



HAL
open science

Modifications électrophysiologiques dans le suivi longitudinal de patients aphasiques : une revue de la littérature

Sophie Arheix-Parras

► **To cite this version:**

Sophie Arheix-Parras. Modifications électrophysiologiques dans le suivi longitudinal de patients aphasiques : une revue de la littérature. Sciences cognitives. 2020. dumas-03084341

HAL Id: dumas-03084341

<https://dumas.ccsd.cnrs.fr/dumas-03084341v1>

Submitted on 21 Dec 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Année universitaire 2019-2020

COLLEGE SCIENCES DE LA SANTE
Centre de Formation Universitaire d'Orthophonie

Mémoire (U.E. 7.5) pour l'obtention du

CERTIFICAT DE CAPACITE D'ORTHOPHONISTE
Grade Master

Présenté et soutenu publiquement en juin 2020

par Sophie ARHEIX-PARRAS

née le 10/01/1995 à Tarbes

**Modifications électrophysiologiques dans le suivi
longitudinal de patients aphasiques : une revue de la
littérature**

**Sous la direction de :
Bertrand GLIZE et Grégoire PYTHON**

Membres du jury :

Madame Mélanie ENGELHARDT, Orthophoniste, Service MPR Pr DEHAIL, USN Tastet
Girard - Hôpital Pellegrin, CHU de Bordeaux

Madame le Docteur Isabelle HESLING, Enseignant-chercheur IMN, team 5 GIN, Université
de Bordeaux

Année universitaire 2019-2020

COLLEGE SCIENCES DE LA SANTE
Centre de Formation Universitaire d'Orthophonie

Mémoire (U.E. 7.5) pour l'obtention du

CERTIFICAT DE CAPACITE D'ORTHOPHONISTE
Grade Master

Présenté et soutenu publiquement en juin 2020

par Sophie ARHEIX-PARRAS

née le 10/01/1995 à Tarbes

**Modifications électrophysiologiques dans le suivi
longitudinal de patients aphasiques : une revue de la
littérature**

Sous la direction de :
Bertrand GLIZE et Grégoire PYTHON

Membres du jury :

Madame Mélanie ENGELHARDT, Orthophoniste, Service MPR Pr DEHAIL, USN Tastet Girard - Hôpital Pellegrin, CHU de Bordeaux

Madame le Docteur Isabelle HESLING, Enseignant-chercheur IMN, team 5 GIN, Université de Bordeaux

Titre : Modifications électrophysiologiques dans le suivi longitudinal de patients aphasiques : une revue de la littérature

Résumé : Deux types de mesures peuvent être enregistrées par la magnétoencéphalographie et l'électroencéphalographie : les mesures en continu, principalement enregistrées pendant le repos ou le sommeil, ou les mesures de potentiels/champs magnétiques évoqués (ERPs/EMFs), liées à des événements. Les ERPs/EMFs peuvent être analysés par l'étude des formes d'onde, du temps-fréquence ou de la topographie. Cette revue résume les études longitudinales de la récupération de l'aphasie post-AVC étudiée par imagerie temporelle, en continue ou liée à un événement. Nous avons recherché dans MEDLINE via PubMed et Scopus le 26 mars 2020 des articles en anglais publiés de 1950 à 2020. Les études admissibles concernaient l'exploration de l'aphasie post-AVC par EEG ou MEG en repos ou pendant différentes tâches. Nous avons inclus 38 études : 11 études non interventionnelles suivant la récupération (176 patients) et 27 essais cliniques de médicaments (48 patients), de méthodes de réadaptation spécifiques (178 patients) ou de neuromodulation (122 patients). Les études non interventionnelles ont établi une corrélation entre la récupération spontanée et certains biomarqueurs, comme le lien entre une mauvaise récupération et des ondes lentes au repos. Les essais cliniques tentent de lier améliorations comportementales et mesures électrophysiologiques : plusieurs études se sont concentrées sur la N400 en tant que biomarqueur des effets positifs induits par la thérapie. Les possibilités analytiques de l'imagerie temporelle sont intéressantes dans le suivi de la récupération spontanée ou induite par la thérapie dans le cadre de l'aphasie post-AVC, et pourtant peu exploitées. Le peu d'études via imagerie à haute résolution et le manque de connaissances sur l'analyse topographique ou de temps-fréquence sont probablement les principales raisons de leur faible utilisation. Quant à l'identification des biomarqueurs des effets induits par la thérapie, elle semble plus fiable en analyse ERP/EMF qu'avec l'EEG en continu.

Mots clés : aphasie, accident vasculaire cérébral, électroencéphalographie, magnétoencéphalographie, potentiel évoqué relatif, champ magnétique évoqué

Title: Electrophysiological modifications in post-stroke aphasia: a systematic review

Abstract: Two principal types of measures can be recorded by magnetoencephalography and electroencephalography: continuous, mostly recorded during resting or sleep, or event-related potential/evoked magnetic field (ERP/EMF) measures, that involves a specific and repetitive task. ERPs/EMFs can be analyzed by waveforms, time-frequency, or topography analysis. This systematic review aimed to summarize longitudinal studies about the recovery of post-stroke aphasia studied by temporal imagery, both continuous and event-related. We searched MEDLINE via PubMed and Scopus

on March 26, 2020, for English articles published from 1950 to 2020. Eligible studies involved post-stroke aphasia exploration by EEG or MEG during resting state or different tasks. We included reports of 38 studies: 11 were non-interventional studies following recovery (176 patients) and 27 were clinical trials with drugs (48 patients), specific rehabilitation methods (178 patients), or neuromodulation (122 patients). Non-interventional studies correlated spontaneous recovery with biomarkers, like the link between poor recovery and slow-wave activity. Clinical trials wanted to correlate behavioral improvements and electrophysiological measures: lots of studies focused on the N400 component as a good biomarker of therapy-induced effects. To conclude, the contribution of EEG and MEG measures is interesting for the following of spontaneous or therapy-induced effects recovery in post-stroke aphasia, but poorly exploited. The few number of high-resolution imagery studies and the lack of knowledge about topographical or time-frequency analysis are probably the main reasons why they are little used. As for, the identification of biomarkers of therapy-induced effects, it seems more reliable with ERP/EMF than through continuous EEG.

Keywords: aphasia, stroke, electroencephalography, magnetoencephalography, event-related potential, evoked magnetic field

Nombre de pages : 76. Nombre de références : 81

Unités de recherche

Handicap Activity Cognition Santé (U1219 Inserm), Université de Bordeaux

Remerciements

Tout d'abord, je souhaite remercier chaleureusement mes directeurs de mémoire. Dr Bertrand Glize pour son implication, son positivisme à toute épreuve et Dr Grégoire Python, pour ses précieux conseils et ses relectures méticuleuses.

Je remercie les membres du jury, Madame Mélanie Engelhardt et Dr Isabelle Hesling, pour l'attention portée à mon travail.

Je remercie également mes proches qui n'ont eu de cesse de m'encourager durant cette année dense, et plus particulièrement mes relecteurs qui ont eu à cœur de m'aider : Caroline pour ses remarques pertinentes, Claire pour ses retours constructifs et Hannah pour son avis « objectif ». Je remercie également ma mère, mon frère, ma sœur et Peter pour leur regard extérieur sur mon travail. Je remercie également Charline pour ses conseils qui m'ont fait gagner un temps précieux.

Je remercie l'ensemble des maîtres de stage qui m'ont accompagnée durant ma formation et m'ont aidée à peu à peu construire ma posture de future professionnelle : plus particulièrement, je tiens à remercier Isabelle Méreuze pour son soutien, son temps et ses remarques toujours justes, et Valérie Michelet pour m'avoir guidée pas à pas et avec qui les échanges ont été des plus riches.

Enfin, je remercie enfin l'ensemble de l'équipe pédagogique du centre de formation de Bordeaux pour leur effort attaché à proposer une formation de qualité, pour leur support et leur écoute plus particulièrement durant cette dernière année.

Table des matières

Remerciements.....	4
I. Introduction	7
1. Imagerie temporelle.....	7
1.1. <i>L'électroencéphalographie (EEG)</i>	8
1.2. <i>La magnétoencéphalographie (MEG)</i>	9
1.3. <i>Analyse de l'activité spontanée</i>	10
1.4. <i>Analyse en potentiels évoqués relatifs (ERP) ou champs magnétiques évoqués (EMF)</i>	10
2. Aphasie	14
2.1. <i>Définition et généralités</i>	14
2.2. <i>Récupération post-AVC : plasticité cérébrale et facteurs de récupération dans l'aphasie</i>	14
3. Objectifs de la revue de littérature	16
II. Article	17
III. Perspectives	62
1. Perspectives cliniques	62
2. Perspectives de recherche	63
IV. Conclusion	67
Bibliographie	68

Index des figures

Figure 1: comparaison des techniques d'imagerie en fonction de leur résolution spatiale et temporelle.....	7
Figure 2: repères pour le positionnement des électrodes selon le modèle 10-20.....	9
Figure 3 : principales composantes d'un potentiel évoqué auditif.....	12
Figure 4 : proposition de plan expérimental pour une étude sur l'évaluation de la rTMS par le biais d'analyses ERP	66

Index des tableaux

Tableau 1 : caractéristiques des rythmes cérébraux	10
Tableau 2 : représentation des principales composantes de l'ERP	12
Tableau 3: principales temporalités et localisations observées lors d'une tâche de dénomination d'images auprès de sujets sains	13

I. Introduction

Ce mémoire traitera des modifications électrophysiologiques retrouvées dans le suivi longitudinal de patients aphasiques. Ces modifications seront objectivées par imagerie temporelle, en électroencéphalographie ou en magnétoencéphalographie, tant lors d'enregistrements en continu que grâce à l'étude de potentiels évoqués. Ces derniers pourront être obtenus lors de tâches de perception, de compréhension ou de production.

1. Imagerie temporelle

L'intérêt principal de méthodes d'imageries, telles que l'électroencéphalographie (EEG) et la magnétoencéphalographie (MEG), est la précision temporelle de l'ordre de la milliseconde : elles nous permettent d'étudier le déroulement temporel des activations cérébrales par le recueil en temps réel de l'activité électrique du cerveau (Garnero, 2001).

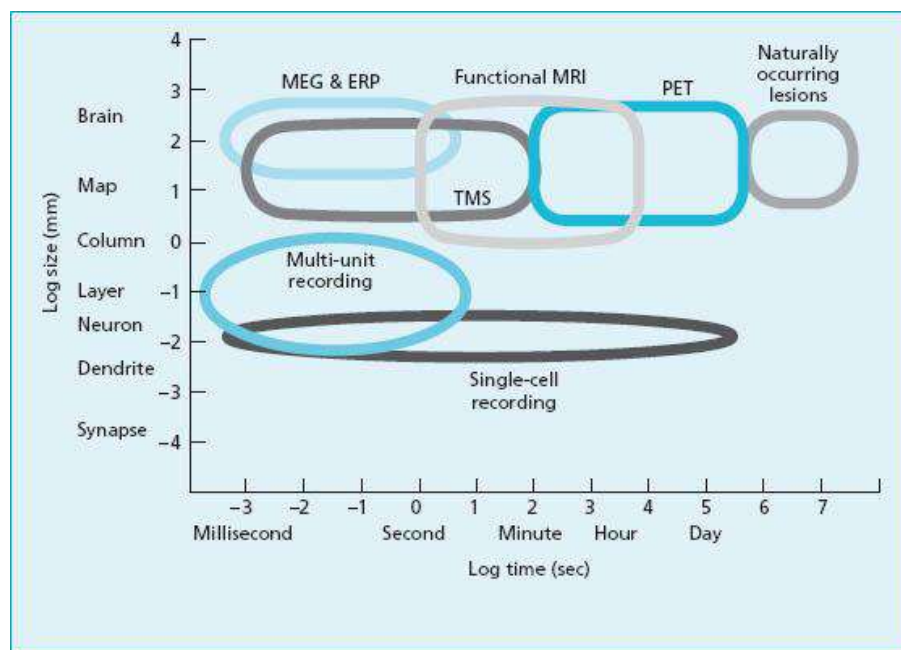


Figure 1: comparaison des techniques d'imagerie en fonction de leur résolution spatiale et temporelle
L'EEG et la MEG sont les outils non invasifs qui permettent la meilleure résolution temporelle, mais présentent une résolution spatiale moindre par rapport à l'imagerie par résonance magnétique fonctionnelle (IRMf).

1.1. L'électroencéphalographie (EEG)

Principe

L'EEG est une méthode permettant d'enregistrer l'activité électrique du cerveau et de l'analyser. Il est possible d'enregistrer l'activité en continu, auprès d'une grande population de neurones pour recueillir différents rythmes d'ondes, ou encore lors d'un événement particulier (*comme la présentation d'une image à dénommer par exemple*), afin d'extraire un signal, appelé potentiel évoqué relatif, par sommation d'une petite population de neurones (Vion-Dury & Blanquet, 2008).

Son faible coût ainsi que son excellente résolution temporelle font de l'EEG une technique très intéressante. L'EEG par enregistrement à la surface du crâne peut être utilisée sur une population variée car il s'agit d'une technique non invasive, contrairement à l'EEG intra-crânienne. Cette dernière consiste à implanter des électrodes directement sous la surface du crâne ; il s'agit d'une technique invasive, utilisée notamment dans le cas particulier d'épilepsies pharmacorésistantes, et ne sera pas traitée dans ce mémoire.

La limite de l'EEG est sa précision spatiale qui dépend notamment du nombre d'électrodes présentes sur le bonnet d'enregistrement : plus leur nombre est important, plus la mesure sera précise. On propose en général 21, 32, 64, 128 ou 256 électrodes. Il est à noter qu'un trop grand nombre d'électrodes peut entraîner des « ponts électriques » entre elles du fait de leur proximité lors de la pose du gel permettant la conduction électrique, et diminuer ainsi la précision recherchée.

Le Montage 10/20

Le montage classiquement retrouvé dans la littérature est le système 10/20 (Vion-Dury & Blanquet, 2008), qui a été proposé initialement par Jasper (Jasper, 1958).

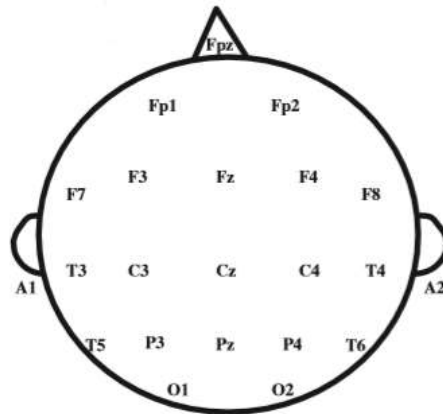


Figure 2: repères pour le positionnement des électrodes selon le modèle 10-20, à partir du modèle de Vion-Dury & Blanquet, 2008

Dans ce montage (Figure 1), les électrodes paires sont situées au niveau de l'hémisphère droit, les impaires sur l'hémisphère gauche et les électrodes situées sur la ligne médiane, reliant le nasion (jonction entre l'arête du nez et le front) à l'inion (point proéminent de l'os occipital), sont désignées par la lettre « z ». Les lettres majuscules correspondent aux différentes localisations en fonction des lobes cérébraux (F : Frontal ; Fp : Fronto-polaire ; P : pariétal ; C : Central ; O : Occipital ; T : Temporal) et des oreilles (A : Auriculaire) (Vion-Dury & Blanquet, 2008).

Cette configuration est identique pour tous les sujets et calculée à l'aide des os fixes du nasion et de l'inion.

1.2. La magnétoencéphalographie (MEG)

Principe

La MEG est une méthode permettant d'enregistrer et d'analyser les variations de champ magnétique cérébral (Vion-Dury & Blanquet, 2008). Cependant, les champs magnétiques cérébraux étant de très faible amplitude, il est nécessaire de les isoler des champs magnétiques externes ; le système le plus efficace consistant à réaliser les mesures dans une pièce blindée formée de parois en μ métal (alliage de nickel et de fer permettant de bloquer les champs magnétiques entrant et sortant) (Garnero, 2001). Ceci explique en partie le coût élevé de la MEG en comparaison avec l'EEG.

La précision temporelle de la MEG est comparable à celle de l'EEG, tandis que sa précision spatiale, nettement supérieure, est de l'ordre de 2-3 millimètres (Vrba & Robinson, 2001).

1.3. Analyse de l'activité spontanée

L'activité électrique spontanée à la surface du crâne peut être analysée et classifiée en fonction de rythmes principaux (alpha, bêta, gamma, delta, thêta) qui apparaissent selon l'état d'éveil du sujet.

Le tableau ci-dessous (Tableau 1) résume les différents rythmes, leurs bandes de fréquences, les activités et localisations cérébrales correspondantes.

Rythme	Bande de fréquences	Localisation	Activité
γ	> 30 Hz	Antérieur et moyen	Veille active Sommeil paradoxal
β	14 - 30 Hz	Antérieur et moyen	Veille calme Sommeil paradoxal
α	8 - 13 Hz	Postérieur	Veille calme
θ	4 - 7,5 Hz	Centrotemporal	Veille Sommeil paradoxal
δ	< 4 Hz	Diffus	Sommeil à ondes lentes Apparition durant d'autres activités dans le cadre de lésions cérébrales

Tableau 1 : caractéristiques des rythmes cérébraux,
adapté de Vion-Dury & Blanquet, 2008 et Vieth et al., 1996

Vieth et al. (, 1996) ont fait partie des premières équipes à relever l'apparition d'ondes lentes dans le cadre de lésions cérébrales, hors sommeil lent, ondes qui pourront par la suite être utilisées à des fins cliniques mais également de recherche comme nous le verrons dans la revue présentée (Hensel et al., 2004; Meinzer et al., 2004).

1.4. Analyse en potentiels évoqués relatifs (ERP) ou champs magnétiques évoqués (EMF)

L'enregistrement de potentiels évoqués (en anglais Event Related Potentials : ERP) ou de champs magnétiques évoqués (en anglais Evoked Magnetic Fields : EMF) concerne de petites populations de neurones qui ont été activées durant une tâche (*dénomination d'images, jugement sémantique, etc.*) répétée un certain nombre de fois. A partir de l'enregistrement de l'activité cérébrale totale durant ces stimuli répétés de façon régulière, il est possible d'extraire

le potentiel évoqué de l'activité en moyennant l'ensemble des essais réalisés (Vion-Dury & Blanquet, 2008).

Il existe plusieurs types d'analyses pouvant être recueillies par le biais des ERP ou des EMF :

- **L'analyse de la puissance de champ global** (global field power) **ou des formes d'ondes** (waveform) : on mesure à un instant donné la stabilité du champ électrique global (Laganaro, 2014).
- **L'analyse topographique** : pour cela, on recherche les périodes de stabilité du champ magnétique ou électrique dans une certaine zone (couvrant un minimum d'électrodes adjacentes) et durant un certain temps, qui correspondent souvent à des processus cognitifs particuliers (*ex : processus sémantiques, processus phonologiques, etc.*) (Garnero, 2001; Laganaro, 2014).
- **L'analyse en temps-fréquence** qui étudie les variations de la fréquence en fonction de la temporalité (Herrmann et al., 2014).

