労災疾病臨床研究事業費補助金

高次脳機能障害者の診断・リハビリ・社会復帰促進パスの策定

平成28年度　総括・分担研究報告書

研究代表者　　　村井俊哉

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研究要旨
平成 13 年度から行われた実態調査によって、高次脳機能障害の中心となる認知機能障害が、注意障害、記憶障害、遂行機能障害、社会的行動障害であることが判明し、以後高次脳機能障害という用語が徐々に人口に膾炙しつつある。しかしながら、このような認知機能障害が、どのような脳損傷あるいはネットワーク損傷に伴って後遺症として生じやすいのか、さらにはそれがどのような形で社会参加に影響をあたえるのか、あるいは急性期からの経過はどのようなものなのか、といったことはまだよくわかっていない。実際の臨床場面でも、慢性期の症例の診察においては、原因となる疾患や事故の発症から年数がたち、すでに急性期の情報へのアクセスができない状態であることもしばしば経験される。そのような中、今回の研究では、急性期から慢性期、あるいは逆に慢性期から急性期への情報提供を行えるように、社会復帰までを見通したクリニカルパスを作成することを目的とした。さらに、その目的のために必要な下位研究として、①社会復帰に寄与するリハビリテーション・代用手段の獲得（担当：神戸大学：種村）②高次脳機能障碍者の社会復帰の現状の把握（担当：京都府立医科大学：武澤）③慢性期の症候学的検討とその脳内基盤の探索（担当：京都大学：上田）を行った。

A. 研究目的

高次脳機能障害は、主に注意障害、記憶障害、遂行機能障害、社会的行動障害からなり、麻痺などの明らかな身体的後遺症のない患者の社会復帰を難しくする要因になっていることが分かっている。特に、外傷性脳損傷は、若年男性に多く認められ、事故後の長い人生を考えた場合、社会復帰ができるかどうかは非常に大きな問題といえるだろう。一方、少なくとも日本の現状では、脳損傷の急性期にかかわる医療従事者が、症例の慢性期までを見通したケアを行っていることはまれであり、逆に慢性期にかかわる医療従事者が、急性期の情報まで理解していることもまれである。その大きな原因として、急性期から慢性期、あるいは慢性期から急性期への情報提供が少なく、共通した理解を持ちがたい、ということがあげられる。このことを解決するためには、熱心な一部の医療者に任せるような方法よりは、よりシステマティックな、個人に依存しない連携パスの作成が必須であると考えられる。翻って、脳損傷慢性期の症候学がすでに十分確立しているか、ということも疑問である。少なくとも、症候学的特徴と、その神経基盤である脳損傷部位あるいは神経回路との関連については、まだわかっていないことも多い。さらに、障害された能力のリハビリテーションについては、近年ようやくリハビリテーションの成果が問われるようになり、より焦点化されたより効率の良いリハビリテーション・代償手段の獲得方法が要請されている。そのため、今回の研究では、高次脳機能障碍者の社会復帰の実態把握、特に社会復帰に有効なリハビリテーション・代償手段の獲得の方法の探索、社会的行動障害の基盤となる社会認知の障害も含めた症候学的特徴とその神経基盤の探索を目的とし、最終的に急性期から社会復帰までの連携パスを作成することを目標とした。

B. 研究方法

1. 脳卒中症例の高次脳機能障害有病率、およびそのアウトカム評価

京都府下で臨床的に利用されている脳卒中クリニカルパスを利用し、そのデータから、脳卒中症例における高次脳機能障害がどれぐらいの症例に認められるのかを調査し、さらに、そのような症例にはどのような特徴があるのかを抽出した。

2. 就労版「あらた」の改変

高次脳機能障害の支援アプリケーションである「あらた」の就労版の開発を目標とする。現

行版についての利用者・非利用者での比較検討を行い、現行版が利用者に与える影響について検討を行う。また就労支援施設職員へのアンケート結果から、就労版についてどのような改変が必要かについて検討を行う。

3. 症候学的特徴とその神経基盤の探索

慢性期の高次脳機能障害者を対象に、社会認知機能を含めた認知機能検査、QOL を含めた行動評価、睡眠、易疲労性などの身体的特徴の評価を行い、３TMRI で撮像した脳画像と比較検討することで、障害の神経基盤を探索する。アミロイドの沈着の評価のために、アミロイド PET を行い、画像を取得する。合わせて、脳損傷症例の継時的な MRI 画像の撮像を行い、経年変化についての検討を行う。

倫理的配慮に関して

本研究は「世界医師会ヘルシンキ宣言（平成25年10月改定)」および「人を対象とする医学系研究に関する倫理指針(平成27年4月1日施行)」を遵守して実施する。また、分担研究においては各大学の倫理委員会の承認を経て行っている。

C. 現在までの進捗と研究結果

1. 就労支援の現状と支援方法

アンケート回収状況は、高次脳機能障害支援拠点からは74/104の回答を得、地域障害者職業センターでは、(独）高齢･障害・求職者雇用支援機構の協力があり、52 ヶ所すべてから回答、就労移行支援事業所では、1539/34374 の回答を得た。本格的な解析は平成28年度の研究として行うが、現在の試験的な解析では、地域障害者職業センターの利用者のうち、特にジョブコーチの利用が、社会復帰を促進する因子と考えられた。

2. 就労支援の現状と支援方法

「あらた」の使用群、非使用群合わせて80名のデータが集まり、解析を行った。このような information and communication technology (ICT)ツールの利用は、直接症例の能力の改善に繋がることはないが、自己効力感を改善するためには役立つことが示唆された。

3. 症候学的特徴とその神経基盤の探索

慢性期の外傷性脳損傷症例を中心に脳神経画像（MRI 画像）と神経心理検査、行動尺度などの収集を行っており、現時点で局所脳損傷45名・び漫性軸索損傷25名のデータを集積した。脳幹体積の検討からは、脳幹の体積変化が、急性期の意識障害の程度と相関することが示唆された。また、慢性期の脳萎縮の進行に関係するとされるアミロイド蛋白の沈着については、滋賀県立成人病センターとの共同研究の形で、アミロイドPET を用いた研究を開始し、すでに7名のPET画像を撮像した。現在までのところ、外傷性脳損傷症例のアミロイド沈着の特徴としては、基底核を中心としたアミロイドの沈着を認めているが、これについてはもう少し症例数を増やして確認が必要と考える。

また、あわせて症状の評価シートの作成を行っており、将来的に急性期病院から慢性期リハビリテーション病院、さらには福祉支援まで活用できることを目指す。

D. 考察および今後の展望

現在、各研究は比較的順調に進行しており、すでに平成28年度中に、ある程度の結果を出すことができた。いくつかの成果については既に英語論文化され、発表しているが、それ以外についても、公表準備中である。就労支援、および脳卒中症例の現状からは、どのような環境因、あるいは病状の特徴が就労を阻害するのか、ということが確認され、就労版「あらた」の作成は、そのように確認された要因を軽減するためのツールとして使用することが可能な方向に工夫される予定である。症候学的特徴とその神経基盤の探求、評価シートの作成は、高次脳機能障害の症状理解に貢献し、急性期から慢性期、社会復帰時期までをつなぐパスの作成に欠かせないものであると考えられる。外傷性脳損傷症例は平成28年度に予定以上の症例数を蓄積できたため、平成29年度については、外傷以外の原因による脳損傷症例について、データの蓄積に注力する予定である。前脳基底部損傷などの特殊な損傷部位を有する症例についての検討は既に開始しているが、こういった脳損傷症例の損傷部位ごとの特徴をあぶり出す作業については、今年度も継続する予定である。評価シート、日常の行動障害の評価尺度(Social Living 77)は、既に暫定版のコンピュータ化を終了したため、本年度は実地的に運用を開始し、改善を重ねた上で、他の医療機関にも使ってもらえる形に持っていくことを目標としている。

E. 結論

引き続き症例を蓄積し、高次脳機能障害者の症候学的特徴と神経基盤の探求を行う。高次脳機能障害の実態調査に基づき社会復帰に必要なパスの作成を進める。さらに同一症例の追跡によりリハビリテーションおよび代替手段の開発を継続していく。

F. 健康危険情報

特記すべき報告事項はない。

G. 研究発表

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H. 知的財産権の出願・登録状況

1. 特許取得

本年度はなし

2. 実用新案登録

本年度はなし

3. その他

特になし。

臨床研究事業費補助金
分担研究報告書

外傷性脳損傷患者の神経心理・画像検査

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研究要旨

外傷、特に交通外傷に伴う脳損傷は、若年者に生じやすく、その後の長い人生を考えると、外傷性脳損傷とその後遺症である高次脳機能障害の影響は甚大である。今回の研究では、交通外傷を主とする様々な原因による脳損傷症例を対象として、古典的認知機能、社会的認知機能、QOL などの行動評価を行い、あわせて３T MRI 画像を撮像し、損傷部位、あるいは損傷の原因別の症候学的特徴、その神経基盤について検討を行うことを目的としている。また、外傷性脳損傷では、慢性期にアミロイドの沈着が生じ、それが脳萎縮に関連するという報告が、慢性外傷性脳症（chronic traumatic encephalopathy）を対象とした研究でなされており、本研究の対象者に対しても、アミロイド PET を用いて、アミロイドの沈着を評価することを開始した。また、高次脳機能障害の評価シートについては、作りこみを続け、バージョンアップを行い、臨床目的に耐えるシートをほぼ完成させた。研究協力者の川上が作成、試用している Social Living77（社会生活評価ツール）と合わせ用いることで、各症例についての包括的な評価と理解が可能になるよう工夫している。

A. 研究目的

高次脳機能障害を呈する疾患には、脳血管障害、頭部外傷、脳炎、脳腫瘍などが存在する。急性期の意識障害を呈する病態から、いわゆる通過症候群を経て、慢性期の、固定された高次脳機能障害に至るまでの期間は、一般に想定されているより長く、症例によっては半年、1年といった期間を要する。一方で、現状の医療のもとでは、この間に複数回の転院を重ねる、あるいは主科となる担当科が変更となることにより、必要な医療情報が抜け落ち、結果として慢性期の評価が十分なされないまま放置されることも多い。このような事態が生じる大きな原因として、１脳損傷に伴う後遺症自体があまりよく知られていない、２臨床データが急性期から慢性期にかけて十分に伝達されていない、ということが挙げられる。さらに、慢性期においては、漫然とした経過観察のみが行われ、脳萎縮の進行を評価し、その危険因子について検討する、ということはほとんど行われていない。本研究では、そもそもあまりデータベースが存在しない、外傷性脳損傷の後遺症症例を中心に、データベース作成を行い、症状と脳損傷部位との関連について、得られたデータベースをもとに検討を行うことを第一の目的としている。第二の目的は、急性期から慢性期にかけて、過不足なく臨床情報を伝達する仕組みづくりであり、その第一歩として、高次脳機能障害の評価シートの作成を行っている。さらに、外傷性脳損傷を対象として、脳萎縮や神経心理検査の経年的変化を検討することを開始し、経年的変化に対するアミロイドの沈着の影響を調べるため、アミロイド PET を行うことで、アミロイドの沈着についても評価を開始することとした。

B. 研究方法

１．症候学的特徴と脳内基盤

Ｉ．被験者

被験者は、分担研究者が行っている京都大学医学部附属病院精神科あるいは脳神経外科の外来、御所南リハビリテーションクリニック、京都市地域リハビリテーション推進センターのいずれかに通院中の外傷性脳損傷患者、または協力機関である京都府立医科大学、京都市心身障害者福祉センター附属リハビリテーション病院、京都大原記念病院、京都医療センター、滋賀県立成人病センターに通院中の外傷性脳損傷の症例からリクルートした。年齢は学童期以上 65 歳以下とし、それ以外の除外基準はもうけなかった。つまり、通常であれば精神疾患、神経疾患などの既往は除外基準として設定するものであるが、これ自体が予後に影響する因子となりうることから、これを除外基準とはしなかった。ただし、現在予備的に行っている画像解析では、精神疾患、神経疾患の既往のある患者は除外している。

II. 評価項目

質問用紙

EMC、FrSBe、 GSES、GSE、 CIQ、FAI、Zarit 介護負担尺度、VAS、自己効力感調査表、使用後の感想（本人、家族）

認知機能

MMSE、 RBMT、 WMS-R の論理的記憶、 WAIS－Ⅲ、TMT-A、TMT-B

倫理的配慮に関して

本研究は「世界医師会ヘルシンキ宣言（平成25 年10 月改定）」および「人を対象とする医学系研究に関する倫理指針（平成27 年4 月1 日施行）」を遵守して実施する。また、京都大学医の倫理委員会の承認を経て行っている。

III. 画像の取得と解析

京都大学に設置された研究用 3 TMRI を用いて、T1、T2、FLAIR、SWI の撮像法による構造画像、Tractography を行うための DTI 画像、さらに resting state fMRI 画像を撮像した。

T1 画像は 1mm^3 に再構成し、Voxel-Based Morphometry 解析に使用した。その際、損傷部位の確認のため、T2, FLAIR, SWI の各画像を参照した。

脳幹体積については、T1 強調画像を FreeSurfer を利用して中脳・橋・延髄に分け、それぞれの体積を健常者と比較し、急性期の意識障害などの指標、慢性期の易疲労性・睡眠障害の指標との関連を検討する。

２. 評価シートの作成

将来的に急性期病院から慢性期リハビリテーション病院、さらには福祉支援まで活用できることを目指して、高次脳機能障害評価シートの作成をほぼ終了した。

３. PET 画像検査

Ｉ. 被験者

被験者は、分担研究者が行っている京都大学医学部附属病院精神科あるいは脳神経外科の外来、御所南リハビリテーションクリニック、京都市地域リハビリテーション推進センターのいずれかに通院中の外傷性脳損傷患者、または協力機関である京都府立医科大学、京都市心身障害者福祉センター附属リハビリテーション病院、京都大原記念病院、京都医療センター、滋賀県立成人病センターに通院中の外傷性脳損傷の症例からリクルートした。

II. 画像の取得

滋賀県立成人病センター研究所との共同研究として、第二世代のアミロイドイメージング製剤として開発された 5-(5-(2-(2-(2-Fluoroethoxy)ethoxy)ethoxy)benzofuran-2-yl)-N-methylpyridin-2-amine ([18F]FPYBF-2)を用いて、脳内のアミロイド蛋白の沈着を評価する。

C.D. 研究結果と考察

１. 症候学的特徴と脳内基盤

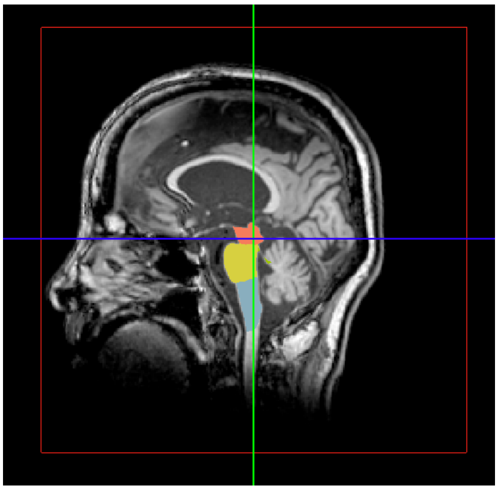
リクルート人数 20(男性 15 名女性 5 名)

