相吉宛
参加受付e-mail：tomomiaiyoshi@gmail.com

慶應義塾大学　戦略的研究基盤形成支援事業・
コミュニケーション行動の生涯発達研究拠点

第3回　fNIRSセミナーシリーズ

本研究拠点ではコミュニケーション行動について心理学・理工学部・医学部による分野横断的研究を行います。その一環として本セミナーシリーズではfNIRS(functional Near-Infrared Spectroscopy)を使った研究手法を正しく理解し，脳機能計測手法として有効に活用していくための連続教育講演を行っています。今回は実際的な実験手法や解析の概略を学ぶとともにfNIRSを実際に体験するセミナーです。

日時

2017年
3月11日（土）15時～18時

場所：慶應義塾大学　日吉キャンパス 第8校舎3階　831教室
http://lsdcom.keio.ac.jp/access/index.html
会場の都合により、定員35名（先着順）とさせていただきます。

教育講演

15:00～16:30
「fNIRSによる認知機能の測定：実験計画と解析」
皆川　泰代（慶應義塾大学文学部心理学研究室）

【要旨】fNIRSは比較的簡便に認知活動に伴う脳内活動を明らかにしてくれる装置であるが，実際にはその原理，計測する信号や脳部位，心理実験手法などの様々な知識なしには標的とする脳活動データは得られない。本講演はその中でも知覚や認知機能を研究するためのfNIRSを使った実験の方法について解説する。プローブ配置，刺激の呈示，実験タスクなどを含む実験計画法について解析手法との関連も含めて説明する。

実験体験

16:50～18:00
「光脳機能測定装置fNIRSを実体験してみよう」
大橋　三男（株式会社スペクトラテック）

【概要】赤外光による脳内の血液量変化を計測する装置fNIRSを使って，何に注意して脳機能の測定をするのか実際に自分の手で実験体験をする。あわせて，計測信号に混在する皮膚血流成分を除去するデモを行う。

お問合せ　慶應義塾大学 日吉心理学研究室 コミュニケーション行動の生涯発達研究拠点
皆川　minagawa@flet.keio.ac.jp

参加希望申込　同研究拠点　事務局　相吉宛　　会場の都合により定員35名とさせていただきます
参加受付e-mail：tomomiaiyoshi@gmail.com

第 4 回 fNIRS セミナー（解析編）

コミュニケーション行動の生涯発達研究拠点では fNIRS セミナーを定期的に行っています。今回は第 4 回セミナーとして fNIRS の解析ソフトである POTATo を使ったデータ解析の方法を学びます。参加される方は Matlab をインストールしたノートＰＣをご準備ください。詳細は下記の「ＰＣの事前準備について」を御覧ください。

日時：5 月 18 日（金）10:15-14:00 途中休憩あり
場所：慶應義塾大学日吉キャンパス第八校舎 831 教室
講師：星野英一（慶應義塾大学 LSDCOM 研究員）

参加希望の方はお名前、ご所属を事務局の相吉（tomomiaiyoshi[at]gmail.com）までメールにてお知らせ下さい。先着順で定員 20 名にて締め切らせて頂きます。

主催：戦略的研究基盤形成支援事業・コミュニケーション行動の生涯発達研究拠点
問合せ先：慶應義塾大学日吉心理学研究室・皆川 minagawa[at]flet.keio.ac.jp

ＰＣの事前準備について
【PC】
- Matlab R2012a 以前のものがインストールされた PC(OS は問いません)
- Signal Processing Toolbox
- Image Processing Toolbox

上記の Toolbox は、塾内で借りる Matlab をインストールすると、通常はインストールされます。もし、インストール時に Toolbox を選ぶように指示が出た場合は、すべて追加するようにしてください。

【ダウンロードしておくファイル】
1. POTATo (Hitachi)
http://www.hitachi-hightech.com/jp/products/ind_solutions/ict/human/brain/ot/analyze/kaiseki_ja.html

2. 当日使うプログラム及びデータ
https://drive.google.com/file/d/1KOO4b3QWRwdqczqB_vzLOBi02t7UNekT
(zip のパスワードは当日お知らせします。)