Un tracé ERP est composé de plusieurs variations d'amplitudes appelées composantes (component). Elles sont caractérisées et nommées par rapport à leur latence suivant un stimulus et leur polarité (Herrmann et al., 2014).

Dans les prochains paragraphes, nous développerons les principales caractéristiques des potentiels relatifs lors de la perception auditive, puis ceux obtenus lors de tâches de compréhension de mots isolés et enfin les potentiels observés lors de la production de mots en tâche de dénomination d'images.

Un potentiel évoqué auditif (AEP : auditory evoked potentiel) étudie le trajet électrique entre la cochlée et le cortex auditif en passant notamment par le tronc cérébral (Hallett, 2016). Le trajet peut être découpé en trois fenêtres temporelles (Picton & Hillyaro, 1974) contenant chacune des composantes différentes (Figure 3) :

- **Entre 0 et 8ms après le stimulus** : activation de la cochlée et des noyaux auditifs du tronc cérébral. Ces ondes sont des ondes précoces (composantes représentées par les chiffres romains de I à VI) de la conduction au niveau du tronc cérébral et ne sont pas impliquées dans la recherche sur l'aphasie, mais sont utiles pour diagnostiquer des surdités ou anomalies d'origine ORL.

- **Entre 8 et 50ms suivant le stimulus** : activation du thalamus et du cortex auditif, les composantes de latence intermédiaire sont les suivantes No, Po, Na, Pa, Nb
- **Entre 50 et 300ms après le stimulus** : activation de régions frontales notamment, avec les composantes de latence tardive, P1, N1, P2, N2 (Tableau 2).

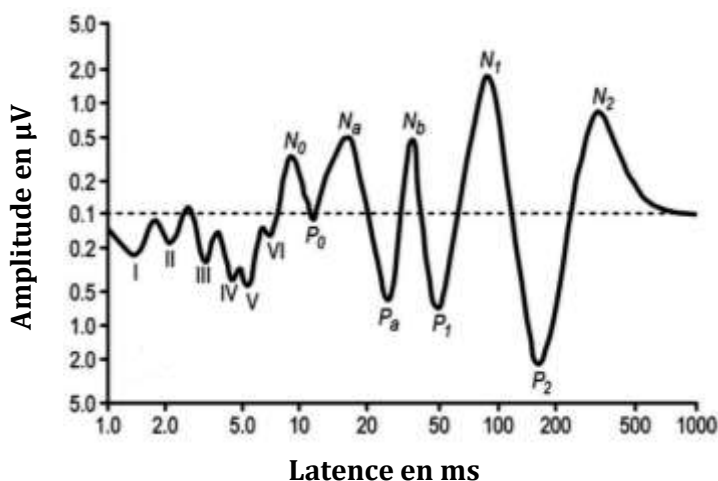


Figure 3 : principales composantes d'un potentiel évoqué auditif, à partir de la représentation de Pérez-González & Malmierca, 2014

Les principales composantes de l'ERP en perception/compréhension de mots sont détaillées dans le tableau ci-dessous (Tableau 2).

Composante	Localisation	Activité
P100	Aires occipitales	Potentiel évoqué visuel
P300	Aires pariétales	Potentiel attentionnel, conscient
N200	Frontal, pariétal et central	Contrôle cognitif voire inhibition (go/no-go)
N400	Large distribution centropariétale (plutôt dans l'hémisphère droit que gauche lors de présentations visuelles)	Traitement sémantique (anomalies sémantiques, mots isolés, non-mots)
MMN	Aires temporales	Stimulus déviant (auditif ou visuel)

Tableau 2 : représentation des principales composantes de l'ERP en tâche de perception/compréhension

P : polarité positive / N : polarité négative / Nombre suivant la lettre : latence approximative du potentiel en ms.
Sources : MMN (Mismatch negativity) : Näätänen et al., 1978 / P100 : Woldorff et al., 1997 / P300 : Sutton et al., 1965 / N200 : Pfefferbaum et al., 1985 / N400 : Lau et al., 2008

La négativité de discordance (MMN : mismatch negativity) est une onde enregistrée à la suite d'un stimulus rare et/ou déviant apparaissant parmi d'autres stimuli fréquents ou identiques. C'est une onde non consciente qui apparaît sans que le sujet ne prête une attention active aux stimuli, contrairement à la P300 (Vion-Dury & Blanquet, 2008).

Au niveau de la production de mots, plusieurs études au cours desquelles l'activité cérébrale est enregistrée par le biais d'EEG révèlent auprès de sujets sains une certaine homogénéité (temporelle et localisationnelle) dans les processus cérébraux de dénomination d'images à partir de 175 ms et jusqu'à 100 ms avant la production orale du mot (Laganaro, 2017). Les principaux résultats issus d'une méta-analyse (Laganaro, 2017) auprès de sujets sains en tâche de dénomination d'images sont présentés dans le tableau ci-dessous (Tableau 3).

Temporalité	Localisation	Processus
+ 170 ms + 275 ms	Lobe temporal gauche Lobe temporal moyen droit Lobe occipital bilatéral	Sélection lexicale (correspondant à la P200)
- 450 ms	Gyrus temporal supérieur gauche (Wernicke) Lobe occipital bilatéral	Processus phonologiques et phonétiques
	Gyrus frontal médial et parahippocampique bilatéral	
- 100 ms	Gyrus frontal inférieur gauche (Broca) et gyrus temporal moyen antérieur droit	Monitoring / processus articulatoires

Tableau 3: principales temporalités et localisations observées lors d'une tâche de dénomination d'images auprès de sujets sains

Les temporalités positives correspondent au temps suivant le stimulus et les temporalités négatives correspondent au temps précédent la réponse articulatoire, ceci afin de diminuer les variations inter-sujets, les temps de latence pouvant être très différents (Laganaro et al., 2012).

2. Aphasie

2.1. Définition et généralités

L'aphasie, comme définie par Trousseau en 1864, est un trouble du langage caractérisé par des troubles de la compréhension et/ou de la production sur les versants écrit et/ou oral (Brin-Henry et al., 2011). Ce trouble est consécutif à une lésion cérébrale située le plus souvent dans l'hémisphère gauche. Dans la plupart des cas, elle fait suite à un accident vasculaire cérébral (AVC), mais elle peut aussi être la conséquence d'un traumatisme crânien, d'une tumeur cérébrale, d'une inflammation ou d'un processus neurodégénératif. Entre 21 et 38% des personnes victimes d'un AVC présenteront une aphasie (Brust et al., 1976; Pedersen et al., 1995).

2.2. Récupération post-AVC : plasticité cérébrale et facteurs de récupération dans l'aphasie

La sévérité initiale de l'aphasie ainsi que la taille et la localisation de la lésion sont les facteurs principaux qui influent sur la récupération (Pedersen et al., 1995; Watila & Balarabe, 2015).

Différents stades se succèdent après une lésion cérébrale : la phase hyperaiguë (24h), aiguë (1 semaine), subaiguë (entre 1 semaine et 6 mois) et la phase chronique (après 6 mois) (Hartwigsen & Saur, 2019). La récupération principale de l'aphasie a lieu durant les 3 mois suivant la lésion (Demeurisse et al., 1980). La phase chronique, quant à elle, est caractérisée par une stagnation des processus de récupération spontanée (Pedersen et al., 1995).

La récupération suite à un AVC est sous-tendue par deux mécanismes principaux :

- ❖ D'une part, **la récupération par rétablissement** : celle-ci fait suite à la résolution de la lésion cérébrale. La reperfusion du tissu appartenant à la pénombre ischémique permet ainsi une récupération spontanée significativement importante (Hillis et al. 2006). Le diaschisis (terme proposé par Monakow en 1914) est un phénomène qui explique qu'une zone cérébrale à distance de la lésion peut être dysfonctionnelle car déconnectée du fait de cette lésion. La levée de ce diaschisis participe donc également à la récupération par rétablissement (pour une méta-analyse voir Carrera et Tononi 2014; Luauté et Luauté 2005).

- ❖ D'autre part, la **récupération par substitution** : on va pouvoir observer une réorganisation des réseaux cérébraux qui s'opère au niveau intrahémisphérique, grâce au recrutement de zones périlésionnelles, mais également interhémisphérique avec le recrutement de zones homologues (Hartwigsen & Saur, 2019). Si la réorganisation interhémisphérique est bénéfique au début de l'atteinte, la récupération sera d'autant meilleure que le patient recrutera moins les régions homologues contralésionnelles au fil du temps et que la balance interhémisphérique sera rétablie (Karbe et al., 1998). Dans le cadre de l'aphasie, on observe des activations de régions droites, homologues de régions gauches précédemment dédiées au langage, notamment au niveau gyrus frontal inférieur, suite à la levée de circuits inhibiteurs (pour une revue voir Geranmayeh, Brownsett, et Wise 2014).

Cette récupération neurobiologique peut être potentialisée par différents facteurs, en particulier par la rééducation comportementale. Plusieurs études ont montré l'effet positif de la rééducation orthophonique dans le cadre des aphasies, qui serait d'autant plus bénéfique que la prise en charge est intensive (entre 4 à 15 heures par semaine, pour deux revues, voir Brady et al. 2016; Stephens 2017). Ces effets sont observables au niveau communicationnel, mais aussi pour l'écriture, la lecture et l'expression orale (pour une revue, Brady et al. 2016). L'intérêt de la prise en charge des patients au stade aigu est controversé et les conclusions des études divergent, allant d'une récupération deux fois plus importante que la récupération spontanée à la non perte de chance si la prise en charge est plus tardive (Brady et al. 2016; Robey 1998). Bien que la récupération spontanée ne soit plus observée au stade chronique, une méta-analyse démontre encore un bénéfice de la rééducation à ce stade (Robey 1998).

Des techniques de stimulation cérébrale non-invasive (NIBS : non-invasive brain stimulation) peuvent également jouer un rôle dans la récupération, notamment la stimulation magnétique transcrânienne (TMS : Transcranial Magnetic Stimulation), mais aussi la stimulation transcrânienne par courant continu (tDCS : transcranial Direct Current Stimulation) (Glize et al., 2014).

Enfin plusieurs recherches entreprennent des investigations avec des médicaments pouvant avoir un impact positif sur la récupération de l'aphasie : on relèvera les études sur le Donepezil (Berthier et al., 2006; Woodhead et al., 2017), un inhibiteur de l'acétylcholinestérase, et la Memantine, (Barbancho et al., 2015), dont l'utilité a déjà démontré des bénéfices pour le

traitement des troubles du langage et de la communication dans les maladies d'Alzheimer et de Parkinson.

3. Objectifs de la revue de littérature

La revue de littérature va être présentée sous forme d'un article en anglais. Elle traitera des modifications électrophysiologiques dans le cadre de l'aphasie post-AVC observées par le biais de l'imagerie temporelle (EEG/MEG). Nous inclurons à la fois les études enregistrant l'activité de fond en continu et les études en ERP/EMF, lors de tâches de production et de perception/compréhension, en modalités orales et écrites.

Dans le cadre de lésions cérébrales et de leur récupération, nous allons observer des modifications des rythmes cérébraux et des tracés ERP, notamment au niveau de leur latence et des pointes d'ondes attendues (Vion-Dury & Blanquet, 2008). Cette revue de littérature permettra d'avoir une vue d'ensemble des variations en imagerie temporelle (EEG/MEG) lors des différentes étapes de la récupération post-AVC, de la phase aiguë à la phase chronique, et d'investiguer la stabilité possible de cette dernière phase. Nous objectiverons également les modifications engendrées par les différentes méthodes de rééducation, de médication et de stimulation cérébrale non-invasive.

Quelles sont les modifications électrophysiologiques observées dans la récupération de l'aphasie, associée ou non à de la rééducation orthophonique, à des prises médicamenteuses ou à des stimulations cérébrales non invasives ? Nous rechercherons deux types d'études longitudinales traitant de l'aphasie post-AVC, en EEG ou en MEG, à la fois par le biais d'enregistrements en continu et avec des analyses ERP/EMF : celles qui font état de l'évolution spontanée et celles dont l'évolution est potentialisée par différents facteurs (rééducation, stimulations cérébrales non invasives, essais médicamenteux).

II. Article

Electrophysiological modifications in post-stroke aphasia: a systematic review

Sophie Arheix-Parras^{1,2}, Grégoire Python^{3,4}, Bertrand Glize^{1,2,3,5}

¹ EA4136 handicap activity cognition health, university of Bordeaux, 33000 Bordeaux, France

² Institut Universitaire des Sciences de la Réadaptation, university of Bordeaux, 33000 Bordeaux, France

³ Faculty of Psychology and Educational Sciences, University of Geneva, Geneva, Switzerland

⁴ Neurorehabilitation Unit, Department of Clinical Neurosciences, Vaudois University Hospital Center and University of Lausanne, Lausanne, Switzerland

⁵ Department of physical medicine and rehabilitation, CHU de Bordeaux, 33000 Bordeaux, France

Corresponding author: Bertrand GLIZE, Place Amélie Raba Léon, service MPR, 33076 Bordeaux, France; bertrand.glize@chu-bordeaux.fr; Phone: +33.556795546 / Fax: +33.556796006

Abstract

Background. Two principal types of measures can be recorded by magnetoencephalography (MEG) and electroencephalography (EEG): continuous or event-related potential/evoked magnetic field (ERP/EMF) measures. Continuous measures are mostly recorded during resting or sleep and allow to observe neural oscillation. Event-related recordings rely on ERP/EMF that involves a specific and repetitive task (such as naming, syllables discrimination, etc.) and can be analyzed by waveforms, time-frequency, or topography analysis.

Objective. This systematic review aimed to summarize longitudinal studies about the recovery of post-stroke aphasia studied by temporal imagery (EEG or MEG), both continuous and event-related.

Methods. We searched MEDLINE via PubMed and Scopus on March 26, 2020, for English articles published from 1950 to 2020. Eligible studies involved post-stroke aphasia exploration by EEG or MEG during resting state or different tasks.

Results. We included reports of 38 studies: 11 were non-interventional studies following recovery (176 patients) and 27 were clinical trials with drugs (48 patients), specific rehabilitation methods (178 patients), or neuromodulation (122 patients). Non-interventional studies correlated spontaneous recovery with biomarkers, like the link between poor recovery and slow-wave activity. Clinical trials wanted to correlate behavioral improvements and electrophysiological measures: lots of studies focused on the N400 component as a good biomarker of therapy-induced effects.

Conclusion. To conclude, the contribution of EEG and MEG measures is interesting for the following of spontaneous or therapy-induced effects recovery in post-stroke aphasia, but poorly exploited. The few number of high-resolution imagery studies and the lack of knowledge about topographical or time-frequency analysis are probably the main reasons why they are little used. As for, the identification of biomarkers of therapy-induced effects, it seems more reliable with ERP/EMF than through continuous EEG. Many avenues remain to be explored, in particular, the evaluation of non-invasive brain stimulation (NIBS) through topography, which may help to identify biomarkers of good response to these treatments.

Keywords: aphasia, stroke, electroencephalography, magnetoencephalography, event-related potential, evoked magnetic field

1. Introduction

Aphasia affects between one quarter to one third (1,2) of post-stroke patients and it has a major impact on the quality of life (3).

Aphasia usually follows a left-brain lesion. Spontaneous neuroplasticity mechanisms drive an important part of the recovery. However, these mechanisms can be enhanced by speech and language therapy (4,5), drugs, or non-invasive brain stimulation (NIBS). The neuronal reorganization is based on perilesional and contralesional rearrangement. However, the exact contribution of the right hemisphere is still debated: it can provide a good or a bad impact on neuroplasticity during recovery (6). This bilateral reorganization is the base of NIBS effects (for more details, see Biou et al. 2019 (7)).

To explore language reorganization, following spontaneous or therapy-induced effects, most of the studies use Positron Emission Tomography (PET) or functional Magnetic Resonance Imaging (fMRI); even if those methods can precisely investigate spatial components, they provide poor temporal precision. On the contrary, electroencephalography (EEG) or magnetoencephalography (MEG) allow to record precisely every millisecond of electrical activity from the brain. This temporal resolution permits to explore another important aspect of brain reorganization during aphasia recovery.

Two main measures can be recorded by MEG and EEG: continuous or event-related potential/evoked magnetic field (ERP/EMF) measures. Continuous measures are mostly recorded during resting state or sleep and allow to observe neural oscillation. Abnormal slow-wave activity (SWA) has been detected in the vicinity of brain lesions during waking resting state (8) and Dubovik et al. (9) described a reduction of interhemispheric synchronization in the alpha frequency band of post-stroke patients. Such changes in neural oscillations can be explored in people with aphasia (PwA). Event-related recordings rely on ERP/EMF that involves a specific and repetitive task (such as naming, syllables discrimination, etc.) and can be analyzed by waveforms, time-frequency or topography analysis (10,11). Usually, in healthy people, the main evoked potentials are identified in perception/comprehension task or in production task. The analyses of perception/comprehension tasks are based on several ERPs components: the Na, Pa, Nb, P300, N100, N200, N400, and the mismatch negativity (MMN). The MMN is obtained by introducing unexpected/deviant items in a task. Production tasks are often based on picture-naming that follows 3 steps: semantic and lexical steps in the first 300ms after stimulus presentation (based on the P200 component), phonological representations, and after 400ms phonological-phonetic representation (12). Moreover, functional connectivity can

be explored using inverse solution to identify region of interest which are synchronized (electrical or magnetic activity and magnitude) and thus are functionally connected. Such ERPs components and widely ERPs analysis, regarding speech and language perception and/or production, may be different in PwA, and may change during recovery.

The following review aimed to summarize longitudinal studies that explored the recovery of post-stroke aphasia using temporal imagery (EEG or MEG) and both continuous and event-related measures.

2. Methods

This systematic review followed PRISMA guidelines (www.prisma-statement.org). We searched MEDLINE via PubMed and Scopus on March, 26, 2020 for English articles published from 1950 to 2020 by using the following keywords in titles, abstracts and keywords: “aphasia” AND “EEG” OR “electroencephalography” OR “MEG” OR “magnetoencephalography” OR “ERP” OR “Event Related Potential”. Eligible studies involved post-stroke aphasia exploration by EEG or MEG during resting state or different tasks. We excluded articles concerning primary progressive aphasia, epilepsy, cancer, mental disorder, dementia or studies focusing on healthy subjects. Two authors (BG & SAP) assessed the eligibility of articles.