利き手：全員右手

その他、背景情報は次のとおりである。

	DAI (n = 20)	Healthy (n = 20)	statistics
Age (years)	38.30± 12.95	36.25 ± 9.51	non-significant
gender	male : 15	male : 15	
Education(years)	13.1 ± 2.7	14.6 ± 2.2	non-significant
IQ (JART)	101.7 ± 11.1 (n=19)	107.8 ± 7.1 (n=17)	non-significant
IQ (WAIS-Ⅲ)	90.8 ± 19.5 (n=19)		
Month from onset	99.5 ± 88.2 (5-355)		
Severity (PTA days)	43.2 ± 36.5 (0.5-150)		
Severity (GCS)	9.7 ± 4.5 (4-15)(n=11)		
Cause of injury	Traffic accident : Fall :		

<u>画像解析結果</u>



脳幹体積は、上図のとおり中脳、橋、延髄に FreeSurfer を利用して半自動的に分割したうえで測定した。

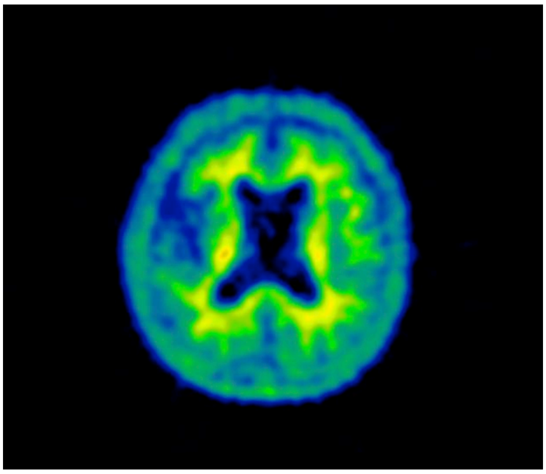
	Pearson Correlation (r)	p-value
Whole brain stem/ICV	-0.564**	0.01
medulla/ICV	-0.361	0.117 NS
pons/ICV	-0.588**	0.006
midbrain/ICV	-0.569**	0.009
SCP/ICV	-0.327	0.159 NS

結果として橋の体積において最も強く、Post Traumatic Amnesia の期間との相関を認めた。この結果については、全脳体積の補正を行うかどうかの検討などを行っており、現在投稿準備中である。

2. PET 画像検査

現在外傷性脳損傷患者 7 名のデータ収集済み（下図）。

今後 MRI の構造変化と合わせて解析予定。



＜その他＞

また、研究協力者と共に、下記の通り前脳基底部損傷症例、びまん性軸索損傷による脳損傷例について、神経心理学的な観点からより詳細に検討を行った。

研究①「前脳基底部損傷例を対象としたエピソード記憶における時間判断の検討」

【背景】

時間情報の処理には，記憶の中の時間情報や，経過時間のような時間知覚が含まれ，これらの処理には前頭葉や側頭葉の機能が重要であるとされている．前脳基底部を損傷した患者では，自伝的記憶の中の時間情報や出来事の順序の想起障害が報告されてきたが，親近性判断のような順序判断課題を用いた検討はほとんどない．また同症例においては，時間知覚のような時間情報の処理過程についても明らかではない．本研究では，前脳基底部損傷例，健常高齢者，並びに健常若年成人を対象として，記憶の中の時間情報の処理過程を検討するために親近性判断課題を，時間知覚の処理過程を検討するために時間知覚課題を行った．本報告では，親近性判断課題における結果を報告する．

【方法】

対象は，京都大学医学部附属病院神経心理外来および山口大学医学部附属病院脳神経外科外来前脳基底部損傷例 9 名（男性 9 名；平均 56 歳；標準偏差 11.3 歳），健常高齢者 47 名（男性 23 名；平均 65.8 歳；標準偏差 2.1 歳），並びに若年健常成人 48 名（男性 25 名；平均 21.4 歳；標準偏差 1.5）であった．親近性判断課題では，連続的に記銘された写真が，テスト段階にてペアで提示され，それらの刺激のどちらがより後に提示されたのかが判断された．また各種神経心理学（全般的認知機能，前頭葉機能，言語性・視覚性記憶，注意など）検査が実施された．

【結果と考察】

各患者群，健常高齢者群，および若年健常成人群における平均正答率を算出し，被験者間 1 要因分散分析を行った．結果，3 群の間で有意な要因の効果が認められた［$F(2, 98) = 29.52$, $p < 0.01$］．下位検定（Ryan 法）の結果，患者群と若年健常成人の間，および健常高齢者群と若年健常成人の間にそれぞれ有意差が認められた（それぞれ，$p < 0.01$）．患者群と健常高齢者群の間に有意な差はなかった（$p = 0.87$）．これらの結果から，前脳基底部損傷例では，出来事の順序の判断において，健常若年成人よりも成績の低下を示したが，健常高齢群との間で成績に差がなかったことが示された．これらのことから，前脳基底部領域が，出来事の順序判断のような処理過程に関与しない可能性が考えられた．今後は，各種神経心理学検査との関連を詳細に検討する予定である．また，前脳基底部領域と経過時間の知覚のような時間情報の処理過程との関連における解析を進めていく予定である．

研究②「びまん性軸索損傷例における外傷後健忘期間と認知機能との関係の検討」

【背景】

びまん性軸索損傷（DAI）は, 外傷性脳損傷（TBI）により引き起こされる，白質の広範な損傷である．先行研究では，DAI において，認知機能の低下や日常生活上の問題が残存することが示されている．また，TBI における外傷後健忘（PTA）期間を用いた重症度評価により, 知能や日常生活動作（ADL）の予後が予測されることが示唆されている．しかし，DAI における PTA の期間が，神経心理学的症状や日常場面における問題をどの程度予測できるのかについてはほとんど明らかになっていない．本研究では，DAI 患者，および大脳皮質限局性脳損傷患者を対象とし，認知機能の低下や日常生活場面での困難の程度と，PTA 期間との関係の特徴を検証した．

【方法】

対象は，京都大学医学部付属病院脳神経外科神経心理外来に通院する DAI 症例 16 名（男性 13 名；平均 38.6 歳；標準偏差 14.3 歳），および大脳皮質限局性脳損傷症例 32 名（男性 20 名；平均 43.3 歳；標準偏差 13.4 歳）であった．症例における PTA の期間は，主治医によって評定された．認知機能検査として, ウェクスラー成人知能検査（WAIS-III），ウェクスラー記憶検査（WMS-R），前頭葉機能検査（FAB），トレイル・メーキングテスト（TMT），語流暢性課題，前頭葉システム行動スケール（FrSBe 本人版/家族版），および遂行機能障害症候群行動評価（BADS）を用いた．日常生活に関する検査として，リバーミード記憶検査（RBMT），日常記憶チェックリスト（本人版/家族版），WHO-QOL26（QOL26），および WHO 障害評価尺度（WHODAS；家族による評価）を用いた．本研究では，DAI における PTA 期間の長さにどのような検査項目が関連するのかにおける特徴を抽出するために，DAI 群と，TBI 群（DAI 群＋大脳皮質限局性脳損傷患者群）に分類し，重回帰分析を行った．

【結果と考察】

本研究では，本人視点と家族視点を区別し，2 つの重回帰分析を行った．①PTA 期間を従属変数とし，WMS-R の遅延再生と注意集中，BADS，FAB，患者の主観的な日常生活検査である日常記憶チェックリスト（**本人版**），および QOL26 の各得点を独立変数として，DAI 群と TBI 群でそれぞれ重回帰分析を行った結果，前者では BADS（β=-0.67, F=11.69, p<.01），後者では BADS（β=-0.36, p<.05）と FAB（β=-0.36, p<.05）を含むモデルによって，PTA 期間の長さが有意に説明された（F=13.68）．②WMS-R の遅延再生と注意集中，BADS，FAB，客観的な日常生活検査である日常記憶チェックリスト（**家族版**），および **WHODAS** を独立変数とする重回帰分析を行った結果，DAI 群では BADS（β=-0.41, p<.05）と WHODAS（β=0.57, p<.01）を含むモデルが（F=15.95）, TBI 群では BADS（β=-0.36, p<.05）と FAB（β=-0.36, p<.05）を含むモデル（F=13.68）が, PTA 期間の長さを有意に予測した．結果から，DAI の特徴として，前頭葉機能の低下に加え，WHODAS のような家族により評価される客観的な日常生活上の困難が PTA 期間を説明することが示された. DAI では, PTA 期間が長いほど，自身の状況を適切にモニターし評価する機能が低下しうることが考えられた．今後、更なる解析を進める予定である。

E. 結論および今後の展望

今年度は、症例数については、当初の予定よりも多く集積ができた。外傷性脳損傷の症例数はある程度蓄積できてきたため、今後、脳卒中を含む、他の疾患についても、症例の蓄積を進める予定である。

症例評価シートについては、暫定版がほぼ完成したため、実際に使用を開始していく。まずは、当研究グループ内での使用を開始し、改定が必要かどうか検討を行う。一定の使用経験ののち、評価シートを使ってもらえる医療機関を検討し、相談を行っていく。

PET 画像については、現在で 7 例の画像の取得が終了した。外傷性脳損傷例の PET 画像については、これまであまり研究がなく、15 例から 20 例の症例を蓄積し、MRI の構造画像データと比較検討を行い、どのような損傷のタイプがアミロイドの沈着を生じるのかなどについて検討を行っていく。より詳細な神経心理学的検討についても、今後も行っていく予定としている。

G. 研究発表

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H. 知的財産権の出願・登録状況

特記なし

労災疾病臨床研究事業費補助金
分担研究報告書

就労版「あらた」の改変に関する研究

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研究要旨

10歳代から60歳代の高次脳機能障害者の多くは就労を目標にリハビリテーションを受療している者が多い。高次脳機能障害は失語症や半側空間無視など症状は様々だが、その中でも記憶障害が最も多いと言われている。記憶障害のリハビリテーションには要素的障害としての記憶力低下を改善する方法と代償手段を指導する方法が選ばれる。この代償手段にはメモリーノートが一般的であるが、近年は IT の進歩で電子ツールの利用が始まっている。2014 年に生活を補綴する ICT ツール「あらた」の開発を行った。パイロット試験では一部効果を認める症例もいたものの治療効果は明らかではなかった。今回は現「あらた」の治療効果の検証を行い、その結果及び就労支援員の意見をもとに就労版「あらた」への改変を目的とする。

A. 研究目的

高次脳機能障害を呈する疾患として脳血管障害や頭部外傷が挙げられる。近年では交通事故や転落事故以外にスポーツ等で生じる軽度の外傷性脳損傷の報告も増えている。その外傷性脳損傷の原因の多くを占める交通事故は 10 代から 30 代と就労世代に多くみられる。彼らのリハビリテーションでの目標は生活の自立、次に就労を含む社会復帰である。脳に損傷を負うと身体機能障害や高次脳機能障害を呈し、社会復帰の妨げとなっていることも多い。高次脳機能障害は失語症や半側空間無視と症状は様々だが、高次脳機能障害モデル事業の調査では 90%が記憶障害を呈すると報告もあり、高次脳機能障害のなかでも記憶障害を呈する割合が最も多い。記憶障害のリハビリテーションには要素的障害としての記憶力低下を改善する方法と代償手段を指導する方法が選ばれる。この代償手段にはメモリーノートが一般的である。近年は IT の進歩で電子ツールの利用が始まっているが、多くはメモなどの紙媒体を利用している。紙媒体の場合は自らメモを見ないと意味を成さないといった問題がある。

我々は2014年に記憶障害者支援のひとつである外的補助手段のアプリケーション「あらた」を企業と共に開発した。すでに少人数でパイロット試験を行い、利用者からは肯定的な意見を頂き、アプリケーションの基本的な操作性を確認した。そこで今回、「あらた」の効果を無作為割り付け比較試験での検証と就労支援施設の職員からのアンケート調査にて、就労版「あらた」改変を検討した。

本研究では、以下のことを目的とする
1）生活を補完する ICT「あらた」による
生活面、職業能力面での改善効果
2）生活を補綴する ICT「あらた」を使用
することでの認知機能の改善効果

これらに対応して、本研究における仮説は以下を含む

① 生活補綴する ICT「あらた」は記憶障害者の外的補助手段は従来のメモリーノートよりも効果があり、生活の自立度があがる
② 「あらた」を使用することにより自身で行動する機会が増え、介助量が軽減し家族のストレスが軽減する
③ 「あらた」は写真機能や文字記入が工夫されていること、また家族が代わりに記入できることでメモリーノートとしての利用頻度が増す
④ 日々ＩＣＴを利用することで生活の向上と操作等の脳活動が増すことで、認知機能が維持、または向上する
⑤ 職場でもＩＣＴ「あらた」は利用可能である

B. 研究方法

Ⅰ.「あらた」の治療効果検証

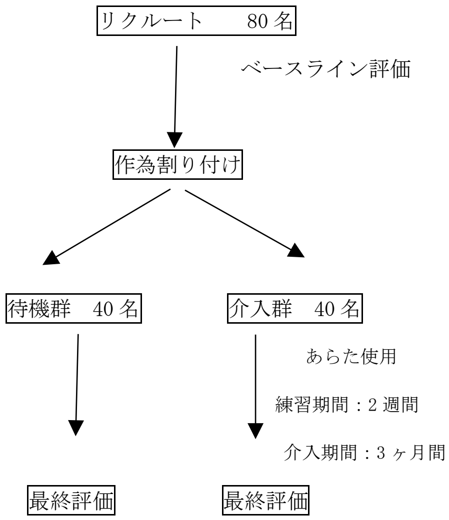
ⅰ. データ取得の向き

前向き研究である

ⅱ. 研究の種類

本研究は、2 群並行群間比較試験であり、非盲検化無作為割り付け臨床試験である。

研究デザイン



対象基準
1）エントリー時：16 歳～65 歳
2）医師の診断にて高次脳機能障害（記憶障害、注意障害、遂行機能障害など）を呈し、生活や仕事で記憶障害に起因する問題を呈している者
3）ＲＢＭＴまたは WMS－R（論理的記憶Ⅰ・Ⅱ、視覚性再生Ⅰ・Ⅱ）が正常値より低い項目があった者
4）京大病院または協力病院及び施設への来院可能な方または近隣病院でリハビリ介入を受けている者
5）本人または家族がタブレットの管理が可能な者

除外基準
1）進行性の認知障害者
2）先天性の発達障害者
3）重度の認知機能障害
(MMSE１８点以下)