慶應義塾大学　戦略的研究基盤形成支援事業
コミュニケーション行動の生涯発達研究拠点
第 1 回 LSDCOM 講演会「言語とコミュニケーションの脳科学」

コミュニケーション行動の生涯発達研究拠点(LSDCOM)ではコミュニケーション行動について心理学・理工学部・医学部による分野横断的研究を行います。LSDCOM 講演会はコミュニケーション行動についての講演会シリーズです。今回は言語とコミュニケーションの脳科学についてお二人の研究者にご講演いただきます。特に Mueller 氏には言語獲得に関連するトピック, 幕内氏には fMRI を用いた成人の文法処理の研究などをお話しいただきます。

日時：2017 年 7 月 31 日（月曜）15 時—17 時

場所：慶應義塾大学三田キャンパス大学院校舎 1 階　312 教室
https://www.keio.ac.jp/ja/maps/mita.html

≪講演≫15：00-16：00
「How the brain uses language as a tool for memory」
Jutta L. Mueller（Universität Osnabrück）

≪講演≫16：00-16：40
「fMRI study of Japanese」
幕内　充（国立障害者リハビリテーションセンター研究所・高次脳機能障害研究室）

上記は質疑を含めた時間です。すべて英語での講演となります（通訳等はございません）。
事前登録等は不要です。
主催：慶應義塾大学日吉心理学研究室・コミュニケーション行動の生涯発達研究拠点
http://lsdcom.keio.ac.jp/　皆川泰代
共催：科学研究費基盤研究（A）「言語と社会認知能力を支える脳機能の定型・非定型発達の解明」
問い合わせ：（担当：相吉）tomomiaiyoshi@gmail.com

慶應義塾大学　戦略的研究基盤形成支援事業
コミュニケーション行動の生涯発達研究拠点
第 2 回 LSDCOM 講演会

LSDCOM 講演会はコミュニケーション行動についての講演会シリーズです。今回は計算論的モデリングを用いた言語プロソディーと単語分節化（文中からの語の切出し）の研究についてご講演いただきます。

日時：2018 年 1 月 26 日（金曜）10 時半—11 時半
場所：慶應義塾大学日吉キャンパス第八校舎３階　831 教室
http://lsdcom.keio.ac.jp/access/index.html
≪講演≫10:30-11:30
「The Role of Prosody and Speech Register in Word Segmentation: A Computational Modelling Perspective」
Bogdan Ludsan（理研 Brain Science Institute）

上記は質疑を含めた時間です。すべて英語での講演となります。
事前登録等は不要です。
主催：慶應義塾大学日吉心理学研究室・コミュニケーション行動の生涯発達研究拠点
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慶應義塾大学　戦略的研究基盤形成支援事業・
コミュニケーション行動の生涯発達研究拠点

LSDCOMシンポジウム
「社会的相互作用の神経基盤研究その最前線」

コミュニケーション行動の生涯発達研究拠点(LSDCOM)シンポジウムはコミュニケーション行動についての講演会，シンポジウムのシリーズです。今回は複数者のコミュニケーション時における社会的信号処理の脳内機構についてfMRIやfNIRSを用いた研究について紹介し，社会脳の機構やその解明方法について議論をします。

日時　2020年 2月21日 金　14時～17時40分

場所：慶應義塾大学　日吉キャンパス 第8校舎3階　831教室
http://lsdcom.keio.ac.jp/access/index.html

プログラム

14:00～14:40　田邊宏樹（名古屋大学）
「MRIによる二人称視点脳機能イメージング研究：共同注意を始まりとして」

14:40～15:20　小池耕彦（生理学研究所）
「二者同時脳機能イメージング研究：過去，現在，そして未来」

15:30～15:50　徐鳴鏑（慶應義塾大学）
「自然な共同作業の相互作用場面でのfNIRSによる二者同時脳機能計測」

15:50～16:30　森本智志（慶應義塾大学）
「行動レベルの相互作用に着目したfNIRS二者同時計測データ解析」

16:40～17:20　白野陽子（自治医科大学/日本学術振興会）
「乳児における社会的相互作用の脳内基盤—随伴性への脳反応—」

17:20～17:40　総合討論

どなたも参加できます。参加費無料，事前登録等は不要です。
主催：慶應義塾大学日吉心理学研究室・コミュニケーション行動の生涯発達研究拠点（皆川泰代）
共催：JST/CREST「ソーシャルシグナルの共有と拡張による共感的行動の支援」（代表：鈴木健嗣・筑波大学）
お問い合わせ：tomomiaiyoshi@keio.jp（担当：相吉）