3. Results

On March 26, 2020, after removal of duplicates, 233 articles were retrieved from the literature search. The flow of articles in the study is in Figure 1. We included reports of 38 studies on post-stroke recovery from aphasia and temporal imaging (EEG/MEG). Among those 38 studies, 11 were non-interventional studies following recovery (176 patients) and 27 were clinical trials with drugs (48 patients), specific rehabilitation methods (178 patients) or neuromodulation (122 patients). Tables 1, 2, 3 and 4 summarize these articles.

3.1. Non interventional studies following recovery

Table 1 summarizes 11 non-interventional studies following recovery in patients with aphasia after a stroke. They regroup 176 patients including one single case study (13).

Comparison with healthy controls

Only one study (14) out of twelve did not have a healthy control group and another (15) used a control group from one of their old studies.

Studies in event-related potential or evoked magnetic field

Seven studies (13,15–20) used ERPs, EMFs or AEPs. They all asked for repetitive tasks but two (19,20) additionally proposed resting and recorded middle latency auditory evoked responses.

Most of them used waveform analysis and focused on main components of ERPs in speech perception/comprehension: N100, N200, N400, P200, P300, and MMN (mismatch negativity). None of these non-interventional studies used time-frequency neither topographic analysis.

Two studies (19,20) also used waveforms but recorded AEPs. They focused their observations on middle and late latency responses: Pa, Na, Nb and N100, P200. Rojas et al. (20) found a correlation between the decrease of latency of Nb and Pa, and the increase in language scores: at 6 months follow-up, the shorter latency was, the better aphasia scores were. Praamstra et al. (19) also found a correlation between abnormal AEP and a tendency of severe auditory comprehension impairments.

Ilvonen et al. used MMN (17) in a watching silent movie task (with impromptus sounds) and found a correlation between the increase of MMN amplitude and improvement in comprehension tests.

Two studies (15,16) found that the P300 amplitude increased during recovery. For Nolfé et al. (18) the presence of the P300 response in the first month post-stroke was correlated with better comprehension improvement in global aphasia. They also found that if the P300 was present at baseline, its amplitude increased in the temporoparietal left areas, and if it was not present at baseline, it appeared in frontal areas.

Becker and Reinvang (15) found that N200 shifted from healthy to damaged hemisphere in 5 out of 8 patients, following recovery from subacute to chronic stage. They also identified the presence of a small N100 in the ipsilesional frontal area as a good predictor for recovery: the smaller it was, the larger the improvement in auditory comprehension was.

Cobianchi and Gianquinto (16) did not find any changes in N400 (normal at baseline) for two patients with expressive aphasia in subacute and in chronic stage.

Gow and Ahlfors (13) found an increase of the left hemisphere (LH) activation during an auditory word-picture verification task, following spontaneous recovery from subacute to chronic stage.

Studies with continuous EEG

Four studies (14,21–23) recorded continuous EEG. Two used resting or at least task-free conditions (21,23), one a semantic categorization task (22) and the last one (14) did not report the task asked to subjects during the recording.

The results of all these studies found slowing in wave activity (mostly around theta and delta rhythms) and these abnormal slow rhythms predicted poor recovery. During recovery, rhythms trended to accelerate from the acute to the subacute and chronic stage, and their frequency seemed to reach a plateau after respectively 6 and 11 months in two studies (14,22). Moreover, two studies highlighted the link between good prognosis of recovery and alpha rhythm. Good recovery was associated with fast alpha rhythm in the contralesional hemisphere at the subacute stage for Jabbari et al (14) and a return to an usual alpha rhythm during resting in the first weeks post-stroke for Nicolo et al (21).

Aphasia stage

In those 11 non-interventional studies, 6 (13–16,19,22) involved patients from subacute to chronic stage. Only 2 of them (14,22) made several continuous EEG measures during the chronic stage without speech therapy (6 months for Jabbari et al. (14) and 11 months for Hensel et al. (22)) but did not find any spontaneous electrophysiological or language changes at this stage.

Table 1: Design and main results of non-interventional studies

Study design	Patients (number, type of aphasia, stage) and controls	Type of temporal imagery, number of channels and task asked	Outcome measure (behavioral and neuroimaging)	Follow-up (time post-stroke), eventually speech therapy	Main results
Gow and Ahlfors, 2017 (13) Short communication Single case	1 Woman, 53 years old RH stroke Subacute to chronic 12 control subjects	MEG 306-channel EEG 70-channel Auditory word-picture verification task (judgement)	PAL, results at the auditory word-picture verification task ERP: source localizations and connectivity based on Granger analysis (identification of ROI)	1 month 7 months	Improvement in the accuracy of the judgment task, increase of activation, and influence of LH network (number of ROI increase). Decrease of influence of the RH. Increase of intrahemispheric connection in the LH but a decrease in the RH (compared with controls). Decrease of inter-hemispheric connectivity compared to healthy subjects.
Nicolo et al., 2015 (21)	24 including 15 LH stroke Mild motor <u>or</u> language impairment at least Subacute 26 matched in age control subjects	EEG 128-channel Task free state	GeBAS Continuous EEG: rhythms (Beta, Alpha and Theta), functional connectivity WND	T0: 3 weeks T1: 3 months	Correlation between larger WND and good clinical improvements in both hemispheres. The coherence between oscillations of language areas at T0 with the entire cortex is correlated with a better improvement in language recovery (same for motor impairment). Usual alpha frequencies during resting state became beta or theta frequencies in the first weeks of a stroke. It is maladaptive if it continues after a while, correlated with poor clinical improvement.

<p>Rojas Sosa et al., 2009 (20)</p> <p>Prospective study</p>	<p>10</p> <p>6 mixed non fluent aphasia 2 sensory aphasia 1 motor aphasia 1 transcortical sensory aphasia</p> <p>Acute to subacute</p> <p>30 matched in age and sex control subjects</p>	<p>EEG</p> <p>2 sources (one active at Cz, one reference at the left mastoid)</p> <p>Sleeping or resting quietly, stimuli = condensation pips</p>	<p>BDAE</p> <p>AEP: waveforms (middle latency auditory responses)</p>	<p>3 days</p> <p>9.6 +/- 4.2 days</p> <p>2 months</p> <p>4 months</p> <p>6 months</p> <p>Individual rehabilitation therapy during the first three months</p>	<p>Language improvements (the most at the 2nd month) depending only on the score at baseline (not type of aphasia, age, or gender).</p> <p>Decrease in the latency of Pa and Nb peaks (towards normalization) for all patients during follow-up. Changes in aphasia scores and Nb latency = inversely related.</p> <p>At 6 months: correlation between aphasia score and Nb peak (shorter latency => higher aphasia scores).</p>
<p>Becker et Reinvang, 2007 (15)</p> <p>Short communication</p>	<p>8</p> <p>including 1 traumatic brain injury and 2 RH stroke</p> <p>3 global aphasia 1 transcortical sensory aphasia 1 Broca 1 Wernicke 1 mixed transcortical aphasia 1 anomic aphasia</p> <p>Subacute to chronic</p> <p>Control subjects from another study</p>	<p>EEG</p> <p>17-channel</p> <p>3 paradigms:</p> <p>Passive syllable discrimination</p> <p>Passive tone discrimination</p> <p>Active syllable discrimination and identification</p>	<p>Norwegian Basic Aphasia Assessment, TT</p> <p>ERP: waveforms, time-window from mean latencies</p>	<p>≈ 90 days (63-130)</p> <p>≈ 208 days (142-297)</p> <p>8-12h of SLT per week (50-80% one to one therapy)</p>	<p>Small clinical improvements and ERPs changes (amplitude and latencies) for all patients.</p> <p>N200: shift of N200 (for 5 patients) overweight from contralesional to ipsilesional hemisphere (= normalization). Activation of the contralesional hemisphere is decreasing with time.</p> <p>1 (mild to moderate auditory comprehension impairments): no shift.</p> <p>1 (severe): contralesional overweight in the first session and became more conventional after 3 months.</p> <p>N100: at the first session, ipsilesional frontal N100 amplitude predicted recovery (smaller it was, the larger the improvement was in auditory comprehension).</p> <p>P300 and N200: increase between baseline and 3 months in ipsilesional frontal areas.</p>

<p>Nolfe et al., 2006 (18)</p>	<p>17 Global aphasia</p> <p>Acute to subacute</p> <p>20 matched in age control subjects</p>	<p>EEG 16-channel</p> <p>Auditive stimuli: low pitch (frequent) and high pitch (rare)</p>	<p>AAT (comprehension and TT)</p> <p>ERP: waveform (P300)</p>	<p>12.9 days (sd = 5.8)</p> <p>Once a month up to 6 months</p> <p>Schuell's aphasia therapy</p>	<p>In the beginning, P300: only found for 7 patients in the RH (6 patients in both hemispheres / 3 patients in all derivations). For others (10 patients) they presented the P100-N200 complex at least.</p> <p>After 6 months: increase in the number of patients who presented a P300, only one on 17 didn't have a P300 response.</p> <p>Patients with P300 at the beginning showed a "higher and well defined amplitude" in the temporo-parietal left areas, negligible in the frontal areas. But for others (late P300) the P300 was in the frontal areas but negligible in the temporo-parietal areas.</p> <p>There is a link between a better evolution of the AAT comprehension subtest and the presence of a P300 response in the first month for patients with global aphasia.</p>
<p>Hensel et al., 2004 (22)</p>	<p>11 (including one ambidextrous)</p> <p>4 Wernicke 1 Broca 2 Amnestic 4 global</p> <p>Subacute to chronic</p> <p>10 control subjects</p>	<p>EEG 30-channel</p> <p>Semantic categorization task (natural or artificial objects)</p>	<p>AAT</p> <p>Continuous EEG: delta rhythm / SWA, source localization</p>	<p>Baseline: during the first 3 months</p> <p>4 other sessions with an interval of 4-5 months between sessions during 2 years</p> <p>Between no therapy and 1-2 hours a week</p>	<p>Improvements in language measures.</p> <p>SWA found in the vicinity of patients' lesion: important LH delta amplitude (and little in RH), not found in controls and delta dipole "located in the LH relative to minute strength in the RH".</p> <p>Decrease of that delta amplitude and dipole strength from 3 months post-stroke to around 11 months post-stroke. No changes after until 2 years post-stroke.</p>

<p>Ilvonen et al., 2003 (17)</p>	<p>8 10 days: 3 global / 3 conduction / 2 Wernicke 3 months: 2 global / 3 conduction / 1 Wernicke / 1 anomic 6 months: 1 global / 2 transcortical sensory / 3 conduction / 1 Wernicke / 1 anomic</p> <p>Acute to subacute</p> <p>8 matched in age control subjects</p>	<p>EEG 9-channel</p> <p>Watching a silent video and ignore tones</p>	<p>Subtests from BDAE and TT</p> <p>ERP: waveforms (MMN)</p>	<p>4 days 10 days 3 months 6 months</p>	<p>Correlation between an increase of MMN amplitude and improvements in speech comprehension tests.</p> <p>4 days post-stroke: attenuated MMN in the right ear stimulated. Question of correlation with the metabolic depression and the edema outside of the primary lesion in the LH.</p> <p>10 days post-stroke: MMN still abnormal for both ears. Question of reduced metabolism, blood flow, and diaschisis in the RH.</p> <p>3 months post-stroke: MMN amplitude increase strongly for the right ear. Question of an increase in metabolism in the LH.</p> <p>6 months post-stroke: MMN amplitude increase for the left ear (more than at 3 months). Changes in the RH during 3 to 6 months after stroke.</p>
<p>Szelies et al., 2002 (23)</p>	<p>23 5 Wernicke 4 Residual aphasia (unclassified) 5 Broca 6 Anomic 2 Transcortical sensoric 1 Conduction</p> <p>Subacute</p> <p>43 matched in age control subjects</p>	<p>EEG 19-channel</p> <p>Resting condition</p>	<p>AAT (including TT)</p> <p>Continuous EEG: quantitative topographical EEG</p>	<p>2 weeks 8 weeks</p>	<p>Prognosis of a good language recovery was associated with theta and delta activity, mostly in inside speech relevant regions.</p> <p>More details: Supplementary motor area: increase of theta power correlated with a bad outcome. Occipital regions: less pronounced alpha power correlated with a good outcome. Disturbances in other areas: Broca's area, Wernicke's area, supramarginal gyrus (F7 T3, T5).</p>

Cobianchi and Giaquinto, 2000 (16)	<p>2</p> <p>Expressive aphasia</p> <p>Subacute to chronic</p> <p>18 control subjects</p>	<p>EEG</p> <p>16-channel</p> <p>Passive oddball paradigm (frequent high and infrequent low pitch) (for P300)</p> <p>Stimulus : word LEONE (no instruction) (P340)</p> <p>5 letter words (high frequency, nouns, adjectives and pseudo-words) (N400)</p>	<p>AAT</p> <p>ERP: waveform (P300, P340, N400)</p>	<p>Patient 1: 47 days</p> <p>Patient 2: 73 days</p> <p>6 months</p> <p>1 year</p> <p>Training program</p>	<p>No expressive aphasia improvement.</p> <p>Increase (toward normalization) of the P300.</p> <p>Both patients: lacked a defined P340 at baseline but slow reappearance with recovery with a frequently inverted polarity.</p> <p>N400: almost normal since baseline (longer than healthy subjects).</p>
Praamstra et al., 1993 (19)	<p>20</p> <p>(including 2 hematoma, divided in 2 groups)</p> <p>6 global</p> <p>5 anomic</p> <p>7 Wernicke</p> <p>2 Broca</p> <p>10: moderate / recovered auditory comprehension impairment at T2</p> <p>10: severe auditory comprehension impairment at T2</p> <p>Subacute to chronic</p> <p>2 groups of 15 control subjects</p>	<p>EEG</p> <p>14-channel</p> <p>Late AEP</p> <p>Stimuli: 1Hz tone bursts of 50ms duration including rise and fall times of 10ms</p> <p>Middle AEP</p> <p>Resting to sleep</p> <p>2 to 4 series of 1500 stimuli per ear, rate 10/sec</p>	<p>AAT, TT</p> <p>AEP at T2: waveforms (late N100, P200, and middle Na, Pa, latency auditory responses), dipole source analyzing</p>	<p>T1: mean group one 2.4 (1-8) months and group two 5.4 (1-36) months</p> <p>T2: mean group one 51.2 (13 – 94) months and group two 45.5 (12-79) months</p>	<p>Intergroup differences: severe auditory comprehension impairments correlated more likely with abnormal AEP.</p> <p>AEP generation: in the posterior superior temporal lobe => most patients in the severe groups showed a lesion in this area (CT scans) and from the other group, mostly preserved.</p> <p>But they can't conclude about a relationship between AEP abnormalities and speech perceptual deficit because the evaluation was based on auditory discrimination performance only.</p>

<p>Jabbari et al., 1979 (14)</p>	<p>52 12 Broca 36 Mixed and Global 4 Wernicke</p> <p>Subacute to chronic</p>	<p>EEG 16-channel</p> <p>Activity not specified</p>	<p>Benson and Geschwind's approach to aphasia, PICA</p> <p>Continuous EEG: alpha, slow waves</p>	<p>2 to 4 weeks</p> <p>Every 4 to 6 months along during at 12 to 18 months</p> <p>44 received regular speech therapy</p>	<p>Link between degrees of focal slowing in EEG at baseline and language improvements: the more there were slow waves, the poorer was the recovery.</p> <p>Link between alpha rhythm in the contralateral hemisphere, recovery and initial severity: faster it goes, the better recovery was.</p> <p>Normal EEG was related with very good improvement in language, only with mild aphasia at baseline (but every type) and complete recovery of aphasia at discharge.</p> <p>Correlation between improvement of EEG and PICA scores.</p>
--------------------------------------	--	---	--	--	---

AAT: Aachen Aphasia Test

AEP: auditory evoked potentials

CT: computerized tomography

BDAE: Boston Diagnostic Aphasia Examination

GeBAS: Geneva Bedside Aphasia Score

MMN: mismatch negativity

PAL: Psycholinguistic Assessment of Language

PICA: Porch Index of Communicative Ability

QEEG: quantitative EEG

RH/LH: right hemisphere / left hemisphere

ROI: region of interest

sd : standard deviation

SWA: slow wave activity

TT: Token Test

WND: weighted node degree

3.2.Clinical trials

Tables 2, 3, and 4 regroup clinical trials in patients with aphasia by testing drugs, rehabilitation techniques, and non-invasive brain stimulation (NIBS). They recorded 420 patients with aphasia including three single case studies (25–27).

Drugs associated with specific rehabilitation method

Table 2 summarizes two double-blind, placebo-controlled studies (28,29) that tested two different drugs associated with different speech and language treatment on patients with chronic aphasia. They both used ERP/EMF to relate their behavioral results to electrophysiological modifications. The first study (28) demonstrated that Earobics therapy improves comprehension but Donepezil was deleterious on speech comprehension, especially for severe aphasia. The second study (29) showed that, associated or not with constraint-induced aphasia therapy (CIAT), Memantine had a good impact on chronic aphasia. These improvements were always associated with electrophysiological changes in the grand-average ERP performed in a silent reading task.

Table 2: Design and main results of treatment trials

Study design	Patients (number, type of aphasia, stage) and controls	Drug tested, dose, frequency, design	Speech training, frequency	Type of temporal imagery, number of channels and task asked	Outcome measure (behavioural and neuroimaging), follow-up	Main results
Woodhead et al., 2017 (28) Double-blind placebo-controlled, cross-over	20 9 global 11 Wernicke Chronic	Donepezil Placebo than drug or drug than placebo : weeks 0-5 : drug (5 mg) or placebo weeks 5-10 : drug (10mg) & Earobics or placebo & Earobics weeks 10-15 : Wash Out weeks 15-20 placebo or drug (5 mg) weeks 20-25 : placebo & Earobics or drug (10mg) & Earobics	Earobics version 1 : phonological training 10 hours / week during 5 weeks training block	MEG (18 subjects) 274-channel and EEG (2 subjects) 128-channel Spoken syllable (standard and deviant stimuli)	CAT, SART, ASHA FACS ERP: waveforms (MMN), source localization Follow-up : baseline, before drug condition and after, before placebo condition and after	Phonological training + placebo: improve in speech comprehension + stronger modulation of the left STG's self-connection and connection from left HG to STG and interhemispheric connections in severe aphasia. Phonological training + donepezil: decrease in speech comprehension. The severe subgroup showed stronger effects in both cases.