ⅲ. 評価項目

1）生活での問題について
・Everyday Memory Checklist :EMC

・Community Integration Questionnaire: CIQ
・Frenchay Activities Index 自己評価: FAI
・General Self‐Efficacy Scale: GSES
・General Self‐Efficacy:GSE
・Zarit 介護負担尺度
・Frontal Systems Behavior Scale: FrSBe

２）認知機能の測度として
・Wechsler Adult Intelligence Scale-Third Edition: WAIS－Ⅲ（知識、数唱、符号）
・Wecheler Memory Scale-Reviseed: WMS-R の論理的記憶Ⅰ・Ⅱ、視覚再生Ⅰ・Ⅱ
・Rivermead Behavioural Memory Test: RBMT
・Trail Making Test:: TMT‐A、TMT‐B

倫理的配慮に関して

本研究は「世界医師会ヘルシンキ宣言（平成25 年10 月改定）」および「人を対象とする医学系研究に関する倫理指針（平成27 年4 月1 日施行）」を遵守して実施する。
また、京都大学医学部附属病院倫理委員会2016年2月と神戸大学保健学研究科2016年2月にて倫理委員会の承認を得ている。

対象者に対する配慮

① 待機群の者にも研究終了後に３ヶ月間「あらた」使用を可能とする。
② 個人情報の保護
③ 不利益は評価時に時間的拘束が発生する。
④ 研究の説明と同意を得た後でも研究参加を断ることが可能。

Ⅱ．あらたの使用状況及びアンケート調査

あらたの効果検証研究であらたを使用した被験者 80 名と就労支援職員 12 名に現在のあらたの使いやすさや改変項目を調査する。また就労支援員には就労支援の施設で使用して頂き就労場面での改変機能についてご意見を頂く。

C．研究結果

Ⅰ．「あらた」の治療効果検証

参加者 80 名の内 2 名が脱落し、78 名（男性 53 名　女性 25 名）にて研究を実施した。参加者の平均年齢は 43±12.6 歳,MMSE27.4±3.4 であった。参加者は発症 1 年以上を経過し、自宅で生活を行なっていた。

介入群と待機群の質問紙結果を表 1 と認知機能の神経心理検査結果を表 2 に示す。質問紙の結果については健忘の度合いを評価する EMC（本人評価・家族評価)、QOL 評価の CIQ、ADL の自立度の尺度の FAI、介護負担尺度の Zarit 介護負担尺度、前頭葉機能検査（アパシー・脱抑制・遂行機能）評価の FrSBe は介入群、待機群ともに治療前後で有意な変化は示さなかった。自己効力感の尺度である GSES（$p=0.001$)、GSE（$p=0.027$）があらたを実際に使用した介入群で有意な向上を示した。認知機能評価の神経心理検査については、あらたを使用した介入群、使用せずに従来の手帳等を用いて生活していた待機群の両群とも初期評価から 3 ヶ月後には一部有意な向上を示した。介入群は WAIS-Ⅲの知識（$p=0.033$)、WMS-R の論理記憶Ⅱ（$p=0.003$）が有意な向上を示し、待機群は WAIS‐Ⅲの数唱（$p=0.018$)、WMS-R の論理記憶

Ⅰ（ｐ＝0.008）、視覚再生Ⅱ（ｐ＝0.046）と有意な向上を示した。

また、介入群のあらたの使用頻度には個人差があり、毎日使用する者、または週 3 回程度の者もいた。使用頻度が少ない要因としては、タブレットを持ち歩けない、生活に変化がなく入力する内容がない、操作が難しい、忘れるなどが挙げられた。

表１）質問紙評価結果

	質問用紙	あらた開始前 平均±標準偏差	あらた使用３ヵ月後 平均±標準偏差	p値
介入群	EMC（本人）	19.17±8.4	18.23±6.78	0.93
	EMC（家族）	13.97±6.22	14.26±8.01	0.105
	CIQ	13.03±8.19	13.13±4.82	0.79
	FAI	21.38±8.19	21.41±9.09	0.873
	GSES	6.13±3.91	7.59±3.47	＊＊0.001
	GSE	71.74±11.58	76.77±14.88	＊0.027
	Zarit 介護負担尺度	34.24±14.87	34.44±16.61	0.169
	FrSBe（本人）	68.41±10.88	67.94±7.42	0.636
	FrSBe（家族）	75.73±17.02	74.9±15.34	0.922
	質問用紙	初期 平均±標準偏差	３ヵ月後 平均±標準偏差	p値
待機群	EMC（本人）	15.33±8.17	14.82±7.15	0.549
	EMC（家族）	16.89±12.03	16.7±16.26	0.584
	CIQ	13.56±4.95	13.31±4.27	0.494
	FAI	20.28±8.29	21.26±9.187	0.137
	GSES	7.97±6.27	7.18±3.79	0.968
	GSE	73.1±7.4	72.18±9.25	0.674
	Zarit 介護負担尺度	30.92±24.52	30.03±11.31	0.556
	FrSBe(本人）	71.02±10.2	69.68±8.82	0.092
	FrSBe（家族）	72.93±11.1	71.66±9.15	0.364

Wilcoxon の符号順位和検定　ｐ＜0.05＊　ｐ＜0.01＊＊

表 2）神経心理検査結果

	検査名	あらた開始前 平均値±標準偏差	あらた使用 3 ヶ月後 平均値±標準偏差	t値	p値
介入群	符号（WAIS-Ⅲ）	6.13±4.03	6.28±3.92	-0.758	0.453
	数唱（WAIS-Ⅲ）	7.69±3.14	8.44±3.75	-1.577	0.123
	知識（WAIS-Ⅲ）	6.69±3.23	7.46±3.35	-2.214	＊0.033
	論理記憶Ⅰ（WMS－R）	14.15±8.33	14.49±8.33	-0.272	0.787
	視覚再生Ⅰ（WMS-R）	29.79±10.91	31.44±9.1	-1.211	0.234
	論理記憶Ⅱ（WMS－R）	7.1±7.65	9.85±8.24	-3.123	＊＊0.003
	視覚再生Ⅱ（WMS-R）	18.62±13.11	20.44±13.69	-1.757	0.087
	RBMT	14.69±5.6	15.41±5.98	-1.21	0.234
	TMT-A	145.05±73.01	147.28±73.86	-0.319	0.752
	TMT-B	184.54±81.65	178.72±77.34	-0.573	0.57
待機群	検査名	初期 平均値±標準偏差	3 ヵ月後 平均値±標準偏差	t値	有意確率
	符号（WAIS-Ⅲ）	6.21±3.29	6.26±3.33	-0.208	0.836
	数唱（WAIS-Ⅲ）	7.41±2.92	8.10±3.4	-2.471	＊0.018
	知識（WAIS-Ⅲ）	7.05＋2.96	7.51＋3.02	-1.966	0.057
	論理記憶Ⅰ（WMS－R）	12.21±6.71	14.7＋7.81	-2.814	＊＊0.008
	視覚再生Ⅰ（WMS-R）	32.69±7.52	34.36±5.47	-1.371	0.178
	論理記憶Ⅱ（WMS－R）	8.79±8.8	9.67±8.35	-0.697	0.49
	視覚再生Ⅱ（WMS-R）	22.36±12.59	25.1±11.92	-2.061	＊0.046
	RBMT	15.33±5.89	14.18±5.65	1.675	0.102
	TMT-A	134.18±69.98	136.56±54.5	-0.348	0.73
	TMT-B	169.33±103.634	164.69±68.12	0.362	0.72

T 検定　p＜0.05＊　p＜0.01＊＊

Ⅱ．あらたの使用状況及びアンケート調査の結果

あらた効果検証研究に参加した介入群と待機群 45 名に研究終了後にあらたの使用状況について、また就労支援施設職員 12 名に現在のあらたを就労版に改変するための意見調査を実施した。参加者の使用状況を表 3〜5、改善項目を表 8 に記載し、就労支援員の回答を表 6 と 7、就労版に向けての追加項目を表 9 に示す。まず参加者によるアンケート調査では、ICT ツールへの便利さは理解するものの、従来の手帳などの代償手段からの変更に抵抗感や不安を呈する症例も多く、特に

50～65 歳の ICT ツールを経験が少ない層において同様の意見がみられた。また使用頻度が少ない要因としては、「操作を覚えることが難しく使いこなすことが難しい」、若い症例の多くは「タブレットが鞄に入らないため持ち運びができず外部でのスケジュール変更が難しかった」、「生活リズムが決まっている」、「入力する予定がない」との意見もあった。あらたの使いやすさについての質問では、「全ての機能を覚えることは難しい」との回答があり、殆どの症例が、予定入力と日記など一部の機能のみを使っていた。またタブレットの文字入力に失敗し、時間を要する症例も多くみられた。更に、殆どの参加者が予定入力と日記を使用し、日記については楽しかったといった意見もあった。

就労支援員への調査では一部改変すれば就労場面でも使用が可能との意見が大半であった。現在のあらたで使用できる機能としては予定入力が多かった。改変内容についてはあらた自体の操作の簡素化と新たな機能追加が必要との意見であった。追加項目の内容としては、仕事の順番や手順がわかるように ToDo リストや動画・静止による作業手順の説明機能が挙がった。

また、参加者、就労支援員ともにあらたで便利と思われる機能は予定入力と日記機能であった。

表 3）あらたの使用頻度

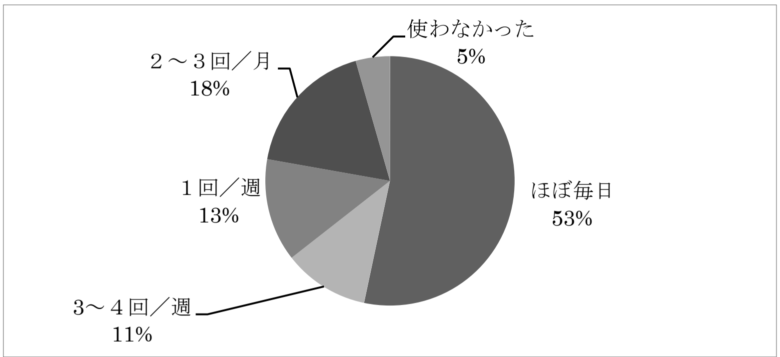


表 4）あらたの使いやすさ

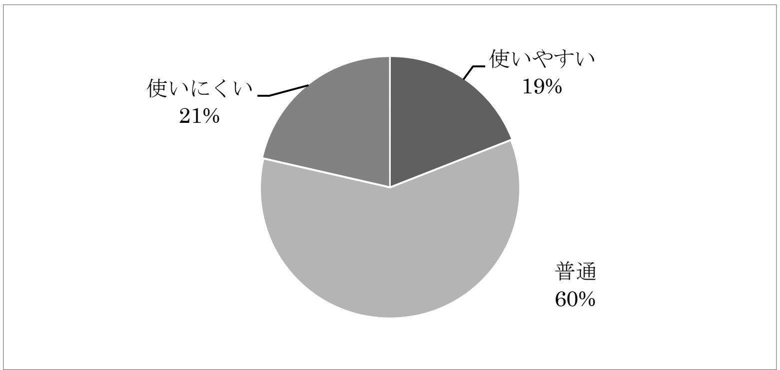
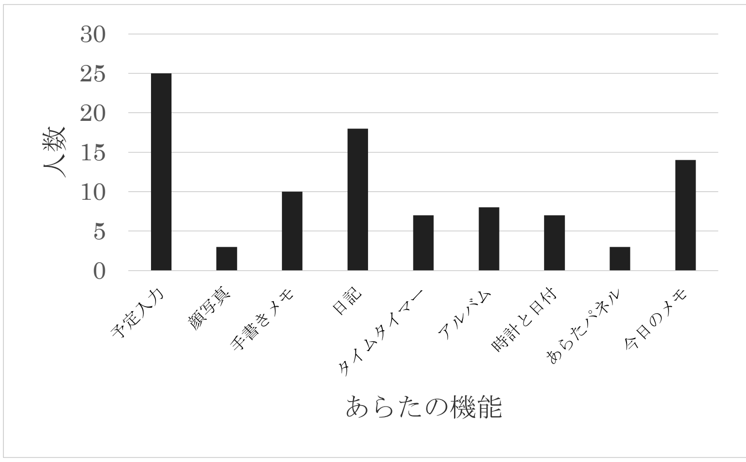
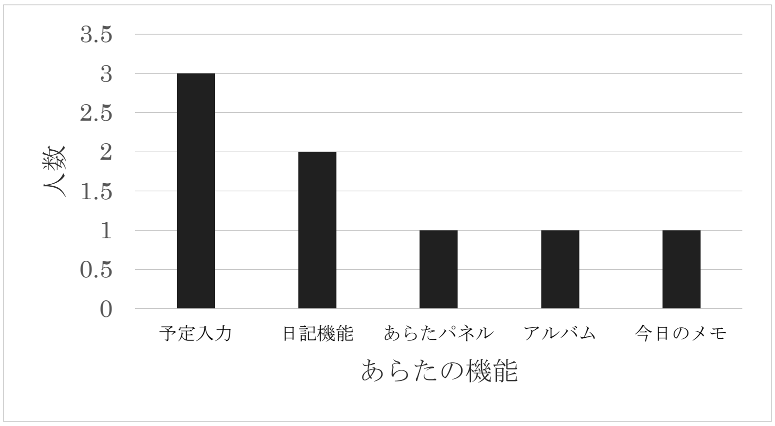


表 5）あらたの便利な機能（参加者）



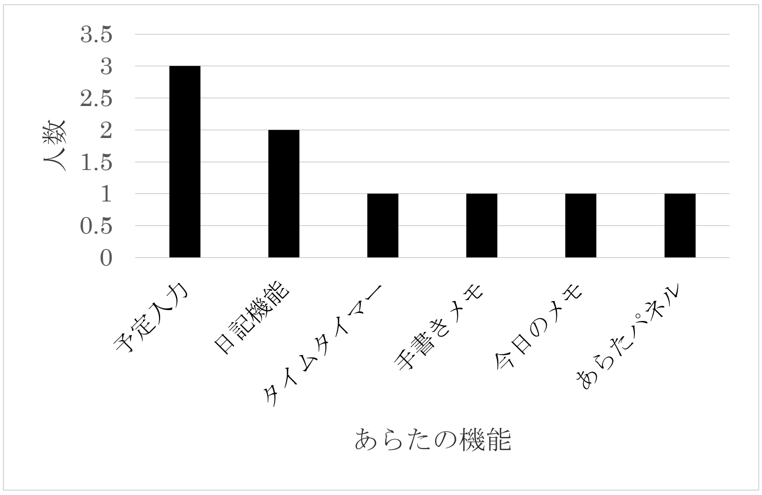
（複数回答あり）

表 6）あらたの便利な機能（支援員）



（複数回答あり）

表 7）就労場面で使用できる機能



（複数回答あり）

表 8）あらたの改変項目

・インターフェース回数を減らす
・インターフェース回数を減
・カレンダーからのアクセスで全ての機能につながる
・リマインダー機能の時間設定が難しい
・携帯できるサイズにして欲しい
・買い物リストが欲しい
・音を徐々に大きくする

