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rTms-Based Treatment for Primary Progressive Aphasia: A Critical Review

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Abstract

Primary progressive aphasia (PPA) is a neurodegenerative disease associated with gradual deterioration of language function. To date, no standard treatment is available for this condition. Behavioural treatments are the most studied option, offering positive results. Little is known about other pathways such as neuromodulatory techniques. This paper summarizes rTMS studies directed to PPA individuals and provides critical judgments on its implications for future clinical guidelines.

Keywords: Primary progressive aphasia; rTMS; Neuromodulatory techniques

Introduction

Primary progressive aphasia is a neurodegenerative condition associated with atrophy of the frontotemporal region of the left hemisphere. A gradual and isolated impairment of language function for at least 2 years is the core feature of this disease, while cognitive and behavioural skills remain relatively preserved at the initial stages [1,2]. Three clinical presentations have been recently recognized in the literature: semantic variant (svPPA); non-fluent variant (nfvPPA) and logopenic variant of PPA (lvPPA) [1]. Language profile and brain atrophy vary as a function of PPA subtype [3]. Semantic variant, characterized by impaired semantic knowledge, word finding, and confrontation naming, is associated with anterior temporal hypometabolism. Non-fluent variant, characterized by deficits in motor programming and complex syntax comprehension, is associated with left inferior frontal and insular atrophy. Logopenic variant, characterized by naming difficulties, poor sentence comprehension and speech pauses, is associated with left posterior temporal cortex damage as well as inferior parietal lobule [1-3]. Over the years, there has been an attempt to develop treatment options within the context of PPA, such as the use of pharmacological agents (e.g: acetylcholinesterase inhibitors and galantamine), omental therapy, neuromodulatory techniques (e.g., transcranial direct current stimulation – tDCS and repetitive transcranial magnetic stimulation – rTMS), and behavioural interventions. Apart from behavioural interventions, most of these management pathways have not proven valid and its application to PPA is highly experimental [4]. This paper focus on the rTMS studies directed to PPA individuals and provides critical judgments on its implications for future clinical guidelines.

rTMS Intervention

rTMS is a non-invasive tool used to induce cortical excitability when applied with high frequency (10-20Hz) or cortical inhibition when applied with low frequency (1-5Hz). A coil is placed on the patient's scalp and brief pulses of electrical current are discharged, in order to modulate neuronal activity [5,6]. A study conducted by Cotelli et al. (2012) [7] compared the effects of rTMS applied to right and left dorsolateral prefrontal cortex

(DLPFC) in two different PPA subgroups, nfvPPA (n=10) and svPPA (n=4). Subjects diagnosed with nfvPPA improved action-naming performance during rTMS stimulation. On the contrary, no main effect was found for object-naming skills. In svPPA patients, no significant benefits from bilateral stimulation were observed in either action-naming or object-naming tasks. The different response to treatment in these two groups of Subjects are attributed to the fact that svPPA patients have impaired semantic knowledge while nfvPPA patients, in the face of preserved semantic content, experience inefficient access to semantic knowledge. Another study revealed significant improvements in oral and written language skills (e.g., phonemic verbal fluency, reduction in the number of semantic written errors) after left DLPFC stimulation in a patient diagnosed with lvPPA [8]. This facilitating effect was temporary and language-specific, as cognitive function remained unchanged after real and placebo stimulation. The authors defend that effective rTMS stimulation facilitated semantic and syntactic processing by promoting a synaptic rearrangement. A third study investigated the effects of rTMS delivered over the left prefrontal cortex on linguistic abilities in a PPA patient [9]. The subject significantly improved verb production following anterior midfrontal gyrus stimulation, as compared to baseline and control conditions. Once again the gains post-rTMS were language-specific, given that patient's accuracy in memory tasks maintained the same.

Conclusion

Overall, the mechanism by which high frequency rTMS strengthens linguistic skills in PPA remains unclear. Treatment gains seem to be language-specific and tend to disappear over time. No beneficial effects were observed on cognitive function when this domain was included in treatment protocol, perhaps because language areas were targeted during treatment. In the future, authors should select the region of rTMS stimulation according to PPA subtype, as each variant presents with different lesion sites. Future studies should seek for long-term benefits, either by increasing treatment duration or manipulating other parameters of the protocol (e.g., intensity).

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