<p>Barbancho et al., 2015 (29)</p> <p>Single-center, randomized, placebo-controlled, double blind, parallel-group study</p>	<p>27 (including 13 placebo) 14 anomic 8 Broca 3 conduction 2 transcortical motor 1 Wernicke</p> <p>Chronic</p> <p>15 control subjects</p>	<p>Memantine, 10mg, twice daily</p> <p>weeks 0-16: memantine or placebo alone weeks 16-18: memantine or placebo + CIAT weeks 18-20: memantine or placebo alone</p>	<p>CIAT</p> <p>30h: 3h/day during 2 weeks</p>	<p>EEG</p> <p>21-channel</p> <p>ERP in a silently reading task</p>	<p>WAB-AQ scores</p> <p>ERP: waveform (P100 and N400)</p> <p>Follow-up: baseline to endpoints at weeks 16,18 and 20</p>	<p>Baseline: ERP in patients with aphasia showed an increase in brain activity (N400 and P100).</p> <p>Week 16: ERP (N400 and P100) decreased more in the memantine group than the placebo group. Increase of the WAB-AQ in the memantine group only.</p> <p>Week 18: WAB-AQ increased more in the memantine group. ERP (N400 and P100) increased in both groups.</p> <p>Week 20: changes remained stables.</p> <p>All the electrophysiological changes were in both hemispheres: bilateral reorganization of language network through this protocol.</p> <p>In the memantine group, there was a correlation between RMS, P100 and the WAB-AQ at baseline and at all time points.</p>
---	--	--	---	--	---	---

ASHA FACS : Social Communication and Daily Planning from the Functional Assessment of Communication Skills for Adults

CAT : Comprehensive Aphasia Test
CIAT : Constraint-Induced Aphasia Therapy
HG : Heschl's gyrus

SART : Sustained Attention to Response Test
STG : Superior Temporal Gyrus

WAB-AQ: Western Aphasia Battery-Aphasia Quotient

Specific speech training method

All 19 studies regrouped in Table 3 tested the effects of specific speech rehabilitation for aphasia by assessing behavioral and electrophysiological modifications.

Among them, nine studies (25,30–37) tested intensive constraint induce speech therapy based on the same principle: ILAT (Intensive language action therapy), CIAT (constraint-induced aphasia therapy) or CILT (constraint Induced Language Therapy). Wilson et al. (38) provided an InteRACT program, that is also an intensive therapy (5 hours per days, 5 days a week during 4 weeks). Four studies provided computer-assisted rehabilitation (39–42) for a lexical-phonological or IMITATE therapy. Iyer et al. (43) studied the impact of SFA/PCA (phonological components analysis/semantic feature analysis) protocol and Cornelissen et al. (44) used the CPT (Contextual priming technique), that had similarities with the SFA protocol. Aerts et al. (45) investigated the difference of benefits between intensive versus conventional therapy (according to Belgium National Institute for Health and Disability Insurance) on a single case-patient with subacute aphasia. The fifth Breier et al. study (46) used MIT (Melodic Intonation Therapy). The last study of Stojanovic et al. (47) didn't precise the type of speech rehabilitation.

All these studies found a positive impact of their rehabilitation protocol and most of them could correlate this positive impact with modifications on electrophysiological measures. Fifteen out of 19 studies used ERP/EMF (25,30–34,36–38,41–46) and most parts focused their analysis on main ERP/EMF components like the MMN, the P300 or the N400. Four studies used continuous EEG focusing on normal SWA during sleep (39,40) or abnormal SWA at rest (35,47).

Table 3: Design and main results of specific speech training method

Study design	Patients (number, type of aphasia, stage) and controls	Speech training, frequency	Type of imagery, number of channels and task asked	Outcome measure, follow-up	Main results
Iyer et al., 2020 (43) Case-control trial	8 Chronic 15 healthy controls	SFA/PCA 3 naming-therapy sessions per week during 4 weeks (12 session)	EEG 128-channel picture-word judgment task	Naming in treated items ERP: waveform and source analysis with DCM (including five ROI + window of 0-600ms to include N200 and N400) Follow-up: prior and immediately following therapy	Improvements in naming for patients who had reduced intrahemispheric coupling in RH areas (i.e., IFG and pSTG) after therapy. Patients with bad naming improvements showed, on the contrary, the highest RH coupling. DCM of EEG can be used to identify cortical connections that contribute to predict treatment inducing recovery in naming.
Lucchese et al., 2017 (33)	10 9 Broca 1 global Chronic	ILAT/CIAT 4 weeks, 3.5 hours, 3 days per week (10.5 per week)	EEG 128-channel Sentences with deviants words (pseudowords) and syntax	AAT (TT, comprehension, Naming and Repetition) ERP : waveform (MMN) and topography Follow-up : 2 days before and after the treatment interval	Significant improvements in language scores (all subtests of the AAT). MMN responses increased (especially over the LH) for all types of stimuli but ungrammatical strings.

Mohr et al., 2016 (36)	12 Broca Chronic	ILAT during 2 weeks, 3-4 hours/day (5 days a week)	MEG 102-channel Meaningful words and pseudowords	BDAE, BNT, TT, CAL EMF: waveform (MMNm) Follow-up : before and after therapy	Clinical improvements in naming, auditory comprehension, and in the quality of communication in everyday life situations. Increase MMNm amplitudes in the left fronto- temporal area only for meaningful words.
Radman et al., 2016 (41) Case report	1 Woman, 52 years old, bilingual (L1: Farsi and L2: French) Broca Subacute	Intensive lexical- phonological computer-assisted therapy (L2) 5 days per week during 4 weeks : phonological therapy of naming using a CAT (16 hours in total)	EEG 64-channel Picture-naming and word-picture verification tasks	BAT ERP : waveform and topography Follow-up: T0: 15 weeks after stroke, (only behavioral tests), T1: week 16, before the start of therapy and T2: after the therapy.	Improvement in naming in L2 but not in L1 (untreated). No cross-language generalization found in EEG (topography) analyses: modified EEG responses to treated L1 but not untreated L2. ERP topographic modulations in 540-500ms time- window post-stimulus in L2 indicate that the brain network involved in the phonetic encoding (late time window) has been modified by lexical- phonological therapy (during picture naming task).

<p>Aerts et al., 2015 (45) Case study</p>	<p>1 Man, 47 years old Non fluent aphasia Acute and post-acute 71 control subjects from a previous study (48)</p>	<p>Intensive / Conventional therapy 3 weeks of intensive therapy: 2 hours / day, 5 days a week (30 hours) 7 weeks following the prescription of the National Institute for Health and Disability Insurance in Belgium: 1 hour / day, 4 days a week (30 hours) 3 weeks of intensive therapy: 2 hours / day, 5 days a week (30 hours)</p>	<p>EEG 23-channel Auditory phoneme discrimination (attentive : P300 and pre-attentive : MMN) Auditory word recognition (N400)</p>	<p>AAT, subtests of PALPA ERP: topography and waveform (P300 / MMN / N400) Follow-up: 10 days post-onset before fist intensive therapy, after first intensive therapy, after 7 weeks conventional therapy, after second intensive therapy, after 6-month period of no intervention</p>	<p>After the whole therapy period: significant improvements in behavioral measures and improvements (towards normalization) in neurophysiological measures (P300, MMN, N400) Increase of P300 in bilateral frontoparietal, N400 (PW) in bilateral anterior frontal + right posterior frontoparietal and MMN (for MoA) in right frontotemporal areas. After the 6 months of no intervention: behavioral improvements maintained or improved again, but neurophysiological measures showed a decline. Between periods of therapy: increase of N400 (to PW) during intensive therapy and decrease during conventional therapy. Decrease of a test comprising PW during conventional treatment. Ceiling effects for lots of behavioral measures.</p>
<p>Sarasso et al., 2014 (40)</p>	<p>13 5 Broca 1 Wernicke 6 anomic 1 conduction Chronic</p>	<p>IMITATE 3.5 hours intensive single session, imitation-based, computer-assisted rehabilitative protocol</p>	<p>EEG 256-channel Sleeping</p>	<p>Subtest of the WAB, subtests of the Apraxia Battery for Adults, BNT Continuous EEG : SWA Follow-up: two sleep recording: before and just after therapy / behavioral measures were conducted before the first night of sleep and after the second night of sleep.</p>	<p>No behavioral changes but improvements in the WAB Repetition score. After therapy: during REM sleep, increase in EEG SWA and β EEG activity over bilateral connections between fronto-parietal networks (changes were more consistently found in the RH).</p>

Stojanović et al., 2013 (47)	<p>32 26 non fluent 6 fluent</p> <p>Subacute</p> <p>86 control subjects</p>	Two months of neurological and speech therapy	<p>EEG 32-channel</p> <p>Resting state (eyes closed and eyes open)</p>	<p>BDAE</p> <p>Continuous EEG : QEEG</p> <p>Follow-up: baseline at 1 month post-stroke and after therapy</p>	<p>Good improvement of aphasia in 17 and poor improvement in 15 patients.</p> <p>Variation of the frequency band (most on theta and delta band) before and after therapy in both hemispheres. Correlations were significant for SWA in the LH and for fast frequencies in both hemispheres (even more with the 2 subgroups of bad and good improvement). Delta band = sign of lesion</p> <p>Good improvement when shifting over LH of EEG variability (all frequencies for eyes closed and fast frequencies in eyes open) and when shifting over RH of beta frequency (in eyes-closed condition) and delta band (in eyes open condition).</p>
Wilson et al., 2012 (38)	<p>9</p> <p>1 transcortical motor 1 conduction 6 anomic 1 Broca</p> <p>Chronic</p> <p>Control subjects</p>	<p>InteRACT program</p> <p>5 hours per day, 5 days a week, during 4 weeks</p>	<p>EEG 64-channel</p> <p>Picture-name matching task</p>	<p>WAB-AQ, Communicative Effectiveness Index, Communication Activity of Daily Living-2</p> <p>ERP: waveform</p> <p>Before and after therapy</p>	<p>Improvements in language measures for 6 out of 9 patients (others had good performances at baseline) and no significant improvement in the picture-naming task.</p> <p>Normal P1-N1-P2 pattern for both groups, before and after therapy.</p> <p>Centro-parietal N400: shift from RH to the LH after therapy correlated with language improvements (not toward normalization of the pattern). No change in amplitude.</p> <p>Decrease in the healthy group of the N400 amplitude (probably due to habituation).</p>

<p>Breier et al., 2011 (32) Case study</p>	<p>1 Man, 62 years old Broca Chronic</p>	<p>CILT 3 hours / days, 4 days a week during 3 weeks (36 hours)</p>	<p>MEG 248-channel Recognition memory task for spoken words DTI</p>	<p>CIU EMF: before the resolution of the N1m, spatiotemporal analysis Follow-up: 3 weeks prior to, immediately prior to, immediately after, 3 months after therapy.</p>	<p>Improvement in language function after therapy and no change between the two pre-therapy and the two post-therapy sessions.</p> <p>“Bilateral increase in MEG activity in the temporal lobe during a receptive language task in areas potentially involved with language function, included inferior frontal lobe/insula, superior and middle temporal gyri, supramarginal and angular gyri in the left hemisphere and homotopic areas in the right hemisphere”.</p> <p>But decrease of MEG activity 3 months after therapy (to baseline for RH).</p>
<p>Breier et al., 2010 (46)</p>	<p>2 2 mixed aphasia Chronic</p>	<p>MIT 2 blocks of two-30min per day, 2 days a week during 3 weeks (total of 12 hours)</p>	<p>MEG 248-channel Silent action-picture naming</p>	<p>CIU ERF: waveform and sources of average waveform Follow-up: before, after the 1st block and after the 2nd block</p>	<p>Improvements in behavioral measures for one out of two patients.</p> <p>Baseline: LH more activated than RH for both (non-responder and responder).</p> <p>After the 1st block: increase in LH activity for both.</p> <p>After the 2nd block: reduction of RH activity for the therapy-responder / increase in RH activation for the other patient.</p>

Sarasso et al., 2010 (39)	4 Non-fluent aphasia Chronic	IMITATE 3.5 hours intensive single session, imitation-based, computer-assisted rehabilitative protocol fMRI study before of original IMITATE therapy (90 minutes daily during 6 weeks)	EEG 256-channel Sleeping fMRI during an “observation” task of a woman articulating syllables	WAB Continuous EEG: SWA Follow-up: two EEG sleep recording : before and just after therapy / behavioral measures were conducted before the first and after the second night of sleep / fMRI : first five sessions were 3 weeks apart, with the third being just before the start of IMITATE therapy, the fifth at the end, the sixth 9 months post- therapy.	Changes in SWA after the intensive session of IMITATE (LH more than RH) Long term reorganization of LH and RH language network during fMRI after original IMITATE therapy (6 full weeks). Increase of repetition scores after both therapy (one day / 6 full weeks)
Meinzer et al., 2009 (34) Pilot study	10 1 Wernicke 5 Broca 2 Global 1 Amnesic 1 not classified Chronic 10 control subjects	CIAT 3 hours / day for 10 consecutive days	MEG 148-channel Automatic word reading design	AAT (profile score and written language) EMF: time-frequency analysis (HFA) Follow-up: the day before and the day after therapy For the control group: two tests with an interval of two weeks	Improvements in language scores after therapy. Control subjects: HFA bilaterally distributed, no distinction between word classes (content, function, and pseudowords) => lexical route. Before therapy for patients: RH dominance for HFA, no distinction between word classes. In high- functioning patients’ subgroup (highest scores in AAT written language), no difference found after the therapy in HFA = similar bilateral pattern than controls. For low-functioning patients (lowest scores in AAT written language), more bilateral pattern after therapy (decrease of RH).

<p>Breier et al., 2009 (31)</p> <p>Case series</p>	<p>23 both expressive and receptive language impairments</p> <p>Chronic</p>	<p>CILT</p> <p>3 hours / days, 4 days a week during 3 weeks (total of 36 hours)</p>	<p>MEG</p> <p>248-channel</p> <p>recognition memory task for spoken words</p>	<p>WAB, CIU</p> <p>EMF: spatiotemporal analysis</p> <p>Follow-up: 3 weeks prior to, immediately prior to, immediately after, 3 months after therapy.</p>	<p>3 subgroups of patients :</p> <ul style="list-style-type: none"> · Those who improved significantly in language after therapy and lost their gain 3 months after greater RH activation than others subgroups. · Those who improved significantly in language after therapy and maintained their performances 3 months later: increase activation in left temporal areas after therapy. · Those who did not improve significantly after therapy showed comparably greater activation in left parietal areas.
<p>Laganaro et al., 2008 (42)</p>	<p>4 including 1 (P3) with herpes encephalitis</p> <p>P1: Wernicke to conduction (phonological impairment)</p> <p>P2: conduction (phonological impairment)</p> <p>P3: transcortical sensory (semantic impairment)</p> <p>P4: fluent (phonological impairment)</p> <p>Subacute</p> <p>15 control subjects</p>	<p>Computer assisted therapy for anomia</p> <p>3-5 weekly sessions</p>	<p>EEG</p> <p>128-channel</p> <p>Picture naming</p>	<p>MT 86</p> <p>ERP: waveform and topography</p> <p>Follow-up: two baselines (a week of interval in-between), post treatment, 2-4 weeks after the end of the therapy, 6 months later for 2 patients</p>	<p>Improvements in behavioral results after training.</p> <p>After therapy, normalization of amplitude and topography in the first 300ms for P1 and P2. In the following time-window abnormal amplitude and topography (new or persistent). Normalization of amplitude at 6 months but not of topography.</p> <p>P3: “increase of amplitudes diverging from the control group, especially during the first 300ms” = visual and semantic processes.</p> <p>P4: “normalization of amplitudes and maps at early time windows. New abnormal maps appeared after 250ms”.</p> <p>Source analysis: RH activation in 3 on 4 patients but at different stages (baseline, after therapy or chronic).</p>

Breier et al., 2007 (25)	1 Women, 62-year-old Expressive and receptive aphasia Chronic One stroke and one healthy control	CILT 3 hours / days, 4 days a week during 3 weeks (total of 36 hours)	MEG 248-channel (co-registered with MRI) Recognition memory task for spoken words	WAB, BNT, Spoken Word Picture Matching and the Sentence Picture Matching, subtests of PALPA ERF: waveform, spatiotemporal Follow-up: one week before, one week after, 3 months after therapy	Behavioral improvement after therapy. Important RH participation even after therapy. Increase in RH activation (superior temporal and supramarginal gyrus), deactivation of inferior frontal gyrus, correlated with clinical improvement (compared with stroke control). 3 months after activation of the bilateral mesial temporal area. Decrease of RH activation in the supramarginal gyrus and increase of LH participation through the middle temporal gyrus.
Breier et al., 2006 (30)	6 5 Broca 1 conduction Chronic	CILT 3 hours / day, 4 days a week during 3 weeks (total of 36 hours)	MEG 248-channel (co-registered with MRI) Recognition memory task for spoken words	Subtests of the WAB, BNT, TX (= performance on the dual card task), CIU ERF (only for 5 of 6): waveform, source localization Follow-up: before and after therapy	The degree of activation in right contralateral areas (homotopic of LH pre-morbid language areas) before the therapy was correlated with language improvements after therapy. No correlation for post-activation areas. “While all patients tended to experience an increase in onset and peak latency within the left hemisphere as compared to the right hemisphere after therapy, this trend was exaggerated in the Non-Responders.”
Pulvermüller et al., 2005 (37)	10 2 Wernicke 5 Broca 1 Amnesic 1 Transcortical one data is missing Chronic	CIAT ≈ 30h over 10 consecutive working days	EEG 29-channel Lexical decision task (with word and pseudoword)	Subtests of AAT (including the TT) ERP: waveform, source localisation Follow-up: before and after therapy	After therapy: improvement in language scores, increased of negativity around 250-300ms for words, no change for PW in both hemispheres. Is the word evoked negativity around 250-300ms after word onset could be an index of recovery?

Meinzer et al., 2004 (35)	28 4 Wernicke 13 Broca 2 Amnesic 3 Global Chronic 25 control subjects	CIAT 3 hours / day for 10 consecutive days: for 18 patients: language exercises with increasing levels of difficulty for 10 patients: model-based intervention	MEG 148-channel Resting period	AAT (profile score and TT) Continuous EEG: SWA / ASWAM, Delta Dipole Density Follow-up: one day before and one day after the end of therapy, months later for behavioral measures	At baseline: abnormal slow-wave activity (in almost all patients) only in the region surrounding the structural lesion. Improvements after training and decrease the amount of slow-wave activity. But for some patients (n = 12), language improvement increases a delta activity surrounding the lesion.
Cornelissen et al., 2003 (44)	3 Conduction Residual aphasia Broca (all had anomia) Chronic	CPT 1 hour, 3 times a week during 3 weeks (6 additional sessions for 1 patient)	MEG 306-channel Picture naming task Resting (eyes open and eyes closed)	Subtests from BDAE and BNT, 106-item naming test EMF: waveforms and source of waveforms + spontaneous brain activity (SWA) Follow-up: 2 pre-tests (2 weeks apart), 2 weeks and 3-4 weeks after training	Improvement in naming only for treated items. SWA (5Hz) surrounding the lesion. Changes after treatment in brain activity only in regions next to the lesion (left inferior parietal lobe) starting at around 300-600ms after the stimulus (and lasting 200-700ms). These changes could reflect therapy-effects on phonological processing. Huge intersubject variability between correct and erroneous responses.