表 9）就労版あらたの追加機能

・体調に関する記入項目
・カレンダー予定に場所と人の記入
・ToDo リスト
・メトロノーム機能
・動画撮影（作業手順記録）
・録音機能（会議の録音）

D. 考察

ICT ツール「あらた」は、生活における健忘や介護度を統計学的に有意な改善までは至らなかった。しかし記憶に対する能力の改善は感じないものの、あらたを用いることで、物事をうまくできると予測する自己効力感が高まり、生活面での不安感は改善や自信に繋がったと考える。また認知機能については、ICT ツールに頼っても認知機能は特に低下を示さず、逆に ICT ツールを操作することで一部の認知機能は向上を示した。しかし、あらたを使用しなかった待機群も介入群よりも若干多くの項目で認知機能の有意な改善を示した。このことより従来の手帳や自己の能力でスケジュールを管理しようとする方が、より認知機能を働かせ認知機能は改善したと考えられる。しかしあらたを用いても、タブレット操作や予定入力などでは認知機能を働かせていると考えられる。また、あらたの機能で日記機能が多くの参加者が気にいり利用されていた、日々の出来事を思い出すといった事を行なうことで論理記憶Ⅱの長期記憶の改善にも繋がったと考えられる。

今回、あらたの効果検証とあらたの使用状況における調査より、ICT ツール「あらた」の効果や便利さは多くの参加者が理解されていたが、実際に生活に役立つツールとして使うには個人差がみられた。使用頻度が少なかった要因としては記憶障害でタブレットの操作方法が覚えられない、運動機能障害や認知機能の問題でタブレットの画面をタッチして文字を入力することが難しいなど障害面も問題もみられた。また、外出頻度が高く、あらたの機能が必要な参加者にとってはタブレットのサイズが鞄に入らない、外で失

くしたら不安などの理由で使用頻度が少なかった。

本研究の被験者、就労支援員ともに予定入力の必要性と便利さを認めている。記憶障害の症例は手帳にスケジュールを記載するが見ることを忘れ、結果的に約束やスケジュールのミスに至ることが多い。あらたの場合はリマインダー機能があり予定表を見ることを忘れていてもあらたがアナウンスすることでスケジュール管理のミスを減少できる。また、就労の場では、多くの仕事内容を覚える、時間内に作業を終了させる必要がある。一度の説明では仕事内容を覚えることが難しい場合に動画や静止画で視覚的なメモができる。そして作業工程の終了時刻を入力することで自己の仕事ペースをフィードバックすることができるなど有効な利用が期待できる。

次に日記機能の評価が高かった。あらたの日記機能はタブレットで撮影した写真を日記に張り付けが可能で、写真の視覚情報によって一日の出来事を想起する手がかりになる。また体調や気分をアイコンで入力し長い文章を書かなくても日記が完成できる。このように ICT だから障害をサポートできる面もあり、また逆に操作の困難さを感じる場合も多い。このことより、より操作の容易な ICT ツールが必要で、操作のサポート体制も必要と考える。

E. 結論

生活を補綴する ICT ツールあらたは、生活面における健忘や介護度の直接的な改善を実感までには至らないが、あらたを使うことで生活や活動をうまくできる自信には繋がると思われる。また ICT ツールを用いても自ら操作することで認知機能は維持向上を示す。しかし、ICT ツールを使いこなすのは記憶障害を呈する高次脳機能障害者には簡単なことではない。今後、障害者が使用しやすいように改変する必要性がある。

生活、就労のどちらの場面でも予定の時間を守るといった展望記憶はとても重要で、予定入力機能は重要な機能の一つである。また、就労の場では多くのことを覚える必要があり、説明の早さも指導員によって異なるため、後で見直せる動画や録音機能が必要である。あらたの改変については日常生活で用いるには、個々の生活スタイルに応じて媒体のサイズが重要となる。ICT ツールを用いることの便利さは実感されているが、日々使用するにはもう少し使用しやすく機能を改変する必要があり、また就労で効果的に用いるには現在のあらたにいくつかの追加機能が必要と考えられる。

G. 研究発表

報告予定

2017 年度　全国作業療法士学会

2017 年度　高次脳機能障害学会

2017 年度　ASEAN Conference on Healthy Ageing 2017

H. 知的財産権の出願・登録状況

1.　特許取得　特になし

2. 実用新案登録　特になし

3. その他　特になし

労災疾病臨床研究事業費補助金
分担研究報告書

職場復帰を促進する要因の検索に関する研究

研究分担者　武澤　信夫　京都府リハビリテーション支援センター長

研究要旨
平成 27 年度に実施した「高次脳機能障害者の就労支援に関する調査」の解析を行い、報告書を作製し、関係者に送付した。また、京都府共通の脳卒中地域連携パスの利用者 801 名の回復期リハビリテーションの効果、高次脳機能障害の実態と職場復帰・在宅復帰等について調査を行い、集計を行った。

A．研究目的

高次脳機能障害者の職場復帰を促進する要因の検索に関する研究のために、就労支援の現状の把握を行い、京都府における脳卒中地域連携パスの高次脳機能障害者の職場復帰・在宅復帰を可能とする要因を検索する。

B．研究方法

郵便法によるアンケート調査（倫理面への配慮）。協力する回復期リハビリテーション病院において、脳卒中パスのデータを匿名化して提供を受け、個人情報を厳重に保護する。

C．研究結果

高次脳機能障害者の就労支援については、都道府県の高次脳機能障害支援拠点において取り組まれ、特に公的リハビリテーションセンターや医療機関が拠点の場合、地域障害者職業センターとの連携が効果的であると思われた。就労移行支援事業所における取り組みは、明らかに充実していた。

2014 年 7 月 1 日から 2015 年 6 月 30 日までの京都府における脳卒中地域連携パスの利用者率は、19.1%の 801 名で、そのうち、90.4%、725 名のデータを回収した。536 名に高次脳機能障害を認め、注意障害、記憶障害、失語症などが高率であった。高次脳機能障害を有する者が、介護保険の認定率が高く、職場復帰・在宅復帰が不良であった。

D．考察

高次脳機能障害者の就労支援においては、医療機関の継続的な診療・支援が必要と考えられ、高次脳機能障害支援拠点や地域障害者職業センターとの連携が重要と思われた。

脳卒中は、高次脳機能障害の原因としては最も多く、今回の調査でも職場復帰率は高次脳機能障害のない者が 17.5%に対して、有する者では 6.2%と非常に不良であったが、その要因の検索が必要である。

E．結論

高次脳機能障害者の就労支援には、医療・福祉・就労支援機関の継続した連携が求められる。
脳卒中を原因とする場合も、医療と福祉・就労支援機関の適切な支援が求められる。

G．研究発表

1. 論文発表
なし
2. 学会発表

武澤信夫、木村彩香、近藤正樹、中川正法、水野敏樹：脳卒中地域連携パス利用者の高次脳機能障害の現状、第 53 回日本リハビリテーション医学会学術集会、京都：2016.6.9

平野哲雄、武澤信夫、東小百合、梅田匡純、安達　徹、吉岡　修、中川正法：京都府丹後圏域における高次脳機能障害者の現状と課題、第 53 回日本リハビリテーション医学会学術集会、京都：2016.6.9

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ORIGINAL ARTICLE

Facial emotion recognition in patients with focal and diffuse axonal injury

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ABSTRACT

Objective: Facial emotion recognition impairment has been well documented in patients with traumatic brain injury. Studies exploring the neural substrates involved in such deficits have implicated specific grey matter structures (e.g. orbitofrontal regions), as well as diffuse white matter damage. Our study aims to clarify whether different types of injuries (i.e. focal vs. diffuse) will lead to different types of impairments on facial emotion recognition tasks, as no study has directly compared these patients. *Methods*: The present study examined performance and response patterns on a facial emotion recognition task in 14 participants with diffuse axonal injury (DAI), 14 with focal injury (FI) and 22 healthy controls.*Results*: We found that, overall, participants with FI and DAI performed more poorly than controls on the facial emotion recognition task. Further, we observed comparable emotion recognition performance in participants with FI and DAI, despite differences in the nature and distribution of their lesions. However, the rating response pattern between the patient groups was different. *Conclusion*: This is the first study to show that pure DAI, without gross focal lesions, can independently lead to facial emotion recognition deficits and that rating patterns differ depending on the type and location of trauma.

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Traumatic brain injury; facial expression; diffuse axonal injury; focal brain injury; emotion recognition

Introduction

Emotion perception is the ability of an individual to infer the emotions of others using body language, facial expressions and context. This ability is crucial in a social setting, as improper interpretation of emotional cues typically leads to lower social competence [1,2]. Since emotions are complex in nature, much of our interpretation of the emotions of others is derived from analysing a combination of non-verbal cues and features. Amongst these cues, facial expressions are perhaps the most distinct representations of human emotion [3–7], and we tend to primarily read and analyse faces to assess the emotional state of others.

Impaired emotion recognition has been reported as a feature of several psychiatric disorders, such as schizophrenia [8–11] and autism [12–15], and contributes significantly to the social impairments associated with these disorders. In addition, emotion recognition deficits can also be induced by traumatic brain injury (TBI). An abundance of studies have demonstrated that patients with TBI are likely to be impaired in terms of their ability to correctly recognize emotional facial expressions [7,16–23]. One particular meta-analysis, which assessed 296 participants with TBI, reported that 39% of the study population had significant difficulties in recognizing emotional facial expressions. The mean recognition ability across all patients was 1.1 standard deviations lower than that of healthy controls [24].

Emotion recognition impairments in patients with TBI are diverse and not consistent across all emotions. Studies have shown that patients with TBI encounter more difficulty when rating the extent to which faces show negative emotions (fear, sadness, disgust and anger) compared with positive emotions (happiness and surprise) [20,25–28]. There is also considerable variability in the degree of impairment reflected by emotion recognition task performance in individuals with TBI, with some patients performing much worse than others [29]. Patients with TBI who have emotion recognition dysfunction, especially those who are unable to successfully interpret emotional facial expressions, may present with behavioural problems, have decreased interpersonal skills, and find it more difficult to reintegrate into society [7,21,30].

Most studies investigating changes in emotion recognition following TBI have examined participants with focal injuries in an attempt to identify the damaged brain areas linked to specific deficits. These studies have implicated several brain regions [31,32], in particular the frontal lobe [31], which is the most common area of injury following TBI. Damage to the frontal lobes is associated with poor performance in facial emotion identification tasks, which we previously found to be due to a liberal cognitive bias (i.e., tendency to endorse an emotion label as matching a facial expression, regardless of whether the label is correct) [17]. This bias may result from impairments in decision-making abilities associated with ventromedial prefrontal damage [33] or with deficits in cognitive flexibility in frontal TBI [34].

Fewer studies have explored how emotion recognition impairment may develop following diffuse axonal injury (DAI) without gross focal lesion. DAI is a type of a brain

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injury in which widespread damage to white matter tracts result from sudden physical acceleration, deceleration or rotational forces that shear the connections between grey and white matter junctions with a typical damage area of less than 15 mm [35]. It has been suggested that white matter disruption can lead to emotion recognition deficits [36]. Green et al. [26] found that dispersed white matter injury in the right posterior hemisphere, in the absence of any gross focal lesion in this region, is sufficient to cause facial emotion recognition deficits. Subsequent studies in which diffusion tensor imaging was used to examine white matter integrity following TBI have additionally demonstrated the specific involvement of the right inferior fronto-occipital fasciculus (IFOF) and the right inferior longitudinal fasciculus (ILF) in emotion recognition deficits in patients with brain injury [37,38]. These tracts appear to be involved in emotion recognition (e.g. matching an emotional label to a face) as well as emotion discrimination (e.g. deciding whether two faces are showing the same emotion) [37,38]. However, studies investigating the relationship between white matter damage and emotion recognition generally involved a DAI patient population with some degree of gross focal injury [26,37].

To the best of our knowledge, no studies have yet investigated facial emotion recognition in patients with pure DAI and compared their performance to those with focal injury. A direct comparison of these groups would yield important information, both theoretically and clinically. First, such a study would make it possible to tease apart the contributions of focal and diffuse brain injuries to facial emotion recognition deficits, and provide additional knowledge on the neurological basis of this facial emotion recognition. From an applied perspective, determining how emotion recognition is affected by focal and diffuse injuries will guide assessment and treatment approaches, which may need to be tailored to the type of lesion.

Our specific objectives in the present study were twofold. First, we aimed to assess facial emotion recognition in participants with DAI, who have widespread white matter injury with no gross focal lesions, and compare their performance to participants with focal frontal-lobe injury and healthy controls. Participants with lesions less than 10 mm^3 in size were considered to have pure DAI. We hypothesized that both participants with DAI and FI would show impaired performance compared to healthy controls, and that our FI group, due to their clinical presentation, lesion size and location, would be relatively more impaired on this task than those with DAI [39,40]. Our second objective was to determine the behavioural response patterns underlying facial emotion recognition performance in each group. We have previously shown that deficits in participants with frontal-lobe FI are due to their tendency to select disproportionately strong emotion intensity ratings for emotional faces, regardless of whether the label is correct; we have coined the term ‘liberal bias’ to refer to this effect [17]. We aimed to see whether this response style also underlies facial emotion recognition in DAI. Because lesions in patients with DAI are by definition diffuse (i.e. not localized), we expected no liberal response bias in this group.

Materials and Methods

Participants

Twenty-eight participants with TBI (14 with frontal FI and 14 with DAI) and 22 healthy control (HC) subjects were included in this study (Table I). Data from the FI and HC participants were collected as part of a previous study and reported in a prior publication [17]; these data were reanalysed here in statistical comparisons with DAI participants. Physicians with expertise in brain injury used magnetic resonance imaging (MRI) data to identify the location of FI and make the diagnosis. The FI lesions were manually drawn, with the highest overlap of lesion maps in the ventromedial orbitofrontal cortex. This group had no focal damage to any other part of the brain, except for two participants who had minor lesions to the right anterior temporal lobe. Patients with DAI were diagnosed based on computed tomography in the early presentation of trauma, and high-contrast fluid-attenuated inversion recovery and susceptibility-weighted imaging (SWI) MRI scans in a more chronic stage. Diagnosis was made by consensus between two expert neuropsychiatrists (UK, TM) using the following criteria: presence of spotty haemorrhages in the brain parenchyma; absence of gross focal lesions (<10 mm^3); injury sustained through significant trauma; and loss of consciousness at the time of injury [41]. It should be noted that focal injuries are inevitably associated with additional diffuse white matter disruption. A more detailed description of the participants with FI can be found in our previous study [17]. Post-traumatic amnesia (PTA) was assessed on the grounds that it serves as a marker of injury severity in TBI, similar to severity and duration of loss of consciousness at onset (Table II).

Table I. Participant characteristics.

