Neurophysiologie Clinique/Clinical Neurophysiology (2017) 47, 35—46

Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com/en

ORIGINAL ARTICLE/ARTICLE ORIGINAL

# Easy methods to make the neuronavigated targeting of DLPFC accurate and routinely accessible for rTMS

## *Méthodes faciles pour rendre le ciblage neuronavigué du cortex préfrontal dorsolatéral précis et couramment accessible pour la pratique de la rTMS*

**Benjamin Pommier**[a,b,c,*], **François Vassal**[a,b,c], **Claire Boutet**[d], **Sophie Jeannin**[e], **Roland Peyron**[b,c,e], **Isabelle Faillenot**[b,c,e]

[a] *Service de neurochirurgie, hôpital Nord, 42055 Saint-Étienne cedex 2, France*
[b] *Inserm U1028, Central Integration of Pain Unit, Lyon Neuroscience Research Center, 69000 Lyon, France*
[c] *Intégration centrale de la douleur, université Jean-Monnet, 42023 Saint-Étienne, France*
[d] *Service de radiologie centrale, hôpital Nord, 42055 Saint-Etienne cedex 2, France*
[e] *Service de neurologie, hôpital Nord, 42055 Saint-Etienne cedex 2, France*

Received 30 August 2016; accepted 3 January 2017
Available online 13 February 2017

**KEYWORDS**
Depression;
DLPFC;
Neuronavigation;
Prefrontal Cortex;
rTMS

**Summary**
*Objectives.* — Dorsolateral prefrontal cortex (DLPFC) is the main stimulation target for rTMS treatment of depression. DLPFC is located in the middle frontal gyrus and corresponds to the lateral part of Brodmann Areas 9 and 46. Current methods to locate the DLPFC are either based on head landmarks that are inaccurate, or based on MRI-neuronavigation. Neuronavigated-methods are based either on standardized stereotactic coordinates translated to the individual patient or on brain landmarks requiring neuroanatomical skills for their identification. We developed a script automating the inclusion of already validated targets into patients' MRI, and also a new method to target DLPFC based on neuroanatomical landmarks. The present study aims to assess this new approach.
*Methods.* — Four targets were compared on 40 hemispheres: three previously validated methods (2 using superimposition of standardized targets on patient MRI and 1 using neuroanatomical landmarks) and the new one presented here. Resulting targets were presented in the individual space and in stereotactic spaces (MNI and Talairach) with the main objective being to reach the middle frontal gyrus and BA9/46. Target dispersion and distances between targets were assessed.

* Corresponding author. Service de neurochirurgie, hôpital Nord, 42055 Saint-Étienne cedex 2, France.
*E-mail address:* benjamin.pommier@neurochirurgie.fr (B. Pommier).

http://dx.doi.org/10.1016/j.neucli.2017.01.007

*Results.* — All targets were located in the middle frontal gyrus. Our proposed neuro-anatomical target was equivalent to or even better than the previously existing one if we consider the criteria of BA46 achievement and dispersion.
*Conclusion.* — The proposed neuroanatomical method and automation of the stereotactic method allow simple and reliable targeting of DLPFC for rTMS treatment.


**MOTS CLÉS**
Cortex préfrontal ;
CPFDL ;
Dépression ;
Neuronavigation ;
rTMS

**Résumé**
*Objectifs.* — Le cortex préfrontal dorsolatéral (CPFDL) est la cible principale dans le traitement de la dépression par rTMS. Il est situé au sein du gyrus frontal moyen et correspond à la partie latérale des aires de Brodmann 9 et 46. Les méthodes pour le localiser sont basées sur des repères externes (méthodes peu précises) ou des systèmes (complexes) de neuronavigation. Les méthodes de neuronavigation sont basées soit sur une translation de coordonnées stéréotaxiques standardisées vers l'IRM de l'individu, soit sur des repères anatomiques nécessitant des connaissances de neuroanatomie. Nous proposons, d'une part, un script permettant l'insertion automatique de cibles existantes dans l'IRM du patient, et d'autre part, une nouvelle méthode de ciblage par des repères anatomiques produisant une nouvelle cible que nous nous proposons d'évaluer.
*Méthodes.* — Quatre cibles ont été comparées sur 40 hémisphères en utilisant trois méthodes préalablement validées (2 utilisant des translations de cibles standardisées et une utilisant des repères anatomiques) et notre nouvelle méthode. Les cibles étaient déterminées dans l'espace de chaque patient et dans les espaces normalisés (MNI et Talairach). L'objectif était d'atteindre le gyrus frontal moyen et les aires de Brodmann 9 et 46. La dispersion des cibles et la distance les séparant étaient évaluées.
*Résultats.* — Toutes les cibles se trouvaient dans le gyrus frontal moyen. Notre nouvelle cible anatomique était équivalente, voire supérieure, dans l'atteinte de l'aire 46.
*Conclusion.* — Nous présentons ici une nouvelle méthode anatomique et une automatisation d'une méthode stéréotaxique de ciblage du CPFDL pour la rTMS.


## Introduction

The dorsolateral prefrontal cortex (DLPFC) is considered as an area of dysfunction in both depression and schizophrenia [8,11]. As such, it is an important target for repetitive Transcranial Magnetic Stimulation (rTMS) both in a research context and in clinical treatment. Stimulating this target has been proven to be effective in major refractory depression [20,21,25,26] and it can also be used to modulate pain [5,32].

DLPFC is a very large cortical area, involved in various functions such as working memory and executive functions. However, defining an anatomical location from a functional definition is neither easy nor accurate. During the past decade, rTMS targeting has been defined on the basis of the approximated ''5—7 cm-method'': DLPFC was targeted 5 to 7 cm anterior to the primary motor cortex [16,20,21,26,27]. Although this is a quick and inexpensive method, it has been criticized since less than half of targets may actually be in the DLPFC [1,13,28]. It has since been proven that therapeutic results depend on targeting [6,9,24], leading to other methods aimed at improving targeting being proposed, such as the ''10—20 method,'' based on the international EEG system. The optimal DLPFC position thus defined according to the electroencephalogram 10—20 system seems to correspond to a point between F3 and F5 [31] or between F3 and AF3 if considering the Modified Combinatorial Nomenclature [7]. It has also given rise to different methods to simplify this approach [3]. However, these approaches seem to be insufficient, especially when compared to neuronavigation methods. [7].

Theoretically, DLPFC corresponds to the lateral part of Brodmann Areas (BA) 9 and 46 [3,7,29,31]. It is located within the superior (SFG) and middle (MFG) frontal gyri [8,14,33]. Generally, DLPFC is considered as being located in the middle part of the MFG [1,14,23,24] with occasional extensions to the SFG and rare extensions to the inferior frontal gyrus (IFG) [17]. Moreover, recent data using functional connectivity in resting-state fMRI have suggested that BA46 appears to be the most functionally relevant area of the DLPFC to be targeted [9].

Neuronavigation is an essential tool allowing adequate placement of the rTMS coil and accurate targeting [2,6,12,18,19,30]. There are 3 main validated targets that can be integrated within the patient's MRI in different ways (Table 1, Fig. 1):

- targets defined in a standardized Talairach's space based on cytoarchitectonic findings [6,29];
- targets defined in a standardized Montreal Neurological Institute (MNI) space based on functional imaging [9];
- targets defined directly based on the individual patient's anatomy [23].