ASWAM: Abnormal Slow Wave Mapping

BAT: bilingual Aphasia Test

BNT: Boston Naming Test

CAL: Communicative Aphasia Log

CAT: Computerize Aphasia Therapy

CILT: constraint Induced Language

Therapy

CIU: Correct Information Units

CPT: Contextual priming technique

DCM: dynamic causal modelling

DTI: diffusion tensor Imaging

ERF: Event Related Field

HFA: High Frequency Activity

IFG: inferior frontal gyrus

ILAT: Intensive language action therapy

IMITATE: Intensive Mouth Imitation and

Talking for Aphasia Therapeutic Effects

MIT: Melodic Intonation Therapy

MMNm: magnetic Mismatch Negativity

MT 86: Montréal-Toulouse 86

PALPA: Psycholinguistic Assessment of

Language Processing in Aphasia

PCA/SFA: phonological components

analysis / semantic feature analysis

pSTG: posterior superior temporal gyrus

PW: pseudoword

REM: Rapid Eye Movement

Therapy

WAB: Western Aphasia Battery

Neuromodulation

Table 4 summarizes 6 studies that used non-invasive brain stimulation (NIBS) in patients with aphasia. Four (26,49,50) used low rTMS (repetitive Transcranial Magnetic Stimulation) applied on the contralesional hemisphere and two of them (26,27) high rTMS on the damaged hemisphere. One study (51) used anodal tDCS (transcranial Direct Current Stimulation) targeting the left posterior perisylvian areas and the older one (52) used rtACS (repetitive transorbital Alternating Current Stimulation). They all found language improvements which were correlated with electrophysiological modifications. Three studies recorded continuous EEG (27,51,52). The three others were ERP/EMF studies, focusing their analysis on the N400 (49,50) or the P200 (26).

Table 4: Design and main results of NIBS studies

Study design	Patients (number, type of aphasia, stage) and controls	Stimulation parameters (neuromodulation type, frequency, location, intensity etc.)	Number of sessions, frequency, speech training	Type of temporal imagery	Outcome measure, follow-up	Main results
Chantsoulis et al., 2016 (26)	1 Woman, 72 years old RH stroke Transcortical sensory aphasia Chronic 35 control subjects	rTMS 25 repetitions 1Hz (LH) 5Hz (right temporal posterior area, T6)	20 sessions Aphasia therapy with “a comprehensive model of rehabilitation”	EEG 19-channel Variant of the cued go/no go task	PL-WAB ERP: waveform (at T6, P200), maps of ERP and QEEG Follow-up: baseline, 6 months later	Improvements in language and cognitive control functions. Decreasing in abnormal neuronal excitability (P2) over T6 in the right hemisphere. “ERPs in a GO/NOGO task can be used in the assessment of functional brain changes and during treatment in those patients with crossed aphasia”.
Wu et al., 2015 (51) Blinded VS Sham	12 8 Broca 2 mixed 1 anomic 1 conductive Post-subacute (3-6 months) 12 control subjects	tDCS Anodal: left posterior perisylvian region 1.2 mA, 20 min T1: speech therapy + sham tDCS T2: speech therapy + tDCS T3: speech therapy + sham tDCS	20 sessions Everydays during 4 weeks of picture-naming and auditory word-picture identification conducted by a computer-system	EEG 16-channel Resting condition Word repetition task	PACA Continuous EEG: ApEn Follow-up: baseline, T1, T2, T3	Improvement in picture-naming and auditory word-picture identification. Before therapy: EEG ApEn indices was higher in P3 and lower in right Broca point and T4 in repetition compared with resting. After therapy: more left activation, higher EEG ApEn in left Wernicke and Broca points, in C3, P3, T3 but also in P4 and right Wernicke point. Correlation between higher activation level in wide areas of the LH and isolated areas of the RH and behavioral improvement.

Dammekens et al., 2014 (27)	1 Woman, 55 years old Non-fluent aphasia Chronic Matched in age control subjects	rTMS IIFG 80% RMT 10Hz	15 sessions, 5 sessions a week for 3 consecutive weeks No speech training	EEG 19-channel Resting condition	AAT Continuous EEG: Beta and theta rhythms Follow-up: before, after and 4 months after the treatment	After stimulation, decrease in rIFG activity post rTMS and normalization for the IIFG for beta3 frequency band (significant effect). Increase in right supplementary motor area activity for beta3 frequency band. Improvements in repetition tests, naming, and comprehension. Increase functional connectivity with the link between the IIFG and the rIFG for theta and beta frequency band.
Barwood et al., 2012 (49) Single blind VS sham	12 6 sham / 6 real Mild to global non-fluent aphasia Chronic	rTMS Anterior portion of right PTR (BA 45) 90% RMT 1Hz 20min	10 sessions, 5 times a week for 2 consecutive weeks No speech training	EEG 32-channel Written word-picture semantic judgement task	BDAE, BNT ERP: waveform (focused on N400) Follow-up: baseline (prior to stimulation), 1 week, 2 months, 8 months and 12 months post stimulation	N400 response over time (up to 12 months) improve in the active rTMS group and not in the sham rTMS group. This improvement was accompanied by improvements on the ERP task and the semantically incongruent condition yielded greater sensitivity to electrophysiological changes over time.
Barwood et al., 2011 (50) Double blind VS sham	12 6 sham / 6 real Mild to severe non fluent aphasia Chronic	rTMS Anterior portion of right PTR (BA 45) 90% RMT 1Hz 20min	10 sessions 5 times a week for 2 consecutive weeks No speech training	EEG 32-channel Written word-picture semantic judgment task	BNT, BDAE ERP: waveform (N400) Follow-up: prior to stimulation (baseline), 1 week, 2 months post stimulation	“Significant differences between the real stimulation and control (sham) stimulation groups on ERP (N400) measures of mean amplitude, area under the curve and peak amplitude, 2 months post stimulation for the semantically incongruent paradigm condition” but no significant results at 1 week post-stimulation. Significant improvements for real stimulation group in comparison with the sham group, on participants’ performance between baseline and two months.

<p>Fedorov et al., 2010 (52)</p> <p>Randomized, drug-controlled trial, blinded</p>	<p>23</p> <p>Motor, sensory and mixed forms (in a 98 stroke patients study)</p> <p>Chronic</p>	<p>rtACS</p> <p>200-400 μA inter-pulse intervals: 23-190ms (both eyes separately) 30-40min</p> <p>Drug: depending on the patients individual requirement</p>	<p>rtACS: daily during 12 consecutive days</p> <p>3 groups:</p> <p>D: control group: drug therapies</p> <p>ACS: rtACS only</p> <p>D/ACS combinaison of both</p>	<p>EEG</p> <p>19-channel</p> <p>Resting condition</p>	<p>NIH-NINDS</p> <p>Continuous EEG: Theta, Beta, alpha rhythms</p> <p>Follow-up: before and after treatment, and after 1 month treatment free</p>	<p>Improvement in aphasia values for both groups ACS and D/ACS compared to the control group. Final outcome: the ACS group deficit was stable but the D/ACS group showed further improvements.</p> <p>Improvement of EEG synchronization between both temporal right and left hemispheres, precisely on theta range (which was absent from damage hemisphere at baseline). Link confirmed at 1 month.</p>
--	--	---	---	---	---	---

ApEn: Approximate entropy

BA: Brodmann area

NIH-NINDS: National Institutes of Health Stroke Scale

PACA: Psycholinguistic Assessment in Chinese Aphasia

PL-WAB: Polish version of the Western Aphasia Battery

RMT: Resting Motor Threshold

rIFG/lIFG: right/left Inferior Frontal Gyrus

rtACS: repetitive transorbital alternating current stimulation

rTMS: repetitive Transcranial Direct Current Stimulation

tDCS: transcranial Direct Current Stimulation

Control groups / sham or placebo groups

In all 29 trials studies described below, only 6 used a placebo/sham group of patients : one speech-training study (25), two drug studies (28,29) and three NIBS studies (49,50,52). In 12 studies (25–27,29,34,35,38,42,43,45,47,51), patient data was compared to healthy subjects groups. So only two studies provided both a healthy control and a patient group comparison (25,29).

Stage of recovery

All studies but four (41,45,47,51) involved patients with aphasia at a chronic stage with the aim to neutralize the spontaneous recovery effects. Three of them (45,47,51) were controlled by only a healthy group. The last one (41) was neither controlled by the healthy nor patient group.

ERP/EMF studies

Twenty trial studies used ERP/EMF.

They provided different tasks: go/no go (26), picture naming (41,42,44,46,46), picture-word verification (38,41,43,49,50), semantic/grammatical judgment (33,36,37), auditory discrimination (45), memory task (25,30–32) or automatic word reading tasks (34) to obtain ERP or EMF.

Waveform analysis

17 studies used waveform analysis (25,26,28–30,33,36–38,41–46,49,50).

Six studies (29,38,43,45,49,50) found modification in N400 during judgment tasks (43,49,50), auditory word recognition (45), picture-naming matching tasks (38) and silent reading (29). Aerts et al. and Barbancho et al. (29,45) were the only ones to find a decrease of the N400 component by reducing speech-training intensity for the first one and by administrating drugs for the second one. For Aerts et al., the decrease of N400 was correlated with a decrease or a maintained ceiling in behavioural measures. On the contrary, for Barbancho et al. it was correlated with language improvement. But, by adding speech therapy, the last team found an increase of the N400, as Barwood et al. in two low-rTMS studies and Aerts et al. in the intensive

speech training part they provided (45,49,50). We noticed that Aerts et al. (45) worked with a patient in a subacute stage of aphasia. In a picture-naming task, Wilson et al. (38) recorded an abnormal shift of centroparietal N400 waveform from the right hemisphere to more lateralized left-hemisphere after therapy but no change in amplitude correlated with language improvement.

Barbancho et al. (29) found similar results with another ERP component, the P100 (with the same decrease followed by an increase in amplitudes described above).

For Chantsoulis et al. (26), their study showed that a decrease of the abnormal P200 in go/no go task after therapy in a single-case crossed-aphasia was correlated with improvements in language and cognitive control function. In Wilson et al. study (38), the P200 showed a normal amplitude and no change before and after therapy in a normal P1-N1-P2 pattern of a picture-naming task. All the patients from that study had more expressive than receptive impairments.

One study (37) described after a CIAT therapy an increase of negativity around 250-300ms in a lexical decision task only for words, not for pseudo-words, in both hemispheres.

Topographical analysis

Four of the clinical trials used ERP/EMF topographical analyses (33,41,42,45).

Concerning the positive impact of increased RH activation, Laganaro et al. (42) showed RH activation during a picture-naming task at different stages of recovery, from two weeks to six months post stroke and also before and after therapy.

Three studies (33,45) used the MMN as a neurophysiological biomarker to prove therapy-induced effects. For this purpose, they introduced in their task (lexical or grammatical judgment, auditory stimulus, etc.) unexpected/deviant items (pseudo-words, ungrammatical sentences construction, etc.) and so could calculate the MMN. These studies all found improvement in the MMN responses, especially on left areas for Lucchese et al. (33) during a lexical task with meaningful and pseudowords, and in right frontotemporal areas for Aerts et al. (45) during an impromptu auditory stimulus. More precisely, the MMN amplitude improvement in Lucchese et al. (33) was concerning only meaningful words in the left frontotemporal area.

Aerts et al. (45) studied P300, as a corollary of the MMN. They highlighted an increase in amplitude during two periods of rehabilitation and fluctuations between intensive and conventional therapy.

ERP changes were reported in various time-windows. Laganaro et al. (42) reported an increase of amplitude and topographical changes after therapy in different time-windows: in the first 300ms in a patient with semantic impairments and after 250ms in patients with phonological impairments. Radman et al. (41) reported topographical modification in late time-windows (540-600ms) in a naming task following phonological therapy.

Sources waveform or spatiotemporal studies

Twelve others studies added source localization to their waveforms analysis or did spatiotemporal maps (25,26,28–32,37,38,43,44,46).

In the continuity of topographical studies described above, one study (44) found EMF modification in naming task induced by therapy, based on both lexical-semantic and phonologic representations, started at 300-600ms after picture presentation in regions surrounding left brain lesion, but no more implication of right hemisphere was noticed after therapy. The 3 patients of that study had more phonological impairment than semantic impairment.

Breier et al. (30) described a correlation between the degree of RH activation, at baseline before therapy (during a recognition memory task for spoken words) and language improvements following therapy. In another one-case study, Breier et al. (32) showed a bilateral MEG activity increase in left language areas and homotopics after therapy.

However, other studies found a correlation between decrease of RH implication and recovery like Breier et al. in 2010 (46) who showed a correlation between response to MIT (Melodic Intonation Therapy) and reduction of RH activity in a two-patients study at chronic stage. For the same team in 2009 (31), an increase in left temporal area activation in a naming task after therapy was associated with language improvement and long-term maintain of their performances. At the contrary, patient with more RH activation did not maintain their behavioral improvement at 3 month following-up.

In another study of Breier et al. (25), they found an increase in RH areas activation right after therapy in a recognition memory task for spoken words. However, after 3 months without

therapy, they observed an increase of LH participation and a decrease of the contralesional hemisphere.

By using MEG in an MMN task with patients in a chronic stage, Woodhead et al. (28) linked language improvement with stronger modulation of the left superior temporal gyrus' self-connection, connection from left Heschl's gyrus to superior temporal gyrus and in interhemispheric connections.

One study by Iyer et al. (43), in a Dynamic causal modeling (DCM) based on two-time windows including N200 and N400 during phonological and semantic tasks, found a link between high level of naming improvement after therapy and low intrahemispheric coupling in the right hemisphere, especially in inferior frontal gyrus and posterior superior temporal gyrus.

Time-frequency analysis

Only one study provided time-frequency analysis (34). The authors analyzed variation of frequencies with time during a reading-task, more precisely HFA (High Frequency Activity), mostly in gamma band. They related improvement in language after therapy to a decrease of HFA in the RH (towards normalization of a bilateral activation pattern).

Continuous EEG

Among the 7 studies with continuous EEG (27,35,39,40,47,51,52), two were sleeping studies of Sarasso et al. (39,40) that investigated the impact of an intensive single session of IMITATE therapy on patients with chronic aphasia. They found an improvement in behavioral measures (repetition) correlated with an improvement of SWA (slow-wave activity) during REM sleep. These changes were bilateral in both studies but more consistently in the ipsilesional hemisphere for the first one (39) and in the healthy hemisphere for the second one (40).

Another study (35) focused on abnormal SWA, not during sleep, but at a rest. That abnormal activity was in the vicinity of the lesion and for most of the patients, improvements after speech therapy induced a decrease of that activity (16 patients of 28).

Two studies (27,52) found an improvement of interhemispheric connectivity after therapy correlated with language improvement, showed by synchronization on beta3 and theta waves

for Dammekens et al. and only for theta range for Fedorov and collaborators. Dammekens et al. (27) also found a normalization of beta3 band after high rTMS with a decrease in the RH.

Wu et al. (51) used EEG non-linear analysis with ApEn (approximate entropy) which is a statistical measure that quantifies the extent of serial interrelationships (range from 0 if it's perfectly ordered to infinite if measures are random). In their case, when ApEn increased, the irregularity increased too and that could be correlated with "raised nonlinear cell-dynamics or interaction of cortical networks". Wu and collaborators compared two tasks (resting and repetition) in a patient with aphasia and a healthy control. They found a correlation between the increase of EEG ApEn indices in LH and some isolated RH areas and improvement in behavioral measures.

3.3. Methodological differences

Type of imagery

About the type of imagery techniques, 27 of the studies used EEG, 9 used MEG and 2 (13,28) used both EEG and MEG.

Concerning the number of electrodes, only 19 studies of 38 used high-resolution imagery with equal or more than 64 electrodes.

Of the 27 studies using ERP/EMF, 15 did so with high-resolution imagery. Twenty-three analyzed using waveform, 4 using topography (33,41,42,45) and 1 (34) using time-frequency analysis only. In the 15 studies with high resolution, there were 3 that used topography, 11 only waveforms, and the last one (34) used time-frequency analysis. Two of the ERP/EMF studies (26,44) recorded both continuous and EMF measures. However, they recorded spontaneous EEG only to remove SWA from EMF when it was necessary.

The other 11 studies used continuous recording and only 4 of them were in high-resolution imagery.

4. Discussion

4.1. Methodological comments

About placebo/sham conditions, only 6 out of 29 clinical trials used such a control group (25,28,29,49,50,52). The others worked with patients at a chronic stage of aphasia, considering this stage as stable. Indeed, among the non-interventional studies, two reported electrophysiological stability during that phase in continuous EEG (14,22). However, in the study of Barbancho et al. (29), modifications on ERPs waveform analysis were reported for the placebo group composed of chronic patients. Thus, even if there is an apparent consensus about behavioral stability (without any stimulation) during the chronic stage (2), the electrophysiological stability of that phase remains uncertain. Therefore, further studies might enroll sham or placebo groups of patients with aphasia even at a chronic stage. Furthermore, 3 clinical trials (41,45,51) worked with patients at a subacute stage and were not controlled by any placebo group. Electrophysiological variations in that phase have been investigated in several non-interventional studies reviewed here (17,18,20). They all found important modifications in their electrophysiological measures and high interpatient variability, sometimes correlated with language improvements. Working with patients at the subacute stage seems very relevant but would need, according to us, at least a placebo group and a large number of patients.

4.2. Continuous EEG/MEG activity

Main continuous EEG/MEG findings

After a stroke, abnormal rhythm patterns are found in the vicinity of the lesion and more precisely slow wave activity, outside the sleeping period (8). In this review, studies found that recording spontaneous rhythms at rest with EEG/MEG could be a very good predictor for the recovery of aphasia and could determine the severity of aphasia. In the study of Jabbari et al. (14), among their 52 patients, the only one with normal EEG rhythms was a patient with only mild aphasia who completely recovered. We note that when the slowing of brain activity persisted in time it was correlated with bad spontaneous recovery (14,21–23). Moreover, fast rhythms, mostly alpha rhythms, were on the contrary correlated with good improvements (14,21). Furthermore, for Nicolo et al. (21), beta oscillations could be associated with the

creation of new synaptic connections and so – in case of brain lesions – with neural reorganization and recovery.

Analyzing spontaneous EEG also allows some studies to characterize the electrophysiological impact of concomitant speech and language therapy.

The decrease of abnormal SWA at rest, in the vicinity of brain lesions in the study of Meinzer et al. (35) was correlated with language improvement for about 60% of the patients. Therefore in this interventional study, measuring only SWA does not seem to be a reliable biomarker.