	DAI (n = 14)	FI (n = 14)	HC (n = 22)	F (χ^2)	p
Sex (M/F)	11/3	10/4	11/11	3.008	0.222
Age (years)	34.8 (13.7)	38.0 (12.9)	40.0 (7.7)	0.936	0.399
Education (years)	13 (4.1)	13.9 (2.7)	13.5 (2.6)	0.313	0.733
Verbal IQ	89.1 (19)*	99.2 (17.7)	107.3 (15.4)	4.838	0.012
Performance IQ	85.2 (19.5)*†	99.1 (16.8)	109.8 (14.1)	9.482	<0.001

Notes. Mean and standard deviation (SD) in parentheses.
M = male, F = female.
*p < 0.05 compared with HC.
†p < 0.05 compared with FI.

Table II. Characteristics of the patients with diffuse axonal injury.

Patient ID	Time post injury[a]	PTA[b]	Cause of injury
Patient 1	84	60	Traffic accident
Patient 2	104	90	Traffic accident
Patient 3	262	40	Traffic accident
Patient 4	73	60	Traffic accident
Patient 5	146	60	Traffic accident
Patient 6	196	150	Traffic accident
Patient 7	132	75	Traffic accident
Patient 8	12	69	Traffic accident
Patient 9	27	18	Traffic accident
Patient 10	33	14	Traffic accident
Patient 11	166	60	Sports accident
Patient 12	138	30	Traffic accident
Patient 13	189	30	Fall
Patient 14	293	60	Traffic accident

[a]Time post-injury months.
[b]Post-traumatic amnesia (PTA) in days.

Exclusion criteria were a history of neurological disease, psychiatric or serious medical illness, stroke, antipsychotic medication use or substance abuse disorder. One FI male patient had a history of somatization disorder and had received medication, but this participant had sufficient social ability to hold a regular occupation. All participants were right-handed. Written informed consent was obtained after a complete description of the study to the participants. The Committee on Medical Ethics of Kyoto University approved this study.

Although sample size was not pre-determined (but rather based on recruitment rates at our clinic), we used G*Power v.3.1.9.2 to retrospectively calculate sample size requirements for a 3-group (HC, DAI and FI), 6-condition (happy, sad, angry, fearful, surprised and disgusted) repeated-measures design with a 5% error probability and 95% power, using a 25% non-sphericity correction. Results indicate that a total sample size of 33 is adequate (i.e., 11 participants per group).

Neuropsychological assessments

All participants underwent neuropsychological assessment, the methods of which are described in detail elsewhere [17]. Briefly, verbal (VIQ) and performance IQ (PIQ) were assessed using the Wechsler Adult Intelligence Scale Revised/III [42,43]. The participants also completed the Benton Facial Recognition Test (BFRT) [44], in which they were required to match 22 non-emotional human faces to a target face. This step ensures that face recognition abilities are intact before assessing facial emotion recognition abilities. BFRT scores were categorized as Normal (score 41–54), Moderate (score 39–40), Borderline (score 37–38) and impaired (score <37).

Experimental task

Participants completed the Ekman task, a widely used and validated tool in facial emotion expression research, in which they were shown a series of 36 photographs of happy, sad, angry, fearful, surprised and disgusted facial expressions [45]. The photographs were presented to each participant one at a time in random order on a computer screen. The series included six exemplars of each emotional expression. For each photograph, the participants were asked to evaluate the extent to which the face matched each of six emotional labels. For instance, in one block, participants were asked to rate the extent to which a happy face seemed happy, sad, angry, fearful, surprised or disgusted. All 36 faces were rated on a scale from 0 (not at all) to 5 (very much). As such, each of the 36 photographs was rated on all six affect scales.

Data analysis

We first compared the groups on socio-demographic and cognitive variables using a multivariate analysis of variance (ANOVA). Next, we performed a Pearson correlation between patients' raw scores for each of the 36 faces from the experimental task and the average six ratings for the same faces given by the control group. The scores from each control participant were correlated with those of the remaining 21 controls, in order to obtain a measure of how closely each control's performance resembled that of other controls while ensuring that the correlation is not conflated by the inclusion of the participant's own score (which would pull the correlation closer to 1). This resulted in 36 Pearson correlations per subject, which were then Fisher z-transformed [46,47]; higher z' values indicate a stronger correlation with the scores of the control group (i.e., closer to normal performance). Of the 36 z' values, those for the six faces expressing the same emotion (e.g., six happy faces) were then averaged, resulting in a total of six z' per participant (one for each facial expression). All analyses included IQ as a covariate, since IQ is known to contribute to emotion recognition performance [48,49]. In addition, verbal IQ (VIQ) and performance IQ (PIQ) were also found to be significantly different between DAI and FI groups (see Results section). To assess overall facial emotion recognition performance in all three groups, z' values for each of the six facial expressions (happy, surprised, fearful, disgusted, angry and sad) were compared between groups using a 3 × 6 repeated-measures ANOVA followed by planned pairwise between-group comparisons.

In order to test whether a Liberal Bias mediated task performance, a composite Liberal Bias score was calculated by averaging participants' raw scores for all facial expressions. This metric, originally developed by our group [17], is a measure of the average rating attributed to each exemplar; higher scores are indicative of a more liberal rating style (i.e., tendency to endorse labels closer to 5 = very much), regardless of accuracy. The Liberal Bias score was used as a hypothesized mediator in bootstrapping analyses using 5000 bootstrap samples and PIQ and VIQ as covariates. Bootstrapping is a statistical technique, particularly useful in small samples, to determine the accuracy of estimates (in this case, mediation by Liberal Bias) using random resampling [50]. Bias-corrected and accelerated confidence intervals (CIs) were used to determine significance (if zero was included in the interval, the indirect effect was assumed to be null). Statistical analyses were performed using SPSS v.22.0 software for Windows. Statistical significance thresholds were set at $p < 0.05$, and effect sizes are reported as η_p^2.

Results

Participant characteristics

The participant characteristics are reported in detail in Table I. All groups were statistically similar in terms of sex distribution ($\chi^2(2) = 3.008$, $p = 0.222$, age ($F(2,49) = 0.936$, $p = 0.399$) and years of education ($F(2,49) = 0.313$, $p = 0.733$). The members of the DAI, FI and HC groups included both males and females. The cause of injury of participants with DAI was due to traffic accident (12 cases), sports (1 case) and fall (1 case). The cause of injury in FI patients was traffic accident in all cases. The time post injury as well as PTA for each participant with DAI can be found in Table II; unfortunately, these data were not systematically documented in FI participants. We performed subsequent analyses with verbal IQ, and performance IQ as covariates.

Neuropsychological and clinical tasks

The groups differed on VIQ ($F(2,49) = 4.838$, $p = 0.012$) and PIQ ($F(2,49) = 9.482$, $p < 0.001$). DAI participants had lower mean VIQ scores than HC patients, and lower PIQ scores than the FI and HC groups (Table I). The BFRT data showed that, with the exception of one patient belonging to the DAI group, all participants were able to normally process facial features. Despite his BFRT score (score = 28), the patient in question was able to perform comparably with the rest of the DAI group on the facial emotion recognition task.

Experimental task results

Facial emotion recognition in DAI and FI

The task performance of each group is illustrated in Figure 1. Analyses revealed a significant overall effect of Group ($F(2,42) = 8.105$, $p = 0.001$, $\eta_p^2 = 0.278$). Further inspection of the data revealed that task performance for the FI ($p = 0.019$) and DAI groups ($p = 0.001$) did not significantly differ ($p = 0.488$), although the performance of both groups fell significantly below that of the HC participants. We also found a main effect of Emotion ($F(5,210) = 4.482$, $p = 0.009$, $\eta_p^2 = 0.096$), and noted better overall performance on Happy trials compared with Angry ($p < 0.001$), Disgusted ($p < 0.001$), Fearful ($p < 0.001$), Sad ($p < 0.001$) and Surprised ($p < 0.001$) trials. Additionally, performance on Fearful trials was poorer overall compared with Angry ($p = 0.016$), Disgusted ($p = 0.038$), Sad ($p < 0.001$) and Surprised ($p = 0.017$) trials. The Group × Emotion interaction was not significant ($F(10,210) = 0.882$, $p = 0.494$, $\eta_p^2 = 0.040$).

Behavioural response patterns underlying task performance

Bootstrapping results supported an indirect effect of Liberal Bias on ratings of Anger (point estimate of −0.14, 95% BCa CI [−0.39, −0.01]), Disgust (point estimate of −0.14, 95% BCa CI [−0.40, −0.02]), Happiness (point estimate of −0.49, 95% BCa CI [−1.13, −0.04]), Sadness (point estimate of −0.15, 95% BCa CI [−0.41, −0.02]) and Surprise faces (point estimate of −0.27, 95% BCa [−0.59, −0.04]). The indirect effect was not significant for Fear (point estimate of −0.02, 95% BCa CI [−0.12, 0.05]). In FI, results revealed an indirect effect of Liberal Bias on ratings of Anger (point estimate of −0.12, 95% BCa Cl [−0.39, −0.00]), Disgust (point estimate of −0.14, 95% BCa Cl [−0.40, −0.00]), Sadness (point estimate of −0.17, 95% BCa Cl [−0.39, −0.04]) and Surprise (point estimate of −0.27, 95% BCa Cl [−0.64, −0.04]), but not for Fear (point estimate of 0.01, 95% BCa Cl [−0.10, 0.02]) or Happiness (point estimate of −0.22, 95% BCa Cl [−0.67, 0.24]). In DAI, bootstrapping analyses revealed no indirect effect on ratings of any emotional label, with point estimates of −0.01 for ratings of Anger (95% BCa Cl [−0.07, 0.03]), −0.01 for Disgusted (95% BCa Cl [−0.07, 0.02]), 0.00 for Fear (95% BCa Cl [−0.03, 0.01]), −0.07 for Happiness (95% BCa Cl [−0.12, 0.31]), −0.05 for Sadness (95% BCa Cl [−0.17, 0.01]) and −0.07 for Surprise (95% BCa Cl [−0.22, 0.02]).

Considering that liberal responding was not mediating impaired task performance in DAI participants, data were visually inspected to see if another pattern of responding could better explain this group's performance. It was noted that DAI participants tended to give strong, incorrect ratings to most faces, following no obvious pattern (i.e., rated surprised and disgusted faces as sad; angry, sad and disgusted faces as surprised; angry and disgusted faces as fearful; sad, surprised and fearful faces as angry; fearful, sad and surprised faces as disgusted). Interestingly, they additionally failed to endorse *correct* emotional labels for most faces (e.g., low 'happiness' ratings given to happy faces; Figure 2).

Discussion

In the present study, we compared facial emotion recognition in participants with DAI, frontal lobe FI and HC subjects. We first hypothesized that, compared to HCs, DAI and FI participants would show impaired performance on a facial emotion recognition task and second, that participants with FI would exhibit a relatively higher degree of impairment. Further, we expected no liberal pattern of response ratings in DAI.

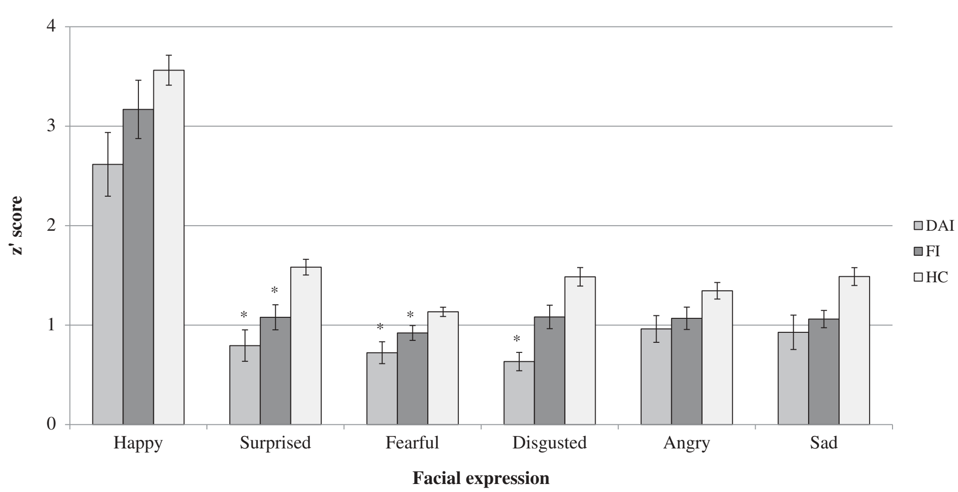

Figure 1. Emotion recognition performance in subjects with focal and diffuse axonal injury compared with healthy controls. Mean (standard error) z' scores for each group on the Ekman task. *Notes.* Higher z' values indicate a stronger correlation with the scores of the control group (i.e., closer to normal performance). *$p < .05$ compared to HC.

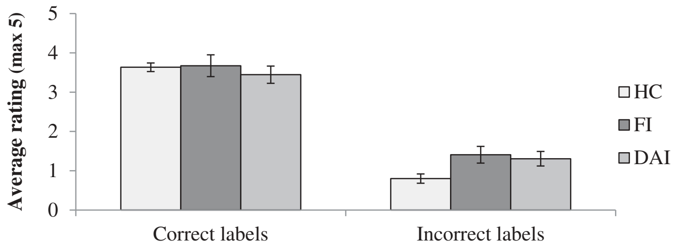

Figure 2. Average ratings given to correct and incorrect labels matching emotional faces in the experimental task, on a scale from 0 (not at all matching) to 5 (very much matching). *Notes*. Correct labels (e.g. 'Happy' label for a smiling face) should be rated near 5 (very much matching), while incorrect labels (e.g. 'Sad' label for a smiling face) should be rated near 0 (not at all matching). Error bars indicate standard error.

Facial emotion recognition in DAI and FI

Consistent with our first hypothesis, our results indicated that participants with focal and diffuse axonal injuries were impaired relative to controls in identifying emotional facial expressions. However, in contrast to our second hypothesis, overall task performance was comparable between these two patient groups. Our initial hypotheses were based on the fact that the frontal lobes are known to play a critical role in facial emotion recognition [39] and, as such, specific focal injury to this area was expected to lead to the most severe deficits. Rather, our results point to similarly severe deficits following disruption of white matter tracts, and support previous research suggesting the crucial role of white matter tracts in facial emotion recognition [26,36]. Thus, intact facial emotion recognition depends not only on the integrity of regions directly involved in the somatosensory representations of emotional expressions, including the frontal lobes [39], temporal regions and the amygdala [51], but also on the integrity of the white matter tracts that serve to connect these networks.