In the 2 sleeping studies reviewed here (39,40), the increase of normal SWA during sleep, after one day of therapy, was a good prognosis for language improvement. Some studies agreed that non-REM sleep (corresponding to the period of SWA) corresponds to declarative learning (53). Indeed, the therapy used in these 2 sleeping studies was based on watching video clips of different people saying words and sentences. These two studies highlighted the fact that rehabilitation could take the same ways as learning by creating new cerebral connections during non-REM sleep, like in memory tasks. However, the IMITATE therapy used in the studies of Sarasso et al. in 2010 and 2014 is very repetitive and so might also be considered as learning. The two last continuous EEG studies that we reviewed here (27,52) focused their analysis on interhemispheric connectivity after NIBS rather than on electrophysiological biomarkers of therapy-induced improvements.

To sum up, if recording continuous brain activity could help to predict language recovery or following interhemispheric connectivity, it does not appear to be sufficient to demonstrate therapy-effects between responders and non-responders of therapy for example.

4.3. ERP/EMF/AEP analysis

Methodology used

Among the 27 studies selected in that review using ERP/EMF, only one used time-frequency analysis whereas 4 used topographic analyses. Most of the ERP/EMF studies focused their analysis on waveforms analysis. Only 15 out of 27 studies used high-resolution imagery. This limitation could partly explain the few number of studies using topographical analyses.

Main ERP/EMF findings

ERP/EMF can be a suitable tool to reflect the effects of therapy for many authors (37). Classically, ERPs/EMFs tend to normalize with recovery and language improvement but, as in Laganaro et al study (42), some increase of abnormalities or new abnormalities in ERPs analysis were also correlated with language improvement. As for the implication of the right hemisphere or perilesional areas after stroke, modifications in electrophysiological measures could also be a good sign for recovery even when it is not towards reaching a normal pattern.

In the case study of Aerts et al. (45) as well as in Becker et Reinvang (15) or Barbancho et al. (29), better language performance was not associated with ERPs components returning to normal. Aerts et al's case study showed after a therapy-free period a decrease in the electrophysiological measures (P300, MMN and N400) which became more deviant than before. Interestingly, those discrepancies were correlated with the continuity of improvements in language scores.

Different steps occur in picture naming for healthy subjects: semantic and lexical steps in the first 300ms after stimulus presentation, then phonological representations are accessed, and finally after 400ms phonological-phonetic take over (12). Some ERP modulations related to patients' impairments have been identified in two studies of Laganaro et al. (54,55). Patients with semantic impairments had topographical and waveform differences in the early time windows (before 300ms), patients with lexical-phonological impairments in the time windows after that and before 400ms, and patients with phonological-phonetic impairments after 400ms. Outside of these impaired time windows, patterns were quite normal as compared to healthy control subjects.

In a study from this review, the same team (42) described an increase in amplitude and topographic changes after therapy in different time windows: in the first 300 milliseconds for a patient with semantic difficulties and after 250ms for patients with phonological difficulties. The team of Radman et al. (41) with a clinical case of a bilingual patient, reported topographic changes in late time windows (540 to 600ms after stimulus onset) following lexical-phonological therapy. Cornelissen et al. (44) found changes in EMF patterns induced by the Contextual Priming Technique therapy from 300-600ms after stimulus onset in perilesional regions. All patients had predominantly phonological (rather than semantic) difficulties. All of these studies described a variety of patterns when compared to control subjects, namely changes

corresponding as much as normalizations, the appearance of discrepancies, or the maintenance of discrepancies.

Overall, modifications in ERP/EMF topographic and waveform analyses seem to be both consistent with clinical difficulties presented (semantic or phonological) but also appear to evolve through targeted rehabilitation methods.

Other studies mentioned ERP components as biomarkers of recovery, prognosis, or therapy-induced effects.

Thus, the N400, mostly found in the studies reviewed during semantic judgment tasks (43,49,50), could be an interesting biomarkers of type of language impairment : it is abnormal in aphasia with comprehension deficits (45), but not in patients with expressive aphasia and relatively spared comprehension in Cobianchi and Gianquinto study (16). The N400 could also be a good measure of therapy effects (45,49,50) and more precisely for Barwood et al. in two studies (49,50), a good measure of improving in lexical-semantic processing or semantic integration.

We can also highlight the MMN component as a potential biomarker of therapy-induced effects or spontaneous recovery (17,33,36,45). All these studies found improvements in all behavioral measures (both expressive and receptive tasks), except the non-interventional study from Ilvonen et al. (17), which only correlated the MMN modulation with comprehension improvements.

Several studies related the presence and/or the increase in amplitude of the P300 component as a good sign for recovery, from acute to the chronic stage (15,16,18). Nolfé et al. (18) even suggested that the P300 could be linked to with the “level of cognitive elementary abilities”. However, only one clinical trial (45) investigated the shape of the P300 as a sign of therapy-induced effects: they found that its amplitude increased and decreased with the intensity of speech and language therapy.

4.4. Conclusion

To conclude, the contribution of EEG and MEG measures is interesting for the following of spontaneous or therapy-induced effects recovery in post-stroke aphasia, but poorly exploited. The few number of high-resolution imagery studies and the lack of knowledge about

topographical or time-frequency analysis are probably the main reasons why there are little used. As for, the identification of biomarkers of therapy-induced effects, it seems more reliable with ERP/EMF than through continuous EEG. Many avenues remain to be explored, in particular, the evaluation of NIBS through topography, which may help to identify biomarkers of good response to these treatments.

References

1. Brust JC, Shafer SQ, Richter RW, Bruun B. Aphasia in acute stroke. *Stroke*. mars 1976;7(2):167-74.
2. Pedersen PM, Jørgensen HS, Nakayama H, Raaschou HO, Olsen TS. Aphasia in acute stroke: Incidence, determinants, and recovery. *Ann Neurol*. 1995;38(4):659-66.
3. Lam JMC, Wodchis WP. The Relationship of 60 Disease Diagnoses and 15 Conditions to Preference-Based Health-Related Quality of Life in Ontario Hospital-Based Long-Term Care Residents. *Med Care*. avr 2010;48(4):380–387.
4. Brady MC, Kelly H, Godwin J, Enderby P, Campbell P. Speech and language therapy for aphasia following stroke. *Cochrane Database Syst Rev* [Internet]. 2016 [cité 2 févr 2020];(6). Disponible sur: <https://www-cochranelibrary-com.docelec.u-bordeaux.fr/cdsr/doi/10.1002/14651858.CD000425.pub4/full>
5. Stephens M. The Effectiveness of Speech and Language Therapy for Poststroke Aphasia. *AJN Am J Nurs*. nov 2017;117(11):19.
6. Hartwigsen G, Saur D. Neuroimaging of stroke recovery from aphasia – Insights into plasticity of the human language network. *NeuroImage*. 15 avr 2019;190:14-31.
7. Biou E, Cassoudeulle H, Cogné M, Sibon I, De Gabory I, Dehail P, et al. Transcranial direct current stimulation in post-stroke aphasia rehabilitation: A systematic review. *Ann Phys Rehabil Med*. mars 2019;62(2):104-21.
8. Kamada K, Sagner M, Möller M, Wicklow K, Katenhäuser M, Kober H, et al. Functional and metabolic analysis of cerebral ischemia using magnetoencephalography and proton magnetic resonance spectroscopy. *Ann Neurol*. oct 1997;42(4):554-63.
9. Dubovik S, Pignat J-M, Ptak R, Abouafia T, Allet L, Gillibert N, et al. The behavioral significance of coherent resting-state oscillations after stroke. *NeuroImage*. 15 mai 2012;61(1):249-57.
10. Herrmann CS, Rach S, Vosskuhl J, Strüber D. Time–Frequency Analysis of Event-Related Potentials: A Brief Tutorial. *Brain Topogr*. 1 juill 2014;27(4):438-50.
11. Laganaro M. ERP topographic analyses from concept to articulation in word production studies. *Front Psychol*. 2014;5:493.
12. Laganaro M. Inter-study and inter-Individual Consistency and Variability of EEG/ERP Microstate Sequences in Referential Word Production. *Brain Topogr*. 1 nov 2017;30(6):785-96.
13. Gow DW, Ahlfors SP. Tracking reorganization of large-scale effective connectivity in aphasia following right hemisphere stroke. *Brain Lang*. 1 juill 2017;170:12-7.

14. Jabbari B, Maulsby RL, Holtzaple PA, Marshall NK. Prognostic Value of EEG in Acute Vascular Aphasia: A Long Term Clinical-EEG Study of 53 Patients. *Clin Electroencephalogr.* oct 1979;10(4):190-7.
15. Becker F, Reinvang I. Event-related potentials indicate bi-hemispherical changes in speech sound processing during aphasia rehabilitation. *J Rehabil Med.* oct 2007;39(8):658-61.
16. Cobianchi, A, Giaquinto S. Can we exploit event-related potentials for retraining language after stroke? *Disabil Rehabil.* 1 janv 2000;22(9):427-34.
17. Ilvonen Titta-Maria, Kujala Teija, Kiesiläinen Anita, Salonen Oili, Kozou Hesham, Pekkonen Eero, et al. Auditory Discrimination After Left-Hemisphere Stroke. *Stroke.* 1 juill 2003;34(7):1746-51.
18. Nolfé G, Cobianchi A, Mossuto-Agatiello L, Giaquinto S. The role of P300 in the recovery of post-stroke global aphasia. *Eur J Neurol.* 2006;13(4):377-84.
19. Praamstra P, Stegeman DF, Kooijman S, Moleman J. Evoked potential measures of auditory cortical function and auditory comprehension in aphasia. *J Neurol Sci.* 1 mars 1993;115(1):32-46.
20. Rojas Sosa MC, Fraire Martínez MI, Olvera Gómez JL, Jáuregui-Renaud K. Early auditory middle latency evoked potentials correlates with recovery from aphasia after stroke. *Clin Neurophysiol.* 1 janv 2009;120(1):136-9.
21. Nicolo P, Rizk S, Magnin C, Pietro MD, Schnider A, Guggisberg AG. Coherent neural oscillations predict future motor and language improvement after stroke. *Brain.* oct 2015;138(10):3048-60.
22. Hensel S, Rockstroh B, Berg P, Elbert T, Schönle PW. Left-hemispheric abnormal EEG activity in relation to impairment and recovery in aphasic patients: EEG-slow-wave activity in aphasia. *Psychophysiology.* mai 2004;41(3):394-400.
23. Széles B, Mielke R, Kessler J, Heiss W-D. Prognostic relevance of quantitative topographical EEG in patients with poststroke aphasia. *Brain Lang.* 2 juill 2002;82(1):87-94.
24. Cobianchi A, Giaquinto S, Mossuto-Agatiello L, Pisarri F, Nolfé G, Merigliano D. Aiming at predicting outcome in patients suffering from global aphasia. *Riv Neurobiol.* 1997;43(4):253-63.
25. Breier JI, Maher LM, Schmadeke S, Hasan KM, Papanicolaou AC. Changes in Language-specific Brain Activation after Therapy for Aphasia using Magnetoencephalography: A Case Study. *Neurocase.* 29 août 2007;13(3):169-77.
26. Chantsoulis M, Pórola P, Góral-Pórola J, Herman-Sucharska I, Kropotov JD, Pačalska M. Application of functional neuromarkers for constructing protocols of neurotherapy and monitoring the success of treatment in chronic crossed transcortical sensory aphasia: A case study. *Acta Neuropsychol.* 2016;14(4):389-400.

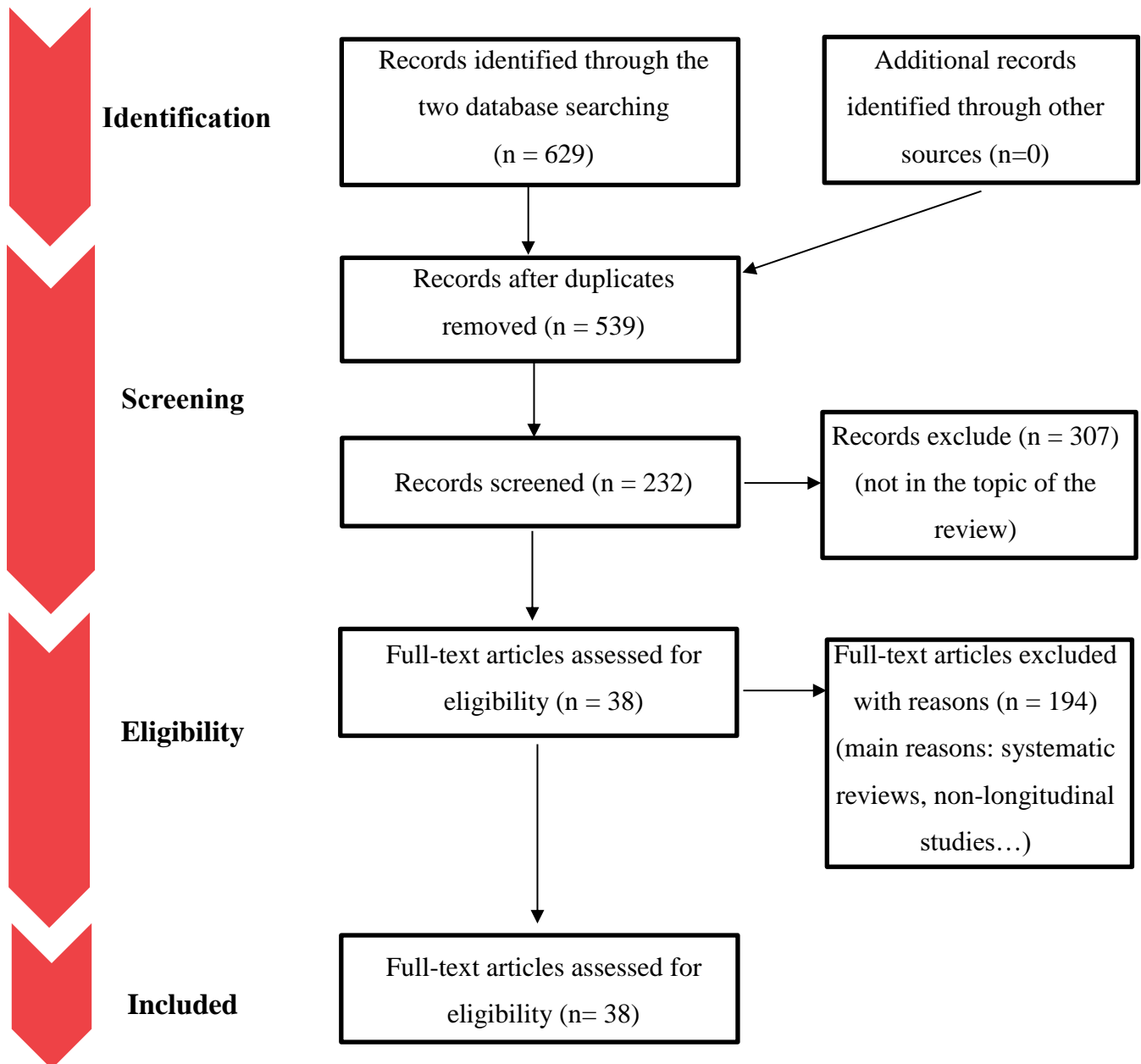
27. Dammekens E, Vanneste S, Ost J, De Ridder D. Neural correlates of high frequency repetitive transcranial magnetic stimulation improvement in post-stroke non-fluent aphasia: A case study. *Neurocase*. 2 janv 2014;20(1):1-9.
28. Woodhead ZV, Crinion J, Teki S, Penny W, Price CJ, Leff AP. Auditory training changes temporal lobe connectivity in 'Wernicke's aphasia': a randomised trial. *J Neurol Neurosurg Psychiatry*. 1 juill 2017;88(7):586-94.
29. Barbancho MA, Berthier ML, Navas-Sánchez P, Dávila G, Green-Heredia C, García-Alberca JM, et al. Bilateral brain reorganization with memantine and constraint-induced aphasia therapy in chronic post-stroke aphasia: An ERP study. *Brain Lang*. 1 juin 2015;145-146:1-10.
30. Breier JI, Maher LM, Novak B, Papanicolaou AC. Functional Imaging Before and After Constraint-Induced Language Therapy for Aphasia Using Magnetoencephalography. *Neurocase*. déc 2006;12(6):322-31.
31. Breier JI, Juranek J, Maher LM, Schmadeke S, Men D, Papanicolaou AC. Behavioral and Neurophysiologic Response to Therapy for Chronic Aphasia. *Arch Phys Med Rehabil*. déc 2009;90(12):2026-33.
32. Breier JI, Juranek J, Papanicolaou AC. Changes in maps of language function and the integrity of the arcuate fasciculus after therapy for chronic aphasia. *Neurocase*. déc 2011;17(6):506-17.
33. Lucchese G, Pulvermüller F, Stahl B, Dreyer FR, Mohr B. Therapy-Induced Neuroplasticity of Language in Chronic Post Stroke Aphasia: A Mismatch Negativity Study of (A)Grammatical and Meaningful/less Mini-Constructions. *Front Hum Neurosci* [Internet]. 2017 [cité 4 avr 2020];10. Disponible sur: <https://www.frontiersin.org/articles/10.3389/fnhum.2016.00669/full>
34. Meinzer M, Paul I, Wienbruch C, Djundja D, Rockstroh B. Electromagnetic brain activity in higher frequency bands during automatic word processing indicates recovery of function in aphasia. *Eur J Phys Rehabil Med*. sept 2009;45(3):369-78.
35. Meinzer M, Elbert T, Wienbruch C, Djundja D, Barthel G, Rockstroh B. Intensive language training enhances brain plasticity in chronic aphasia. *BMC Biol*. 25 août 2004;2(1):20.
36. Mohr B, MacGregor LJ, Difrancesco S, Harrington K, Pulvermüller F, Shtyrov Y. Hemispheric contributions to language reorganisation: An MEG study of neuroplasticity in chronic post stroke aphasia. *Neuropsychologia*. 1 déc 2016;93:413-24.
37. Pulvermüller F, Hauk O, Zohsel K, Neininger B, Mohr B. Therapy-related reorganization of language in both hemispheres of patients with chronic aphasia. *NeuroImage*. 1 nov 2005;28(2):481-9.
38. Wilson KR, O'Rourke H, Wozniak LA, Kostopoulos E, Marchand Y, Newman AJ. Changes in N400 topography following intensive speech language therapy for individuals with aphasia. *Brain Lang*. 1 nov 2012;123(2):94-103.

39. Sarasso S, Santhanam P, Määttä S, Poryiazova R, Ferrarelli F, Tononi G, et al. Non-fluent aphasia and neural reorganization after speech therapy: insights from human sleep electrophysiology and functional magnetic resonance imaging. *Arch Ital Biol.* sept 2010;148(3):271-8.
40. Sarasso S, Määttä S, Ferrarelli F, Poryiazova R, Tononi G, Small SL. Plastic Changes Following Imitation-Based Speech and Language Therapy for Aphasia: A High-Density Sleep EEG Study. *Neurorehabil Neural Repair.* 1 févr 2014;28(2):129-38.
41. Radman N, Spierer L, Laganaro M, Annoni J-M, Colombo F. Language specificity of lexical-phonological therapy in bilingual aphasia: A clinical and electrophysiological study. *Neuropsychol Rehabil.* août 2016;26(4):532-57.
42. Laganaro M, Morand S, Schwitter V, Zimmermann C, Schnider A. Normalisation and increase of abnormal ERP patterns accompany recovery from aphasia in the post-acute stage. *Neuropsychologia.* juill 2008;46(8):2265-73.
43. Iyer KK, Angwin AJ, Van Hees S, McMahon KL, Breakspear M, Copland DA. Alterations to dual stream connectivity predicts response to aphasia therapy following stroke. *Cortex.* 1 avr 2020;125:30-43.
44. Cornelissen K, Laine M, Tarkiainen A, Järvensivu T, Martin N, Salmelin R. Adult Brain Plasticity Elicited by Anomia Treatment. *J Cogn Neurosci.* 4/1/2003 2003;15(3):444-61.
45. Aerts A, Batens K, Santens P, Van Mierlo P, Huysman E, Hartsuiker R, et al. Aphasia therapy early after stroke: behavioural and neurophysiological changes in the acute and post-acute phases. *Aphasiology.* 3 juill 2015;29(7):845-71.
46. Breier JI, Randle S, Maher LynnM, Papanicolaou AndrewC. Changes in maps of language activity activation following melodic intonation therapy using magnetoencephalography: Two case studies. *J Clin Exp Neuropsychol.* mars 2010;32(3):309-14.
47. Stojanovic B, Djurasic L, Jovic S, Paspalj D. EEG study of visual reactivity in aphasic patients. *Acta Chir Jugosl.* 2013;60(3):45-56.
48. Aerts A, van Mierlo P, Hartsuiker RJ, Hallez H, Santens P, De Letter M. Neurophysiological investigation of phonological input: aging effects and development of normative data. *Brain Lang.* juin 2013;125(3):253-63.
49. Barwood CHS, Murdoch BE, Whelan B-M, O'Sullivan JD, Wong A, D. Lloyd, et al. Longitudinal modulation of N400 in chronic non-fluent aphasia using low-frequency rTMS: A randomised placebo controlled trial. *Aphasiology.* 2012;26(1):103-24.
50. Barwood CHS, Murdoch BE, Whelan B-M, Lloyd D, Riek S, O'Sullivan JD, et al. Modulation of N400 in chronic non-fluent aphasia using low frequency Repetitive Transcranial Magnetic Stimulation (rTMS). *Brain Lang.* 1 mars 2011;116(3):125-35.
51. Wu D, Wang J, Yuan Y. Effects of transcranial direct current stimulation on naming and cortical excitability in stroke patients with aphasia. *Neurosci Lett.* 4 mars 2015;589:115-20.

52. Fedorov A, Chibisova Y, Szymaszek A, Alexandrov M, Gall C, Sabel BA. Non-invasive alternating current stimulation induces recovery from stroke. *Restor Neurol Neurosci*. 2010;28(6):825-33.
53. Maquet P. The Role of Sleep in Learning and Memory. *Science*. 2 nov 2001;294(5544):1048-52.
54. Laganaro M, Morand S, Schwitter V, Zimmermann C, Camen C, Schnider A. Electrophysiological correlates of different anomic patterns in comparison with normal word production. *Cortex*. 1 juin 2009;45(6):697-707.
55. Laganaro M, Python G, Toepel U. Dynamics of phonological–phonetic encoding in word production: Evidence from diverging ERPs between stroke patients and controls. *Brain Lang*. 1 août 2013;126(2):123-32.

Flow Diagram

(adapted from PRISMA 2009)



III. Perspectives

Les techniques d'imagerie temporelle telles que l'EEG et la MEG sont largement utilisées dans le cadre de pathologies telles que l'épilepsie. Elles sont beaucoup moins présentes dans la littérature concernant l'aphasiologie, où l'imagerie la plus couramment utilisée demeure l'IRMf. Pourtant, l'IRMf ne permet pas la précision temporelle que fournissent l'EEG ou la MEG.

La revue de littérature est un exercice consistant à synthétiser l'état actuel des connaissances accumulées sur un sujet particulier et d'en comparer les résultats. La revue présentée dans ce mémoire, à propos des modifications électrophysiologiques dans le suivi longitudinal de patients aphasiques à la suite d'un AVC, a permis de montrer l'intérêt de l'imagerie temporelle (EEG/MEG) dans le suivi de ces patients et l'évaluation de protocoles, à la fois par l'étude d'enregistrements en continu mais aussi en potentiels évoqués reliés à des événements (ERP/EMF). Bien qu'ayant un principal intérêt de recherche, ce mémoire illustre également des possibilités au niveau clinique.

1. Perspectives cliniques

Certaines études longitudinales non interventionnelles recensées se sont intéressées à des biomarqueurs électrophysiologiques prédictifs d'une bonne récupération dans le cadre de l'EEG en continu, tels que les rythmes alpha (Jabbari et al., 1979; Nicolo et al., 2015), mais également les éléments prédictifs d'une moins bonne récupération tel que la décréue du rythme de l'activité cérébrale, avec notamment l'apparition de rythmes thêta dans des zones périlésionnelles (Hensel et al., 2004; Jabbari et al., 1979; Nicolo et al., 2015; Szeliés et al., 2002). De leur côté, les études en potentiels évoqués ont notamment révélé la présence de composantes prédictives d'une bonne récupération comme une petite N100 dans les régions frontales ipsilésionnelles (Becker & Reinvang, 2007) ou la présence de la P300 dès la phase subaiguë (Nolfe et al., 2006). Certaines études relèvent également comme facteur de bonne récupération l'augmentation d'amplitude de certaines composantes comme la MMN (Ilvonen Titta-Maria et al., 2003) ou la P300 (Becker & Reinvang, 2007; Cobianchi, & Giaquinto, 2000; Nolfe et al., 2006). Ces biomarqueurs pourraient ainsi constituer des prédictifs de la récupération attendue dès la phase subaiguë de l'aphasie. Bien qu'appartenant toujours

actuellement au cadre de la recherche dans l'aphasie, de telles informations pourraient constituer un complément pertinent aux bilans de suivi.

2. Perspectives de recherche

Cette revue est en premier lieu une mise à jour pertinente pour la recherche en aphasiologie. De manière globale, elle nous permet d'identifier l'ensemble des possibilités qu'offrent l'EEG et la MEG pour évaluer des protocoles de réhabilitation, en mettant en lien les modifications électrophysiologiques avec les modifications comportementales.

Le laboratoire Handicap Activité Cognition Santé (U1219 Inserm) rattaché à l'Université de Bordeaux a récemment fait l'acquisition d'un EEG 128 voies, qui devait permettre cette année d'évaluer par le biais d'une étude pilote l'efficacité d'un protocole rTMS associé à de la rééducation orthophonique. Cette étude devait être basée sur une analyse ERP à partir d'une tâche de dénomination. Le contexte pandémique actuel (confinement de la population de mars à mai 2020) n'a pas encore permis l'aboutissement de cette étude. Ainsi, cette revue de la littérature a eu pour but de constituer un socle théorique notamment pour cette future recherche, qui pourra faire l'objet d'un autre mémoire.

Quatre articles ont été recensés sur l'évaluation par EEG de différents protocoles de rTMS (Barwood et al., 2011, 2012; Chantsoulis et al., 2016; Dammekens et al., 2014). L'un d'entre eux (Chantsoulis et al., 2016) s'est concentré sur le cas clinique particulier d'une aphasie croisée. Ces chercheurs ont retrouvé une diminution de la composante P200 lors d'une tâche de go/no go dans le lobe temporal droit après un protocole de stimulation excitatrice de ce même lobe. Aussi, bien que les résultats puissent être intéressants, notamment à propos de l'impact de la rTMS sur une aphasie consécutive à un AVC droit, ils ne permettent pas de conjecture sur d'éventuels biomarqueurs généraux de bonne réponse à ce type de traitement. Une seconde étude (Dammekens et al., 2014) a observé les modifications au niveau de l'activité électrique en continu, auprès d'un cas clinique. Cette étude illustre l'augmentation de la connectivité interhémisphérique démontrée par une synchronisation des rythmes bêta et thêta, et une diminution des rythmes bêta dans l'hémisphère droit (vers une normalisation de ces rythmes) après stimulation excitatrice de l'hémisphère gauche par rTMS à haute fréquence. Les résultats de cette étude démontrent l'impact positif de ce type de stimulation sur les connexions interhémisphériques, mais ne met en évidence aucun biomarqueur. Enfin les deux études en rTMS

de Barwood et al. (Barwood et al., 2011, 2012), contrôlées par un groupe de patients non stimulés (sham), observent des modifications au niveau des tracés de potentiels évoqués relatifs en tâche de jugement sémantique à partir d'un EEG 32 voies. Ces deux recherches ont retrouvé une modification au niveau de l'amplitude de la N400 pouvant être corrélée avec une amélioration des compétences langagières des patients. Néanmoins, ces deux études en ERP proposent uniquement une analyse au niveau du champ électrique global des tracés et pas d'analyse topographique, probablement du fait de la faible résolution spatiale possible avec un EEG 32 voies.

Bien que les effets positifs de la rTMS, à la fois inhibitrice (rTMS de basse fréquence) au niveau du gyrus frontal inférieur droit, mais aussi excitatrice au niveau de l'aire de Broca (rTMS à haute fréquence), aient été démontrés dans plusieurs études (pour une revue voir Barrios 2019), aucun biomarqueur de bonne réponse à ce traitement n'a donc encore été mis à jour. La découverte de tels biomarqueurs permettrait notamment d'entrevoir les effets induits par cette stimulation non-invasive, mais aussi éventuellement de mieux comprendre pourquoi de telles techniques ne sont pas efficaces pour tous les patients.

L'intérêt d'une telle étude prend donc tout son sens face à cette lacune de la littérature, et nous nous attacherons dans la suite de ce mémoire à décrire un plan expérimental possible d'une telle étude, à la lumière de la revue de littérature qui vient d'être développée.

Les patients recrutés devront être à la phase chronique de leur AVC (> 6 mois), afin d'éviter au maximum les variations électrophysiologiques dues à la récupération spontanée. En effet, deux études longitudinales non interventionnelles à la phase chronique de l'aphasie n'ont pas reporté de changements durant cette phase en enregistrant l'activité électrique en continu (Hensel et al., 2004; Jabbari et al., 1979). D'autre part, quatre autres essais cliniques (Barbancho et al., 2015; Barwood et al., 2011, 2012; Breier et al., 2007) ont utilisé dans leurs études des groupes de patients contrôle : stimulation sham dans le cadre des NIBS (placebo de stimulation), placebo pour l'essai médicamenteux et sans stimulation langagière pour l'étude sur une méthode de rééducation. Parmi ces études, aucune modification électrophysiologique n'est à relever, ni dans les groupes non stimulés pour les deux études de Barwood (Barwood et al., 2011, 2012) au niveau de la puissance de champ global, ni dans l'étude de Breier et al. (Breier et al., 2007). Cependant, l'étude de Barbancho (Barbancho et al., 2015) retrouve des modifications des tracés ERP chez les patients à un stade chronique après la prise d'un placebo (sans rééducation

associée). L'équipe a observé une diminution de la N400 et de la P100, qui suivent les modifications obtenues avec le médicament testé (la Mémantine), bien que les différences observées soient significativement moins importantes dans le groupe placebo que dans le groupe traité.

Aussi bien que la plupart des études convergent vers une stabilité électrophysiologique de la phase chronique de l'aphasie, il semblera pertinent de proposer une stimulation sham de rTMS afin de s'assurer que les modifications soient dues au protocole et non à des modifications spontanées. De plus, il pourra être judicieux de proposer plusieurs lignes de base pour l'enregistrement de l'EEG afin de vérifier la stabilité pré-traitement.

L'équipe de Barwood et al (Barwood et al., 2011, 2012) retrouve une augmentation de l'amplitude de la N400, mais seulement deux mois après la stimulation par rTMS, corrélée avec une amélioration des compétences comportementales. Bien que les progrès langagiers aient pu être observables dès la fin de la stimulation, les modifications électrophysiologiques n'étaient pas visibles directement à la suite du protocole, mais seulement plusieurs semaines plus tard. Aussi, Barwood et al. (Barwood et al., 2011, 2012) discutent d'une possible réorganisation à plus long terme induite par la rTMS. Il semblera alors pertinent dans le design proposé d'évaluer les patients à distance de la stimulation, à la fois au niveau langagier mais aussi électrophysiologique.

Enfin, ces mêmes études (Barwood et al., 2011, 2012) ne proposaient pas de rééducation orthophonique associée à la stimulation. Bien que la rTMS ait démontré des effets sans stimulation orthophonique (pour une revue voir Barrios, 2019), il semble que l'orthophonie pourrait potentialiser les effets d'une telle stimulation. Aussi, une rééducation orthophonique ciblée et intensive sera intégrée dans le protocole proposé. Afin d'homogénéiser un maximum la prise en charge, cette rééducation pourra se baser sur des protocoles de rééducation, notamment des protocoles récents et centrés sur l'anomie comme la SFA/PCA (Semantic Feature Analysis / Phonological Component Analysis). Ces méthodes lexicales sont basées sur de la dénomination d'images aidée par indiçage sémantique pour la SFA et phonologique pour la PCA. Ainsi, le groupe sham de rTMS bénéficiera tout de même de rééducation orthophonique, n'entraînant ainsi pas de perte de chance pour les patients de ce groupe. Les deux groupes rTMS et sham de rTMS seront aveugles quant à leur stimulation effective ou non.

Une proposition de plan expérimental de cette étude est illustrée par le schéma ci-dessous (Figure 4).

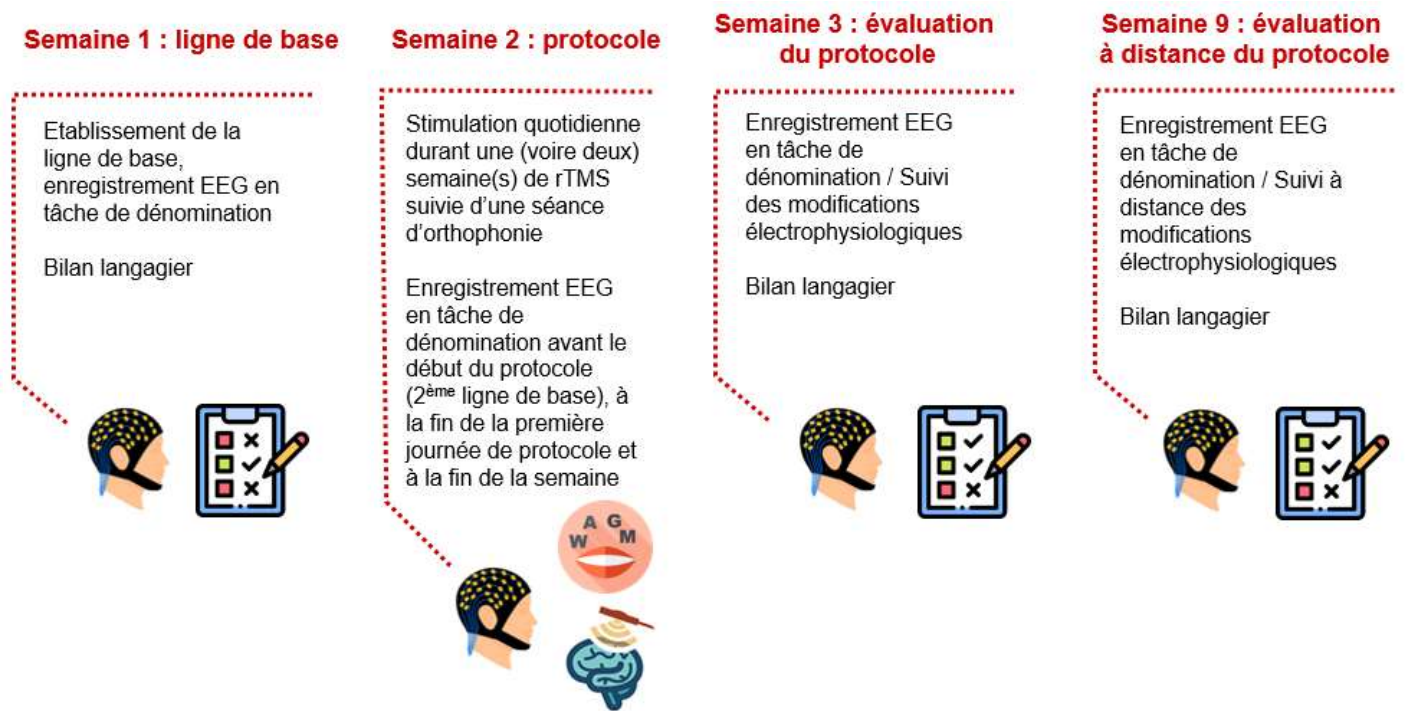


Figure 4 : proposition de plan expérimental pour une étude sur l'évaluation de la rTMS par le biais d'analyses ERP

Les enregistrements EEG pourront être réalisés en tâche de dénomination et de jugement sémantique afin d'en extraire des potentiels évoqués et d'obtenir des données à la fois en production et en compréhension. Grâce à la haute résolution de l'EEG 128-voies dont nous disposons, il sera alors possible de tenter de corrélérer modifications comportementales et changements électrophysiologiques, à la fois sur les formes d'ondes, mais également à partir de modifications topographiques observées.

IV. Conclusion

Ce travail de recherche de littérature et d'élaboration d'un plan expérimental ancré dans les connaissances scientifiques actuelles avait pour objectif de mettre en lumière les modifications électrophysiologiques dans le cadre de l'aphasie post-AVC, observées par le biais de l'imagerie temporelle (EEG/MEG), à la fois en enregistrant l'activité cérébrale en continu mais aussi par le biais de potentiels évoqués en réponse à des tâches précises (ERP/EMF). Par cette revue, nous entrevoyons le champ des possibles de l'imagerie temporelle : à la fois l'opportunité de fournir des biomarqueurs de pronostic de récupération de l'aphasie dès la phase subaiguë, mais également d'évaluer l'impact des protocoles de recherche clinique au niveau de la réorganisation cérébrale.

Le fait qu'un EEG comportant 128 électrodes soit désormais disponible et accessible, notamment aux élèves en orthophonie du centre de formation universitaire de Bordeaux, est une chance, et permettra de futures recherches dans le cadre de la rééducation orthophonique de l'aphasie.