Behavioural response patterns underlying task performance

As anticipated, bootstrap analyses did not support an indirect effect of liberal bias on task ratings in participants with DAI. Several studies have attributed particular patterns of emotion recognition responses to specific brain regions [17,52–55]. We had previously shown that FI participants tended to give strong ratings to incongruent label-emotion pairs emotional labels, and also strong ratings to correct label-emotion pairs [17]. Inspection of our data suggested that, in contrast to subjects with FI, DAI participants tended to give strong, incorrect ratings to emotional faces, but failed to endorse *correct* emotional labels as well. A liberal responding style may thus be specific to frontal-focused lesions. The neuropsychological tests administered in the present study unfortunately do not allow us to draw specific conclusions about the cognitive mechanisms that might explain this cognitive bias in FI. However, it is possible to speculate that impairments in decision making, which have been well established in subjects with damage to the ventromedial prefrontal cortex [56], may lead to a failure to reject incorrect emotion labels based on incongruent facial features. Alternatively, FI subjects' subjective experience of emotion, which has been described as severely blunted in many cases [57], may lead them to perceive others' facial expressions as overstated or exaggerated and endorse very strong ratings when matching labels to these expressions.

In contrast, DAI participants in our study endorsed strong relatively ratings to incorrect emotion labels, and relatively weak ratings to correct labels. Prior studies have pointed to the involvement of the right IFOF and the right ILF in emotion recognition deficits in patients with brain injury [37,38]. Although these studies included participants with focal lesions, one reported a case of isolated damage to the right IFOF and ILF [38]. This patient showed remarkably similar impairments on the Ekman task to our DAI group in terms of *z*-transformed correlation scores [38, Figure 4b], although the authors unfortunately did not report on the response patterns that might account for task performance. The IFOF and ILF connect the occipital lobes to regions involved in facial affect recognition, including orbitofrontal and limbic regions, and their disruption might lead to impaired integration of visual and affective information. The current study did not specifically seek to measure the integrity of IFOF and ILF tracts, and well-designed imaging studies will be necessary to corroborate this hypothesis.

Implications

The evaluation, assessment and treatment of facial emotion recognition deficits in TBI populations are essential [58], because such deficits can be the root of significant social and functional impairment [7,21,30]. Our data indicate that pure DAI is associated with facial emotion recognition impairment independently from focal injuries, and that both focal and diffuse brain injuries can lead to difficulties identifying emotional labels corresponding to facial expressions, yet with different response rating patterns. Thus, widespread white matter injury may have a largely comparable effect on facial emotion recognition to gross grey matter injury in the frontal lobe, which is an area known to be involved in facial emotion recognition [39,51]. Future studies should continue to systematically compare the contribution of grey matter areas involved in facial emotion recognition (i.e. the frontal lobe and amygdala) versus the connections between these regions, in order to further elucidate, whether impaired facial emotion recognition is due to abnormal coordination between specific grey matter areas, their independent effects, or a consequence of the two possibilities.

Furthermore, our results have implications for treatment of facial emotion recognition deficits in DAI and FI populations. Intervention studies have reported that practising analysing emotionally relevant cues using self-instruction and errorless learning in the form of games has been found to effectively improve emotion recognition in participants with focal lesions following TBI [59,60]. The success of such interventions may be improved by taking into account the subtle differences highlighted in our results. Namely, emotion recognition training with FI groups might focus on identifying facial cues that are incongruent with a certain expression (e.g. recognizing that a face is smiling, and therefore probably not sad), while training with DAI groups might focus on identifying relevant cues that may indicate a specific emotion (e.g. recognizing that a face is smiling, and therefore probably happy). In addition, clinicians should be aware of potential emotion-related difficulties in patients even in the absence of focal lesions, and information should be provided to patients and their families. Future studies may be oriented at examining emotion recognition performance in patients with FI having other types of localized lesions (e.g., in the temporal lobes), in order to determine if these participants have their own specific pattern of responding to emotional stimuli.

To the best of our knowledge, previously investigated participants with DAI in TBI studies have exhibited some degree of focal injury [26,37,38]. Thus, the nature and degree of emotion recognition deficits in patients with pure DAI are not well understood. Both focal and diffuse injuries are often present in TBI and interact within a single individual [61], and the FI participants in our sample inevitably had some degree of diffuse white matter damage. However, in order to determine the specific contribution of white matter injury to emotion recognition performance following TBI, care was taken in our study to recruit DAI participants with focal lesions restricted to <10 mm^3, thus effectively isolating the effects of DAI in the absence of any gross focal lesion.

In interpreting our results, we must acknowledge several important limitations of this study. The first limitation is the small size of our sample, especially for our pure DAI and FI groups. This is a common issue in clinical research, particularly when attempting to design samples that are highly homogeneous, as was the case in the present study. Small sample sizes may have prevented us from detecting meaningful differences between our groups, and may have underestimated the effect sizes of our statistically significant between-group comparisons. In addition, our sample only included chronic stage patients, and so these findings cannot be extended to recently traumatically brain-injured individuals. The replication of these results with more robust samples is needed. In addition, information regarding severity and time post injury was not systematically collected from FI participants. Future studies should continue to investigate the relationship between white matter integrity and facial emotion recognition using reliable imaging measures.

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Declaration of Interest

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Disturbance of time orientation, attention, and verbal memory in amnesic patients with confabulation

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ABSTRACT
Confabulation is often observed in amnesic patients after brain damage. However, evidence regarding the relationship between confabulation and other neuropsychological functions is scarce. In addition, previous studies have proposed two possibilities of the relationship between confabulation and false memory, in which patients with confabulation are likely to retrieve false memories, or confabulations are relatively independent of false memories. The present study investigated how confabulation is related to various cognitive functions, including orientation, attention, frontal lobe function, memory, and mental status, and to false memories, as assessed by the Deese–Roediger–Mcdermott (DRM) paradigm. Patients with organic amnesia participated, and confabulations were evaluated using the Confabulation Battery. Amnestic patients were classified into two groups: confabulating (CP) and nonconfabulating patients (NCP). The CP group was significantly impaired in time orientation, attention, and verbal memory, compared to the NCP group and age-matched healthy controls (HC). Results of the DRM paradigm revealed no significant difference in false memory retrieval induced by critical lures across CP, NCP, and HC groups. Confabulating responses in organic amnesia could be in part induced by disturbance of time consciousness and attention control in severe impairment of verbal memories, and confabulation and false memory could be modulated by different cognitive systems.

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Confabulation is often observed in amnesic patients after brain damage, and the symptom is defined as "falsification of memory occurring in clear consciousness in association with an organically derived amnesia" (Berlyne, 1972). Confabulation has been categorized into the two subtypes of spontaneous confabulation, which occurs without apparent prompting, and provoked confabulation, which occurs in response to direct questions probing a faulty memory (Kopelman, 1987; Metcalf, Langdon, & Coltheart, 2007; Schnider, von Daniken, & Gutbrod, 1996). However, little is known about what neuropsychological functions are disturbed in amnesic patients with confabulation, as compared to nonconfabulating amnesic patients. In addition, the specific nature of the relationship between confabulation and false memory remains controversial. The present study investigated these issues by comparing behavioral performance indices of orientation, attention, memory, frontal lobe function, mental status, and false memory across confabulating and nonconfabulating amnesic patients.

Several theories attempt to explain the symptom of confabulation. For example, one researcher proposed that confabulation could depend on covering an exposed memory gap using fictitious memories related to real recent behaviors (Berlyne, 1972). In other theories, confabulation is regarded as a failure to recognize the temporal order of stored information (Schnider et al., 1996), or as a failure to inhibit responses, an inability to monitor behavior, a striking misuse of

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environmental cues, a tendency to be impulsive, and lack of concern about erroneous performance (Stuss, Alexander, Lieberman, & Levine, 1978). In addition, a previous case study of amnesia with confabulation reported that this patient was impaired in episodic memory, executive function, and awareness of memory loss, whereas he showed relatively preserved general semantic memory, visual perception, language, and calculation (La Corte, George, Pradat-Diehl, & Barba, 2011). Thus, we hypothesize that amnesic patients with confabulation could show deficits in time orientation, executive function, memory, inhibition, and impulsivity control, compared to those without confabulation or age-matched healthy participants.

False recognition is the phenomenon in which participants falsely recognize novel items, objects, or events as familiar even if they were not learned or presented in the study phase (Schacter, Norman, & Koutstaal, 1998). Previous studies have often employed the Deese–Roediger–Mcdermott (DRM) paradigm to measure false memories (Deese, 1959; Roediger & McDermott, 1995) and have investigated the relationship between confabulation and false memory using the DRM paradigm (Borsutzky, Fujiwara, Brand, & Markowitsch, 2010; Ciaramelli, Ghetti, & Borsotti, 2009; Van Damme & d'Ydewalle, 2010). For example, one study using this paradigm demonstrated that in confabulating patients, false recognition of critical lures, which were semantically related to targets but not presented during encoding, was not different between divided- and full-attention retrieval conditions, whereas in nonconfabulating patients and normal controls, false recognition to critical lures was significantly greater during divided-attention retrieval than during full-attention retrieval (Ciaramelli et al., 2009). A positive relationship between confabulation and false memory was also supported by another study, in which confabulating patients with rupture of the anterior communicating artery (ACoA) aneurysm exhibited more false alarms during autobiographical memory retrieval than nonconfabulating ACoA patients and normal controls (Gilboa et al., 2006). However, other studies have reported no significant correlations between false memory for critical lures in the DRM paradigm and confabulation (Borsutzky et al., 2010; Van Damme & d'Ydewalle, 2010). Thus, given that previous findings regarding the relationship between confabulation and false memory are not consistent across studies, it remains unclear whether or not confabulating patients are likely to retrieve more false memories (as assessed by the DRM paradigm) than nonconfabulating patients or control participants.

The present study investigated neuropsychological features and false memories in amnesic patients with confabulation. In this study, we employed multiple neuropsychological tests to assess orientation, attention, language, construction, memory, frontal lobe function, and impulsivity control in amnesic patients after brain damage and age-matched healthy participants. DRM paradigm performance was also examined in these participants. On the basis of previous studies, we predicted that amnesic patients with confabulation would be significantly disturbed in time orientation, attention, memory, inhibition, and impulsivity control, compared to nonconfabulating amnesic patients or normal controls. In addition, if DRM paradigm performance is significantly impaired in confabulating patients, the findings would suggest a positive relationship between confabulation and false memory, and vice versa.

Method

Participants

Twelve amnesic patients who regularly attend the outpatient unit of neuropsychology in Kyoto University Hospital participated in this study. They were diagnosed with amnesic disorder due to known physiological condition (F04) based on the International Classification of Diseases–10th Revision (ICD–10). Their etiologies included cerebral hemorrhage, traumatic brain injury, cerebral arteriovenous malformation (AVM), clipping operations for ACoA aneurysm (unruptured), and subarachnoid hemorrhage (SAH) after the rupture of ACoA aneurysm. Damage was identified in the frontal lobes, basal forebrain, parietal lobes, retrosplenial regions, fornix, or more widespread regions. In addition, we recruited 20 age-matched healthy controls (HC) from temporary employment agencies (AGEKKE Corporation and Kyoto City Silver Human Resource Center), for which we asked to recruit participants with no history of neurological or psychiatric disorders and who were working in local communities without evidence of severe health problems. However, data from one amnesic patient and one HC

Table 1. Participant demographic and clinical data.

ID	Sex	Age (years)	Etiology	Damaged regions	Confab rate
CP					
cp001	M	58	Cerebral hemorrhage	Left parietal lobe	.31
cp002	M	38	TBI	Bilateral frontal lobe (basal forebrain spared)	.17
cp003	M	46	SAH after ACoA aneurysm rupture	Bilateral basal forebrain	.17
cp004	F	71	SAH after ACoA aneurysm rupture	Bilateral basal forebrain	.31
cp005	M	66	SAH after ACoA aneurysm rupture	Bilateral basal forebrain	.19
cp006	M	67	Clipping ACoA aneurysm (unruptured)	ACC/fornix, Bilateral basal forebrain	.17
Mean (*SD*)		57.7 (13.1)			.22 (.07)
NCP					
ncp001	M	62	AVM	Retrosplenium	.06
ncp002	M	28	DAI	Diffusion	.06
ncp003	M	62	TBI	Bilateral frontal lobe (basal forebrain spared)	.08
ncp004	M	61	TBI	Bilateral frontal lobe (left basal forebrain included)	.11
ncp006	M	43	AVM	Retrosplenium, left occipital lobe	.06
Mean (*SD*)		49.2 (14.1)			.07 (.03)
HC					
Mean (*SD*)		54.3 (8.4)			.05 (.03)

Note. Confab = confabulation; CP = confabulating patients; NCP = nonconfabulating patients; HC = healthy controls; M = male; F = female; TBI = traumatic brain injury; SAH = subarachnoid hemorrhage; ACoA = anterior communicating artery; AVM = arteriovenous malformation; DAI = diffusional axonal injury; ACC = anterior cingulate cortex; *SD* = standard deviations. Data from ncp005 were excluded from all analyses in this study.

participant were excluded from all analyses. The exclusion reason for the amnesic patient was that in the delayed recognition portion of the Rey Auditory Verbal Learing Test (RAVLT), this patient showed a very high rate of false alarms (85%) for distractor words, while false-alarm rates for the other participants ranged from 0% to 40%. The exclusion reason for the HC participant was that this participant had a neurological history of cerebral infarction. According to the results of the Confabulation Battery (Dalla Barba, 1993; Dalla Barba, Cipolotti, & Denes, 1990; Kanemoto, Natori, Matsuda, & Hamanaka, 1998), all amnesic patients were classified into two subgroups of confabulating (CP) and nonconfabulating patients (NCP), in which CP patients yielded higher rates of confabulation that were at least 2 standard deviations *(SD)* from the average confabulation score for the HC group. By this classification, six CP (1 female and 5 males; mean age = 57.67 years, $SD = 13.10$), five NCP (5 males; mean age = 49.20 years, $SD = 14.13$), and 19 HC (5 females and 14 males; mean age = 54.32 years, $SD = 8.37$) participants were included in this study. An analysis of variance (ANOVA) of mean age with a between-subjects factor of subgroup (CP, NCP, and HC) showed no significant effect of subgroup, $F(2, 27) = 0.91$, $p = .41$, $\eta^2 = .06$. In an ANOVA of confabulation rates, we identified a significant effect of subgroup, $F(2, 27) = 39.42$, $p < .01$, $\eta^2 = .74$, in which confabulation rates in CP (mean = .22, $SD = .07$) were significantly higher than those in NCP (mean = .07, $SD = .03$, $p < .01$) and HC (mean = .05, $SD = .03$, $p < .01$). All participants gave their informed consent to the protocol, which had been approved by the Institutional Review Board (IRB) of the Graduate School of Medicine, Kyoto University (E1812). Detailed profiles of amnesic patients are summarized in Table 1.

Experimental materials

We employed the Japanese-modified version of the Confabulation Battery to examine confabulation severity (Dalla Barba, 1993; Dalla Barba et al., 1990; Kanemoto et al., 1998). This test includes six categories of measures of autobiographical episodic memory, autobiographical semantic memory, orientation, general semantic memory, "I don't know" episodic memory, and "I don't know" semantic memory. Items included in the "I don't know" categories referred to questions to which the appropriate answer was "I don't know." Example items from the Confabulation Battery are shown in Table 2. Six questions were applied into each category, and hence 36 questions were included in this test battery.

We also administered seven neuropsychological tests, including Japanese versions of the Neurobehavioral Cognitive Status Examination (COGNISTAT), RAVLT, Rey–Osterrieth Complex Figure Test (ROCFT), Frontal Assessment Battery (FAB), Behavioral Inhibition System (BIS), Buss–Perry Aggression Questionnaire (BAQ), and the Center for Epidemiologic Studies Depression Scale (CES-D). The COGNISTAT was used to measure three general areas, including level of consciousness,

Table 2. Examples of confabulation battery questions.

Category	Example	No. of questions
Autobiographical episodic memory	What did you do on your recent birthday?	6
Autobiographical semantic memory	What day is your birthday?	6
Orientation	What time is it now?	6
General semantic memory	What is the name of memorial statue created by an artist "Taro Okamoto" in the Osaka International Exposition?	6
"I don't know" episodic memory	What did you do on March 13, 1995?	6
"I don't know" semantic memory	Where was the musical "Dream" held the year before last?	6

Note. Verbal stimuli in this experiment were actually presented in Japanese. English is here used for presentation purposes only.

orientation (to time and place), and attention, and five major ability areas including language (comprehension, repetition, and naming), constructional ability, memory, calculation skills, and executive skills (reasoning and judgment; Kato & Matsuda, 2000; Kiernan, Mueller, Langston, & Van Dyke, 1987). The RAVLT was employed to assess verbal memory (Lezak, 1995; Tanaka, 1998), whereas visual memory was assessed using the ROCFT (Lezak, 1995). The Japanese version of the FAB (Uchida & Kawashima, 2008) assesses frontal lobe functions in terms of conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control, and environmental autonomy (Dubois, Slachevsky, Litvan, & Pillon, 2000). The BIS scale was created to examine individual abilities related to punishment sensitivity and avoidance motivation (Carver & White, 1994), and we employed the Japanese version (Kamide & Daibo, 2005). In addition, the Japanese version of the BAQ was used in the present study to measure individual differences in aggression (Ando et al., 1999; Buss & Perry, 1992). Depression symptoms were assessed using the CES-D (Radloff, 1977).

To investigate false memories, we employed the DRM paradigm (Deese, 1959; Roediger & McDermott, 1995), for which 12 lists of Japanese words were prepared for use in the present study. Each list included one word as a critical lure and eight words that were semantically related to the critical lure. Eight lists of Japanese words were collected from one published source (Hoshino, 2002), and four additional lists were selected from another source (Miyaji & Yama, 2002). In the original lists, one critical lure and 15 related words were used, but we only employed one critical lure and eight related words. This modification enabled amnesic patients to participate in the DRM paradigm without potential fatigue by their memory disturbance. The 12 lists were divided into six lists of target words and six lists of distractor words. The lists corresponding to the target and distractor words were counterbalanced across participants.

Procedure

The present study was conducted in three phases: Administration of general neuropsychological tests, administration of the Confabulation Battery, and administration of the DRM paradigm. Items of Confabulation Battery were divided into two sets. Half of the participants completed all tests in the following order: Confabulation testing (first half), false-memory testing, confabulation testing (second half), and neuropsychological testing. The other participants performed these procedures in the reverse order. The administration order for the neuropsychological tests was RAVLT, ROCFT, BIS, BAQ, CES-D, FAB, and COGNISTAT.

In the assessment of confabulation, participants were given 2 min to answer one question. Oral responses by participants were recorded using a digital voice recorder with their permission. The 36 questions comprising this test were presented in a pseudorandom order. Responses by amnesic patients were corroborated by their families or relatives.

In the DRM paradigm, stimulus presentation and response recoding were controlled using Super Lab 4.5 (http://www.cedrus.com/) run on a Windows PC. During an encoding block, participants were presented with eight words as target stimuli and were instructed to encode them by reading silently. Each word was presented for 3 s with a fixation interval of 2 s. After encoding, participants were required to recall the words learned during encoding within 40 s. The procedure was repeated six times, and hence 48 words (six lists of target words) were encoded in total.

Immediately after encoding, participants were randomly presented with 18 target words, six critical lures related to the target words, 18 distractor words, and six critical lures related to the distractor words and were required to judge whether the words were previously learned (old) or not at two levels of confidence. The target and distractor words consisted of the first, fourth, and eighth words in each list. Eighteen distractor words and six critical lure words related to the distractor words were defined as "unrelated distractors" by collapsing them. Four response options were prepared, namely "Absolutely seen," "Probably seen," "Probably not seen," and "Absolutely not seen," and participants chose one response type by saying one number corresponding to a scale of the response options printed on a white sheet. These responses were recorded by the experimenter pressing a key corresponding to the response type.

Data analysis

Responses of the Confabulation Battery were categorized into (a) confabulation, (b) correct response, or (c) no response. For time information regarding autobiographical episodic memory and autobiographical semantic memory, when the date of events or facts provided by participants were different from five days or more in day, and from five years or more in year, the responses were regarded as (a) confabulation. In addition, when participants answered "I had nothing special to do" to a question, for which an actual day of the events or facts were too difficult to answer, the answers were categorized as (b) correct responses. For time information regarding orientation, when participants provided incorrect responses with a time difference of five days or more in day, or of five years or more in year far from the correct date, the responses were categorized as (a) confabulation. Responses to questions about general sematic memory were categorized as (a) confabulation when the response was replaced by another fact or was otherwise different from the real fact. When participants answered "I don't know," the response was coded as (c) no response. In a question to arrange the order of several historical events as a part of general semantic memory, when any one of the events was not included in participant's responses, the response was coded as (c) no response. For "I don't know" episodic and "I don't know" semantic memory, when participants answered "I don't know" to the questions, the responses were defined as (b) correct responses. Thus, any responses rather than "I don't know" were categorized as (a) confabulation. However, when participants mentioned routine activities such as going to a job, the responses were regarded as (b) correct responses.

For free-recall scores of the DRM paradigm, recalls of target words were defined as hits (Hit), recalls of critical lure words as false alarms to critical lure words (cl-FA), and recalls of new words as false alarms of new words (new-FA). Each of these scores was analyzed using ANOVAs with subgroup as a between-subjects factor. For recognition scores of the DRM paradigm, responses of "Absolutely seen" and "Probably seen" to target words were defined as hits (Hit). When these responses were directed to critical lure words, the responses were categorized as false alarms to critical lure words (cl-FA), and the responses to unrelated distractors were categorized as false alarms to unrelated distractors (ud-FA). The proportions of these types of responses were computed for each participant, and the mean proportions were analyzed using ANOVAs with a factor of subgroup.

Results

Confabulation and general neuropsychological test

Table 3 summarizes neuropsychological test results for the CP, NCP, and HC groups. As illustrated in Figure 1, CP participants were significantly impaired in orientation, attention, and verbal memory, compared to those in the other groups.

In standardized scores of COGNISTAT, an ANOVA for "Orientation" scores showed a significant effect of subgroup, $F(2, 27) = 16.32$, $p < .01$, $\eta^2 = .55$, in which scores in CP were significantly smaller than those in NCP ($p < .01$) and HC ($p < .01$). In addition, given that the test of "Orientation" included the two categories of "place" and "time," we analyzed group differences in these raw scores. This additional analysis demonstrated that scores in CP were significantly impaired in "time" orientation, $F(2, 27) = 19.45$, $p < .01$, $\eta^2 = .59$, whereas all participants showed full marks in the "place" orientation (see Figure 2). Post hoc tests for "time" orientation yielded significant differences between CP and NCP ($p < .01$), and between CP and HC ($p < .01$). There was a significant effect of subgroup for standardized scores of "attention" in COGNISTAT, $F(2, 27) = 4.69$, $p < .05$, $\eta^2 = .26$, for which post hoc

Table 3. Results of general neuropsychological tests.

	CP	NCP	HC	
Test/subtest	Mean (*SD*)	Mean (*SD*)	Mean (*SD*)	Group difference
COGNISTAT				
Orientation	5.83 (3.37)	9.60 (0.89)	9.90 (0.46)	CP < NCP, HC**
Attention	5.00 (4.15)	10.00 (0.00)	8.68 (2.89)	CP < NCP, HC*
Comprehension	7.00 (3.80)	8.80 (2.68)	10.00 (0.00)	CP < HC**
Repetition	9.83 (2.40)	10.60 (0.89)	10.42 (1.35)	
Naming	9.83 (0.41)	9.80 (0.45)	9.73 (0.73)	
Constructional ability	10.50 (1.23)	11.00 (0.00)	10.32 (1.46)	
Memory	6.50 (2.07)	6.60 (1.95)	8.32 (1.11)	CP < HC*
Calculation skills	9.33 (1.63)	10.00 (0.00)	10.00 (0.00)	
Reasoning	9.67 (0.52)	10.40 (0.89)	10.21 (0.71)	
Judgment	10.17 (1.84)	10.40 (1.67)	9.95 (1.08)	
RAVLT				
List A–Trial 1	3.17 (0.98)	4.20 (1.10)	4.79 (1.62)	
List A–Trial 2	6.00 (1.55)	6.60 (0.89)	7.58 (1.92)	
List A–Trial 3	6.17 (1.72)	7.40 (2.70)	9.53 (2.14)	CP < HC**
List A–Trial 4	6.17 (2.48)	8.20 (3.27)	10.58 (1.98)	CP < HC**
List A–Trial 5	6.33 (3.20)	9.00 (3.08)	11.32 (1.86)	CP < HC**
List B–trial	4.00 (0.63)	3.60 (1.52)	5.00 (2.08)	
List A–immediate recall	2.50 (4.23)	6.00 (3.94)	8.53 (3.29)	CP < HC**
List A–20-min delayed recall	1.83 (4.49)	5.60 (3.85)	8.42 (3.37)	CP < HC**
List A–20 min delayed recognition	10.00 (3.90)	12.20 (2.28)	13.79 (1.69)	CP < HC**
ROCFT				
Copy	34.67 (1.63)	35.20 (0.84)	34.73 (2.26)	
3-min delayed recall	11.67 (7.24)	20.40 (3.50)	20.26 (7.92)	
FAB				
Total	15.50 (1.52)	15.40 (1.82)	16.05 (1.78)	
Conceptualization	2.67 (0.52)	2.80 (0.45)	2.32 (0.58)	
Mental flexibility	2.67 (0.52)	2.40 (0.55)	2.84 (0.38)	
Motor programming	2.33 (1.03)	2.40 (1.34)	2.58 (0.84)	
Sensitivity to interference	3.00 (0.00)	2.20 (1.10)	2.90 (0.46)	
Inhibitory control	1.83 (1.17)	2.60 (0.89)	2.42 (1.02)	
Environmental autonomy	3.00 (0.00)	3.00 (0.00)	3.00 (0.00)	
BIS	67.83 (9.02)	65.20 (16.78)	65.11 (8.84)	
BAQ	71.67 (14.67)	70.20 (13.03)	61.79 (10.59)	
CES-D	12.50 (10.13)	12.60 (7.37)	10.63 (6.14)	

Note. CP = confabulating patients; NCP = nonconfabulating patients; HC = healthy controls; COGNISTAT = Japanese version of the Neurobehavioral Cognitive Status Examination; RAVLT = Rey Auditory Verbal Learning Test; ROCFT = Rey–Osterrieth Complex Figure Test; FAB = Frontal Assessment Battery; BIS = Behavioral Inhibition System; BAQ = Buss–Perry aggression questionnaire; CES-D = Center For Epidemiologic Studies Depression Scale.
*p < .05, **p < .01 in F tests.

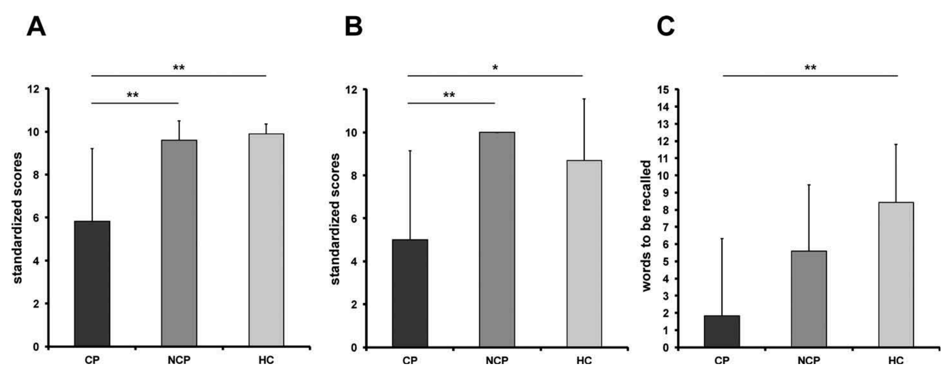

Figure 1. Results of general neuropsychological tests for orientation, attention, and verbal memory. A. "Orientation" scores on the Japanese version of the Neurobehavioral Cognitive Status Examination (COGNISTAT) for confabulating patients (CP), nonconfabulating patients (NCP), and healthy controls (HC). B. "Attention" scores on the COGNISTAT for CP, NCP, and HC. C. 20-min delayed recall scores on the Rey Auditory Verbal Learning Test (RAVLT) in CP, NCP, and HC. Error bars represent standard deviations (*SDs*). *$p < .05$. **$p < .01$.

tests (Bonferroni method) yielded significant differences between CP and NCP ($p < .01$), and CP and HC ($p < .05$). A significant effect of subgroup was also identified for "comprehension" standardized scores of COGNISTAT, $F(2, 27) = 5.63$, $p < .01$, $\eta^2 = .30$, and post hoc tests showed significant

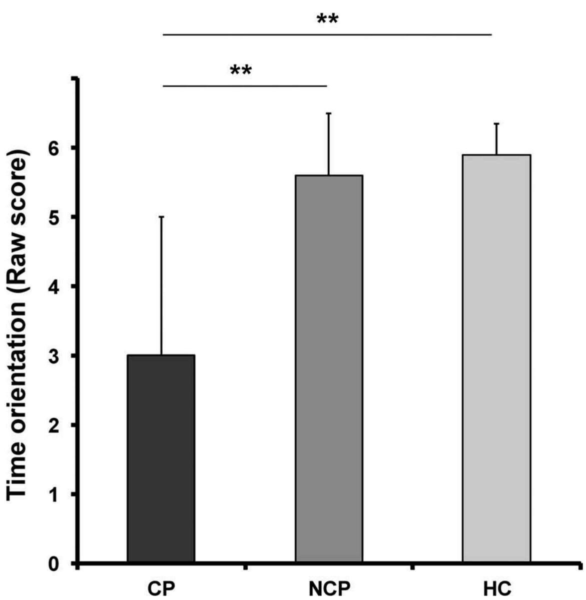

Figure 2. Results of a subtest of time orientation from the "Orientation" of COGNISTAT (Japanese version of the Neurobehavioral Cognitive Status Examination). Raw scores were used to compare performance of time orientation across the subgroups. Confabulating patients (CP) performed significantly worse than Nonconfabulating patients (NCP) and healthy controls (HC) on time orientation raw scores, but place orientation scores were not significantly different across the subgroups. Error bars represent standard deviations (*SD*s). $^{**}p < .01$.

differences between CP and HC ($p < .01$). In addition, an ANOVA for "memory" standardized scores of COGNISTAT revealed a significant effect of subgroup, $F(2, 27) = 5.02$, $p < .05$, $\eta^2 = .27$, which were significantly lower for CP than for HC ($p < .05$). For all other subtests of COGNISTAT, ANOVAs for the standardized scores showed no significant effect of subgroup ["repetition": $F(2, 27) = 0.42$, $p = .66$, $\eta^2 = .03$; "naming": $F(2, 27) = 0.06$, $p = .94$, $\eta^2 = .01$; "constructional ability": $F(2, 27) = 0.55$, $p = .58$, $\eta^2 = .04$; "calculation skills": $F(2, 27) = 2.16$, $p = .13$, $\eta^2 = .14$; "reasoning": $F(2, 27) = 1.75$, $p = .19$, $\eta^2 = .12$; "judgment": $F(2, 27) = 0.24$, $p = .79$, $\eta^2 = .02$.