Bibliographie

- Barbancho, M. A., Berthier, M. L., Navas-Sánchez, P., Dávila, G., Green-Heredia, C., García-Alberca, J. M., Ruiz-Cruces, R., López-González, M. V., Dawid-Milner, M. S., Pulvermüller, F., & Lara, J. P. (2015). Bilateral brain reorganization with memantine and constraint-induced aphasia therapy in chronic post-stroke aphasia : An ERP study. *Brain and Language, 145-146*, 1-10. <https://doi.org/10.1016/j.bandl.2015.04.003>
- Barrios, C. (2019). *Intérêt clinique de la stimulation magnétique transcrânienne répétitive (rTMS) auprès de patients aphasiques : Revue de la littérature et pratique de routine*. Mémoire d'orthophonie.
- Barwood, C. H. S., Murdoch, B. E., Whelan, B.-M., Lloyd, D., Riek, S., O'Sullivan, J. D., Coulthard, A., & Wong, A. (2011). Modulation of N400 in chronic non-fluent aphasia using low frequency Repetitive Transcranial Magnetic Stimulation (rTMS). *Brain and Language, 116(3)*, 125-135. <https://doi.org/10.1016/j.bandl.2010.07.004>
- Barwood, C. H. S., Murdoch, B. E., Whelan, B.-M., O'Sullivan, J. D., Wong, A., D. Lloyd, S. Riek, & A. Coulthard. (2012). Longitudinal modulation of N400 in chronic non-fluent aphasia using low-frequency rTMS : A randomised placebo controlled trial. *Aphasiology, 26(1)*, 103-124. Scopus. <https://doi.org/10.1080/02687038.2011.617812>
- Becker, F., & Reinvang, I. (2007). Event-related potentials indicate bi-hemispherical changes in speech sound processing during aphasia rehabilitation. *Journal of Rehabilitation Medicine, 39(8)*, 658-661. <https://doi.org/10.2340/16501977-0112>
- Berthier, M. L., Green, C., Higuera, C., Fernández, I., Hinojosa, J., & Martín, M. C. (2006). A randomized, placebo-controlled study of donepezil in poststroke aphasia. *Neurology, 67(9)*, 1687-1689. <https://doi.org/10.1212/01.wnl.0000242626.69666.e2>

- Brady, M. C., Kelly, H., Godwin, J., Enderby, P., & Campbell, P. (2016). Speech and language therapy for aphasia following stroke. *Cochrane Database of Systematic Reviews*, 6. <https://doi.org/10.1002/14651858.CD000425.pub4>
- Breier, J. I., Maher, L. M., Schmadeke, S., Hasan, K. M., & Papanicolaou, A. C. (2007). Changes in Language-specific Brain Activation after Therapy for Aphasia using Magnetoencephalography: A Case Study. *Neurocase*, 13(3), 169-177. <https://doi.org/10.1080/13554790701448200>
- Brin-Henry, F., Courrier, C., Lederle, E., & Massy, V. (2011). *Dictionnaire d'orthophonie, troisième édition*.
- Brust, J. C., Shafer, S. Q., Richter, R. W., & Bruun, B. (1976). Aphasia in acute stroke. *Stroke*, 7(2), 167-174. <https://doi.org/10.1161/01.STR.7.2.167>
- Carrera, E., & Tononi, G. (2014). Diaschisis: Past, present, future. *Brain*, 137(9), 2408-2422. <https://doi.org/10.1093/brain/awu101>
- Chantsoulis, M., Półrola, P., Góral-Półrola, J., Herman-Sucharska, I., Kropotov, J. D., & Pačalska, M. (2016). Application of functional neuromarkers for constructing protocols of neurotherapy and monitoring the success of treatment in chronic crossed transcortical sensory aphasia: A case study. *Acta Neuropsychologica*, 14(4), 389-400. Scopus. <https://doi.org/10.5604/17307503.1230927>
- Cobianchi, A., & Giaquinto, S. (2000). Can we exploit event-related potentials for retraining language after stroke? *Disability and Rehabilitation*, 22(9), 427-434. <https://doi.org/10.1080/096382800406059>
- Dammekens, E., Vanneste, S., Ost, J., & De Ridder, D. (2014). Neural correlates of high frequency repetitive transcranial magnetic stimulation improvement in post-stroke non-fluent aphasia: A case study. *Neurocase*, 20(1), 1-9. <https://doi.org/10.1080/13554794.2012.713493>

- Demeurisse, G., Demol, O., Derouck, M., de Beuckelaer, R., Coekaerts, M. J., & Capon, A. (1980). Quantitative study of the rate of recovery from aphasia due to ischemic stroke. *Stroke*, *11*(5), 455-458. <https://doi.org/10.1161/01.STR.11.5.455>
- Garnero, L. (2001). *Les bases physiques et physiologiques de la magnétoencéphalographie et de l'électroencéphalographie*. Laboratoire de Neurosciences Cognitives et Imagerie Cérébrale CNRS-UPR640-LENA. <http://www.labos.upmc.fr/center-meg/media/ecp2001/Meg11.pdf>
- Geranmayeh, F., Brownsett, S. L. E., & Wise, R. J. S. (2014). Task-induced brain activity in aphasic stroke patients: What is driving recovery? *Brain*, *137*(10), 2632-2648. <https://doi.org/10.1093/brain/awu163>
- Glize, B., Guehl, D., Dehail, P., & Sibon, I. (2014). Stimulation magnétique transcrânienne et accident vasculaire cérébral. *MISE AU POINT*, *4*.
- Hallett, (Prénom). (2016). Chapter 6—Neurophysiologic studies of functional neurologic disorders. In M. Hallett, J. Stone, & A. Carson (Éds.), *Handbook of Clinical Neurology* (Vol. 139, p. 61-71). Elsevier. <https://doi.org/10.1016/B978-0-12-801772-2.00006-0>
- Hartwigsen, G., & Saur, D. (2019). Neuroimaging of stroke recovery from aphasia – Insights into plasticity of the human language network. *NeuroImage*, *190*, 14-31. <https://doi.org/10.1016/j.neuroimage.2017.11.056>
- Hensel, S., Rockstroh, B., Berg, P., Elbert, T., & Schönle, P. W. (2004). Left-hemispheric abnormal EEG activity in relation to impairment and recovery in aphasic patients : EEG-slow-wave activity in aphasia. *Psychophysiology*, *41*(3), 394-400. <https://doi.org/10.1111/j.1469-8986.2004.00164x>
- Herrmann, C. S., Rach, S., Vosskuhl, J., & Strüber, D. (2014). Time–Frequency Analysis of Event-Related Potentials: A Brief Tutorial. *Brain Topography*, *27*(4), 438-450. <https://doi.org/10.1007/s10548-013-0327-5>

- Hillis, A. E., Kleinman, J. T., Newhart, M., Heidler-Gary, J., Gottesman, R., Barker, P. B., Aldrich, E., Llinas, R., Wityk, R., & Chaudhry, P. (2006). Restoring Cerebral Blood Flow Reveals Neural Regions Critical for Naming. *Journal of Neuroscience*, 26(31), 8069-8073. <https://doi.org/10.1523/JNEUROSCI.2088-06.2006>
- Ilvonen Titta-Maria, Kujala Teija, Kiesiläinen Anita, Salonen Oili, Kozou Hesham, Pekkonen Eero, Roine Risto O., Kaste Markku, & Näätänen Risto. (2003). Auditory Discrimination After Left-Hemisphere Stroke. *Stroke*, 34(7), 1746-1751. <https://doi.org/10.1161/01.STR.0000078836.26328.3B>
- Jabbari, B., Maulsby, R. L., Holtzapple, P. A., & Marshall, N. K. (1979). Prognostic Value of EEG in Acute Vascular Aphasia : A Long Term Clinical-EEG Study of 53 Patients. *Clinical Electroencephalography*, 10(4), 190-197. <https://doi.org/10.1177/155005947901000403>
- Jasper, H. (1958). Report of the committee on methods of clinical examination in electroencephalography : 1957. *Electroencephalography and Clinical Neurophysiology*, 10(2), 370-375. [https://doi.org/10.1016/0013-4694\(58\)90053-1](https://doi.org/10.1016/0013-4694(58)90053-1)
- Karbe, H., Thiel, A., Weber-Luxenburger, G., Herholz, K., Kessler, J., & Heiss, W.-D. (1998). Brain Plasticity in Poststroke Aphasia : What Is the Contribution of the Right Hemisphere? *Brain and Language*, 64(2), 215-230. <https://doi.org/10.1006/brln.1998.1961>
- Laganaro, M. (2014). ERP topographic analyses from concept to articulation in word production studies. *Frontiers in Psychology*, 5, 493. <https://doi.org/10.3389/fpsyg.2014.00493>
- Laganaro, M. (2017). Inter-study and inter-Individual Consistency and Variability of EEG/ERP Microstate Sequences in Referential Word Production. *Brain Topography*, 30(6), 785-796. <https://doi.org/10.1007/s10548-017-0580-0>

- Laganaro, M., Valente, A., & Perret, C. (2012). Time course of word production in fast and slow speakers : A high density ERP topographic study. *NeuroImage*, 59(4), 3881-3888. <https://doi.org/10.1016/j.neuroimage.2011.10.082>
- Lau, E. F., Phillips, C., & Poeppel, D. (2008). A cortical network for semantics : (De)constructing the N400. *Nature Reviews Neuroscience*, 9(12), 920-933. <https://doi.org/10.1038/nrn2532>
- Luauté, J.-P., & Luauté, J. (2005). La diaschisis de Von Monakow. Historique et devenir d'une découverte. *Annales Médico-psychologiques, revue psychiatrique*, 163(3), 329-333. <https://doi.org/10.1016/j.amp.2005.03.031>
- Meinzer, M., Elbert, T., Wienbruch, C., Djundja, D., Barthel, G., & Rockstroh, B. (2004). Intensive language training enhances brain plasticity in chronic aphasia. *BMC Biology*, 2(1), 20. <https://doi.org/10.1186/1741-7007-2-20>
- Näätänen, R., Gaillard, A. W. K., & Mäntysalo, S. (1978). Early selective-attention effect on evoked potential reinterpreted. *Acta Psychologica*, 42(4), 313-329. [https://doi.org/10.1016/0001-6918\(78\)90006-9](https://doi.org/10.1016/0001-6918(78)90006-9)
- Nicolo, P., Rizk, S., Magnin, C., Pietro, M. D., Schnider, A., & Guggisberg, A. G. (2015). Coherent neural oscillations predict future motor and language improvement after stroke. *Brain*, 138(10), 3048-3060. <https://doi.org/10.1093/brain/awv200>
- Nolfe, G., Cobiauchi, A., Mossuto-Agatiello, L., & Giaquinto, S. (2006). The role of P300 in the recovery of post-stroke global aphasia. *European Journal of Neurology*, 13(4), 377-384. <https://doi.org/10.1111/j.1468-1331.2006.01237.x>
- Pedersen, P. M., Jørgensen, H. S., Nakayama, H., Raaschou, H. O., & Olsen, T. S. (1995). Aphasia in acute stroke : Incidence, determinants, and recovery. *Annals of Neurology*, 38(4), 659-666. <https://doi.org/10.1002/ana.410380416>

- Pérez-González, D., & Malmierca, M. S. (2014). Adaptation in the auditory system: An overview. *Frontiers in Integrative Neuroscience*, 8. <https://doi.org/10.3389/fnint.2014.00019>
- Pfefferbaum, A., Ford, J. M., Weller, B. J., & Kopell, B. S. (1985). ERPs to response production and inhibition. *Electroencephalography and Clinical Neurophysiology*, 60(5), 423-434. [https://doi.org/10.1016/0013-4694\(85\)91017-X](https://doi.org/10.1016/0013-4694(85)91017-X)
- Picton, T. W., & Hillyaro, S. A. (1974). *HUMAN AUDITORY EVOKED POTENTIALS. I: EVALUATION OF COMPONENTS I*. 12.
- Robey Randall R. (1998). A Meta-Analysis of Clinical Outcomes in the Treatment of Aphasia. *Journal of Speech, Language, and Hearing Research*, 41(1), 172-187. <https://doi.org/10.1044/jslhr.4101.172>
- Stephens, M. (2017). The Effectiveness of Speech and Language Therapy for Poststroke Aphasia. *AJN The American Journal of Nursing*, 117(11), 19. <https://doi.org/10.1097/01.NAJ.0000526741.00314.d9>
- Sutton, S., Braren, M., Zubin, J., & John, E. R. (1965). Evoked-Potential Correlates of Stimulus Uncertainty. *Science*, 150(3700), 1187-1188. <https://doi.org/10.1126/science.150.3700.1187>
- Szelies, B., Mielke, R., Kessler, J., & Heiss, W.-D. (2002). Prognostic relevance of quantitative topographical EEG in patients with poststroke aphasia. *Brain and Language*, 82(1), 87-94. [https://doi.org/10.1016/S0093-934X\(02\)00004-4](https://doi.org/10.1016/S0093-934X(02)00004-4)
- Vieth, J. B., Kober, H., & Grummich, P. (1996). Sources of spontaneous slow waves associated with brain lesions, localized by using the MEG. *Brain Topography*, 8(3), 215-221. <https://doi.org/10.1007/bf01184772>
- Vion-Dury, J., & Blanquet, F. (2008). *Pratique de l'EEG - Bases neurophysiologiques—Principes d'interprétation et de prescription*. Elsevier Masson.

- Vrba, J., & Robinson, S. E. (2001). Signal Processing in Magnetoencephalography. *Methods*, 25(2), 249-271. <https://doi.org/10.1006/meth.2001.1238>
- Watila, M. m., & Balarabe, S. a. (2015). Factors predicting post-stroke aphasia recovery. *Journal of the Neurological Sciences*, 352(1), 12-18. <https://doi.org/10.1016/j.jns.2015.03.020>
- Woldorff, M. G., Fox, P. T., Matzke, M., Lancaster, J. L., Veeraswamy, S., Zamarripa, F., Seabolt, M., Glass, T., Gao, J. H., Martin, C. C., & Jerabek, P. (1997). Retinotopic organization of early visual spatial attention effects as revealed by PET and ERPs. *Human Brain Mapping*, 5(4), 280-286. [https://doi.org/10.1002/\(SICI\)1097-0193\(1997\)5:4<280::AID-HBM13>3.0.CO;2-I](https://doi.org/10.1002/(SICI)1097-0193(1997)5:4<280::AID-HBM13>3.0.CO;2-I)
- Woodhead, Z. V., Crinion, J., Teki, S., Penny, W., Price, C. J., & Leff, A. P. (2017). Auditory training changes temporal lobe connectivity in ‘Wernicke’s aphasia’: A randomised trial. *Journal of Neurology, Neurosurgery & Psychiatry*, 88(7), 586-594. <https://doi.org/10.1136/jnnp-2016-314621>

Titre : Modifications électrophysiologiques dans le suivi longitudinal de patients aphasiques : une revue de la littérature

Résumé : Deux types de mesures peuvent être enregistrées par la magnétoencéphalographie et l'électroencéphalographie : les mesures en continu, principalement enregistrées pendant le repos ou le sommeil, ou les mesures de potentiels/champs magnétiques évoqués (ERPs/EMFs), liées à des événements. Les ERPs/EMFs peuvent être analysés par l'étude des formes d'onde, du temps-fréquence ou de la topographie. Cette revue résume les études longitudinales de la récupération de l'aphasie post-AVC étudiée par imagerie temporelle, en continue ou liée à un événement. Nous avons recherché dans MEDLINE via PubMed et Scopus le 26 mars 2020 des articles en anglais publiés de 1950 à 2020. Les études admissibles concernaient l'exploration de l'aphasie post-AVC par EEG ou MEG en repos ou pendant différentes tâches. Nous avons inclus 38 études : 11 études non interventionnelles suivant la récupération (176 patients) et 27 essais cliniques de médicaments (48 patients), de méthodes de réadaptation spécifiques (178 patients) ou de neuromodulation (122 patients). Les études non interventionnelles ont établi une corrélation entre la récupération spontanée et certains biomarqueurs, comme le lien entre une mauvaise récupération et des ondes lentes au repos. Les essais cliniques tentent de lier améliorations comportementales et mesures électrophysiologiques : plusieurs études se sont concentrées sur la N400 en tant que biomarqueur des effets positifs induits par la thérapie. Les possibilités analytiques de l'imagerie temporelle sont intéressantes dans le suivi de la récupération spontanée ou induite par la thérapie dans le cadre de l'aphasie post-AVC, et pourtant peu exploitées. Le peu d'études via imagerie à haute résolution et le manque de connaissances sur l'analyse topographique ou de temps-fréquence sont probablement les principales raisons de leur faible utilisation. Quant à l'identification des biomarqueurs des effets induits par la thérapie, elle semble plus fiable en analyse ERP/EMF qu'avec l'EEG en continu.

Mots clés : aphasie, accident vasculaire cérébral, électroencéphalographie, magnétoencéphalographie, potentiel évoqué relatif, champ magnétique évoqué

Title: Electrophysiological modifications in post-stroke aphasia: a systematic review

Abstract: Two principal types of measures can be recorded by magnetoencephalography and electroencephalography: continuous, mostly recorded during resting or sleep, or event-related potential/evoked magnetic field (ERP/EMF) measures, that involves a specific and repetitive task. ERPs/EMFs can be analyzed by waveforms, time-frequency, or topography analysis. This systematic review aimed to summarize longitudinal studies about the recovery of post-stroke aphasia studied by temporal imagery, both continuous and event-related. We searched MEDLINE via PubMed and Scopus

on March 26, 2020, for English articles published from 1950 to 2020. Eligible studies involved post-stroke aphasia exploration by EEG or MEG during resting state or different tasks. We included reports of 38 studies: 11 were non-interventional studies following recovery (176 patients) and 27 were clinical trials with drugs (48 patients), specific rehabilitation methods (178 patients), or neuromodulation (122 patients). Non-interventional studies correlated spontaneous recovery with biomarkers, like the link between poor recovery and slow-wave activity. Clinical trials wanted to correlate behavioral improvements and electrophysiological measures: lots of studies focused on the N400 component as a good biomarker of therapy-induced effects. To conclude, the contribution of EEG and MEG measures is interesting for the following of spontaneous or therapy-induced effects recovery in post-stroke aphasia, but poorly exploited. The few number of high-resolution imagery studies and the lack of knowledge about topographical or time-frequency analysis are probably the main reasons why they are little used. As for, the identification of biomarkers of therapy-induced effects, it seems more reliable with ERP/EMF than through continuous EEG.

Keywords: aphasia, stroke, electroencephalography, magnetoencephalography, event-related potential, evoked magnetic field

Nombre de pages : 76. Nombre de références : 81

Unités de recherche

Handicap Activity Cognition Santé (U1219 Inserm), Université de Bordeaux