For RAVLT as a verbal memory task, compared to HC, CP was significantly impaired in the learning phase of Trials 3–5, immediate recall after interference, 20-min delayed recall, and 20-min delayed recognition. However, such disturbance was not identified in NCP. For the learning phase of Trials 3–5, an ANOVA showed a significant effect of subgroup [Trial 3: $F(2, 27) = 6.25$, $p < .01$, $\eta^2 = .32$; Trial 4: $F(2, 27) = 8.99$, $p < .01$, $\eta^2 = .40$; Trial 5: $F(2, 27) = 10.56$, $p < .01$, $\eta^2 = .44$], in which scores for CP were significantly lower than those for HC ($p < .01$ for all trials). The same patterns of group differences in RAVLT scores were identified for immediate recall after interference, $F(2, 27) = 6.65$, $p < .01$, $\eta^2 = .33$, 20-min delayed recall, $F(2, 27) = 7.56$, $p < .01$, $\eta^2 = .36$, and 20-min delayed recognition, $F(2, 27) = 6.15$, $p < .01$, $\eta^2 = .31$, and post hoc tests showed significant differences between CP and HC (*ps* < .01). For the learning phases of Trial 1 and Trial 2, as well as the interference trial (List B), we found no significant effects of subgroup [Trial 1: $F(2, 27) = 2.89$, $p = .07$, $\eta^2 = .18$; Trial 2: $F(2, 27) = 2.12$, $p = .14$, $\eta^2 = .14$; interference trial: $F(2, 27) = 1.54$, $p = .23$, $\eta^2 = .10$].

For ROCFT as a visual memory task, ANOVAs showed a significant effect of subgroup for the "delayed recall" phase, $F(2, 27) = 3.36$, $p < .05$, $\eta^2 = .20$, but not for the "copy" phase, $F(2, 27) = 0.12$, $p = .88$, $\eta^2 = .01$. However, post hoc tests for "delayed recall" scores showed no significant differences between any of the subgroups. For FAB to assess frontal lobe functions, no significant effect of subgroup was found for total scores, $F(2, 27) = 0.42$, $p = .66$, $\eta^2 = .03$. ANOVAs for raw scores in subtests of FAB showed no significant effects of subgroup ["conceptualization": $F(2, 27) = 2.01$, $p = .15$, $\eta^2 = .13$; "mental flexibility": $F(2, 27) = 2.15$, $p = .14$, $\eta^2 = .14$; "motor programming": $F(2, 27) = 0.18$, $p = .84$, $\eta^2 = .01$; "inhibitory control": $F(2, 27) = 0.94$, $p = .40$, $\eta^2 = .07$; "environmental autonomy": all participants had perfect scores], except for "sensitivity to interference," $F(2, 27) = 3.47$, $p < .05$, $\eta^2 = .21$. However, post hoc tests revealed no significant differences between any of the subgroups for this function. For tests of mental status, we found no significant effect of subgroup for any of the tests [BIS: $F(2, 27) = 0.16$, $p = .85$, $\eta^2 = .01$; BAQ $F(2, 27) = 2.14$, $p = .14$, $\eta^2 = .14$; CES-D: $F(2, 27) = 0.25$, $p = .78$, $\eta^2 = .02$].

Confabulation and false memory

Table 4 shows results of the DRM paradigm for each subgroup. In general, results of this test demonstrated that false memories of critical lures were not directly associated with confabulation in amnesic patients.

In terms of number of target words recalled, there was a significant effect of subgroup, $F(2, 27) = 6.13$, $p < .01$, $\eta^2 = .31$, for which post hoc tests yielded a significant difference between CP

Table 4. Results of Deese–Roediger–Mcdermott (DRM) paradigm.

Item type	CP	NCP	HC
Number of words recalled			
Hit (*SD*)	22.83 (10.46)	28.20 (2.95)	32.95 (5.24)
cl-FA (*SD*)	0.83 (1.17)	0.60 (0.89)	1.00 (1.60)
new-FA (*SD*)	2.17 (1.72)	2.20 (2.12)	1.37 (1.74)
Recognition rates			
Hit (*SD*)	.65 (.29)	.67 (.18)	0.81 (.14)
ud-FA (*SD*)	.22 (.32)	.11 (.16)	0.03 (.06)
Hit vs. ud-FA (*SD*)	.43 (.36)	.56 (.27)	0.79 (.14)
cl-FA (*SD*)	.64 (.29)	.43 (.25)	0.58 (.28)

Note. CP = confabulating patients; NCP = nonconfabulating patients; HC = healthy controls; cl-FA = false alarms to critical lures; new-FA = false alarms to new items; ud-FA = false alarms to unrelated distractors.

and HC ($p < .01$). False recall was not different across the three subgroups [cl-FA: $F(2, 27) = 0.16$, $p = .85$, $\eta^2 = .01$; new-FA: $F(2, 27) = 0.57$, $p = .57$, $\eta^2 = .04$], but these results of false recall might not be interpretable due to a possible floor effect. In recognition rates of words, an ANOVA for false-alarm rates of unrelated distractors (ud-FA) revealed a significant effect of subgroup, $F(2, 27) = 3.70$, $p < .05$, $\eta^2 = .22$, in which ud-FA rates in CP were significantly larger than those in HC ($p < .05$). For Hit and cl-FA rates in recognition, we found no significant effect of subgroup [Hit: $F(2, 27) = 2.58$, $p = .09$, $\eta^2 = .16$; cl-FA: $F(2, 27) = 0.80$, $p = .46$, $\eta^2 = .06$]. In addition, to investigate whether corrected recognition scores (Hit rates vs. ud-FA rates) were larger than false recognition scores (cl-FA rates) in each subgroup, we performed paired *t* tests between corrected recognition and false recognition scores in each subgroup. In HC, scores of corrected recognition were larger than those of false recognition, $t(18) = 2.90$, $p < .01$, $r = .57$, whereas there was no significant difference between corrected recognition and false recognition scores in both CP and NCP [CP: $t(5) = -1.33$, $p = .24$, $r = .51$; NCP: $t(4) = 0.79$, $p = .47$, $r = .37$].

Discussion

Two major findings emerged from this study. First, the CP group was impaired in time orientation and attention of COGNISTAT, and in verbal memory as assessed by the RAVLT and COGNISTAT. Second, in the DRM paradigm (an assessment of false memory), we found significant differences of performance between the CP and HC groups in terms of recalling studied items and recognizing unrelated distractors. However, false alarms for critical lures related closely to false memories were not different across the subgroups, for both recall and recognition. In addition, HC showed higher rates of corrected recognition (hit rates vs. false-alarm rates for unrelated distractors) than of false recognition (false-alarm rates for critical lures), whereas there was no significant difference between corrected recognition and false recognition in both CP and NCP. These findings suggest that the symptom of confabulation could be associated with disturbance of time orientation, attention, and verbal memory, and that the production of false memories could not be modulated by confabulation severity. Each of these findings is discussed in separate sections below.

Time orientation, attention, and verbal memory in confabulation

The first main finding of this study was that amnesic patients with confabulation performed worse in assessments of time orientation, attention, and verbal memory than those without confabulation or age-matched healthy controls. These findings suggest that confabulation could at least in part reflect deficits in orienting to time, regulating attention or concentration, and verbal memories.

Disturbance of time orientation in confabulating patients has been consistently identified in previous neuropsychological studies. For example, one study of an amnesic case with confabulation reported that this patient showed marked confabulation in response to questions involving access to temporal consciousness (La Corte et al., 2011). A relationship between confabulation and temporal consciousness has been identified in other neuropsychological studies (Dalla Barba & Boisse, 2010; Turner, Cipolotti, Yousry, & Shallice, 2008). In addition, there is also a neuropsychological finding that recovery of confabulation in amnesic patients parallels recovery of temporal context confusion in memory (Schnider, Ptak, von Daniken, & Remonda, 2000). These findings suggest that deficits in time orientation or temporal consciousness could be one critical cause of confabulation in amnesic patients.

In the present study, we found that compared to nonconfabulating patients and healthy controls, confabulating patients were significantly disturbed in attention, which was assessed using the digit span task. This finding is also consistent with previous neuropsychological findings. For example, a case study demonstrated that a confabulating patient with bilateral thalamic infarction was significantly impaired in digit span task as well as in other executive function tasks (Nys et al., 2004). In another study, patients with higher confabulation rates performed worse than those with lower confabulation rates or those without confabulations on the Trail Making Test, which has been used to measure sustained attention, mental tracking, and set-shifting (Cunningham, Pliskin, Cassisi, Tsang, & Rao, 1997). Attention-related deficits in confabulating patients have been frequently observed in other neuropsychological studies (Beeckmans, Vancoillie, & Michiels, 1998; Fischer, Alexander, D'Esposito, & Otto, 1995). Ability of attention in the present study was evaluated only by the digit span task, which is considered as a method to measure short-term memory functions (Conway et al., 2005), and hence the impairment of attention in the CP patients was found only in a relatively specific context. Taken together with evidence from the present and previous studies, however, deficits of attention control could be closely associated with the production of confabulation in amnesic patients.

In the present study, confabulating patients were significantly impaired in verbal memory functions as assessed by the RAVLT, but the impairment was not significant in visual memory functions as assessed by the ROCFT. These findings suggest that confabulation severity could be correlated with individual difference of verbal memory functions, but not of visual memory functions. One study reported that variance in verbal confabulations was explained only by individual difference in RAVLT delayed recall performance, and that variance in graphical confabulations, which was assessed using the ROCFT, was explained only by individual difference in semantic fluency (Pelati et al., 2011). Given that confabulations in our study were evaluated via verbal responses, the present finding of disturbed verbal memory performance in CP patients is consistent with previous findings. The functional dissociation between verbal and visual confabulations reflects the possibility that they could be modulated by different cognitive systems.

False memory in confabulation

The second main finding of our study was that false memories as assessed by the DRM paradigm were not modulated by confabulation severity. This result is in fact consistent with several neuropsychological studies. For example, a previous neuropsychological study using the DRM paradigm reported that ACoA patients showed worse retrieval performance for studied items than healthy control participants (i.e., lower hits), but false alarms for unstudied critical lures and unrelated distractors were not statistically different between these groups (Borsutzky et al., 2010). In another neuropsychological study using the DRM paradigm, Korsakoff patients with confabulation showed a significant correlation between confabulation scores and false alarms to unrelated distractors, whereas they showed no significant correlation between confabulation scores and false alarms to critical lures (Van Damme & d'Ydewalle, 2010). Taken together, confabulation severity could reflect disturbed retrieval of studied memories rather than production of false memory for critical lures as assessed by the DRM paradigm. The present findings, in which confabulating patients were impaired in cognitive functions including time orientation or attention but not in false memories by the DRM paradigm, suggest that false memories assessed by the DRM paradigm could not be directly explained by deficits of time orientation or attention.

The finding of no relationship between confabulation and false memory may be explained by differences in the memories tapped by the Confabulation Battery and the DRM paradigm. In the Confabulation Battery used here, many questions asked participants to access remote memories of autobiographical or public events, whereas in the DRM paradigm, participants were required to retrieve word items immediately after encoding. A functional dissociation between remote and recent memories has been consistently identified in neuropsychological studies. For example, there is neuropsychological evidence that patients with focal retrograde amnesia show severe retrograde amnesia as a form of remote memory loss, with mild or no anterograde amnesia as a form of recent memory loss (Kapur, 1993; Parkin, 1996). On the other hand, a case study reported that a patient, who was damaged only at the CA1 field of the hippocampus, showed marked anterograde amnesia and little retrograde amnesia (Zola-Morgan, Squire, & Amaral, 1986). These findings suggest that remote and recent memories could be at least in part be associated with different systems. Given a functional dissociation between remote and recent memories, confabulations as a form of remote memory error could not appear to be directly related to DRM-driven false memories, as an error of recent memory. However, the present findings of relationships between confabulation and other cognitive functions/false memories may be due to potential artifacts derived from smaller sample sizes of the CP and NCP patients. Further investigations for larger sample sizes of confabulating patients should be carefully performed in future research.

Neural correlates of confabulation

In the present study, brain lesions in CP and NCP patients were variable across them, and hence the relationship between confabulation and brain lesion was not predicted accurately. However, possible neural mechanisms associated with confabulation may be explained by assessing profiles of brain lesions identified in the present and previous studies. As shown in Table 1, four of six CP patients were damaged in the bilateral basal forebrain region, whereas four of five NCP patients were preserved in the basal forebrain region, and one NCP patient showed a focal lesion only in the left side of this region. The importance of the bilateral basal forebrain lesions in confabulation was demonstrated in a previous study, in which patients with basal forebrain lesions continued to confabulate for several months (Schnider et al., 2000). In another neuropsychological study, the relationship between confabulation and focal frontal lesion was investigated by several components in the Confabulation Battery (Dalla Barba et al., 1990), and the most critical lesion associated with confabulation was located in the inferior medial frontal lobe (Turner et al., 2008). Although the contribution of other lesions to confabulation was not denied by evidence available in the present investigations, at least, the bilateral basal forebrain lesion could be one of the most important lesions to cause confabulation in some amnesic patients.

Conclusion

In the present study, we investigated neuropsychological features and false memories in brain-damaged amnesic patients with confabulations. Results demonstrated that confabulating patients showed significant impairments in time orientation, attention, and verbal memory functions, compared to nonconfabulating patients or age-matched healthy controls. In addition, we found that false memory in the DRM paradigm did not differ between confabulating and nonconfabulating patients. These findings suggest that confabulating responses in amnesic patients could be induced by disturbances of time orientation and attention control in the severe impairment of verbal memory functions, and that confabulation and false memory could be modulated by different cognitive systems.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

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