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Review

Transcranial magnetic stimulation in developmental stuttering: Relations with previous neurophysiological research and future perspectives

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HIGHLIGHTS

- TMS is widely used in motor disorders but its potential is underestimated in developmental stuttering (DS).
- TMS data suggest that DS is a symptom of a subtle and complex motor dysfunction.
- TMS sheds light on motor and white matter dysfunctions in DS, highlighted by other techniques.

ABSTRACT

Developmental stuttering (DS) is a disruption of the rhythm of speech, and affected people may be unable to execute fluent voluntary speech. There are still questions about the exact causes of DS. Evidence suggests there are differences in the structure and functioning of motor systems used for preparing, executing, and controlling motor acts, especially when they are speech related. Much research has been obtained using neuroimaging methods, ranging from functional magnetic resonance to diffusion tensor imaging and electroencephalography/magnetoencephalography. Studies using transcranial magnetic stimulation (TMS) in DS have been uncommon until recently. This is surprising considering the relationship between the functionality of the motor system and DS, and the wide use of TMS in motor-related disturbances such as Parkinson's Disease, Tourette's Syndrome, and dystonia. Consequently, TMS could shed further light on motor aspects of DS. The present work aims to investigate the use of TMS for understanding DS neural mechanisms by reviewing TMS papers in the DS field. Until now, TMS has contributed to the understanding of the excitatory/inhibitory ratio of DS motor functioning, also helping to better understand and critically review evidence about stuttering mechanisms obtained from different techniques, which allowed the investigation of cortico-basal-thalamo-cortical and white matter/connection dysfunctions.

Contents

Abbreviations: DS, developmental stuttering; EEG, electroencephalography; EMG, electromyography; MEG, magnetoencephalography; MEPs, motor evoked potentials; PWS, persons who stutter; tES, transcranial electric stimulation; TMS, transcranial magnetic stimulation.

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1. Symptoms, epidemiology, and physiopathology of developmental stuttering

Developmental stuttering (DS) is a disruption in the normal rhythm of speech. People affected may be unable to utter speech in a fluent manner. Its most prevalent form appears during childhood (generally males are usually more affected than females; Craig, 2002), with an onset usually between two and five years of age (Bloodstein, 1995). The principal symptoms of DS are repetitions, prolongations, and tense pauses manifesting speech blocks. This usually happens at the beginning of sentences and words (Bloodstein, 1995). It is often accompanied by secondary, associated movements/spasms, most prevalent but not limited to facial muscular areas (Mulligan et al., 2003; Riva-Posse et al., 2008). DS affects about 5% of children, and can spontaneously remit but remains in about 1% of adults (Yairi and Ambrose, 2005), with different degrees of severity. Persistent DS may be associated with educational and occupational disadvantages, decreased social interaction, isolation, and elevated levels of (social) anxiety (see Craig and Tran, 2014; Iverach and Rapee, 2014; Messenger et al., 2004). The exact causes of DS have not yet been identified. Today DS is considered to be a multifactorial and complex motor disorder (Alm, 2004; Craig-McQuaide et al., 2014; Ludlow and Loucks, 2003), influenced by genetic components (see for example Barnes et al., 2016; Chabout et al., 2016; Fisher, 2010; Drayna and Kang, 2011; Han et al., 2014; Kang and Drayna, 2011, 2012; Kang et al., 2010; Raza et al., 2015), which could influence the correct functions of brain networking and development (Beal et al., 2015; Cykowski et al., 2010). For example, it has been demonstrated that mutations in the lysosomal enzyme-targeting pathway may be mainly related to the presence of a reduced number of vocalizations and longer pauses between them in mice (Barnes et al., 2016).

The most influential hypothesis on DS physiopathology postulated that stuttering was due to an incomplete dominance of speech/motor regions in the left hemisphere (see Travis, 1978), with respect to the homologue regions of the right hemisphere, as it is usually evident in right-handed fluent speakers. This hypothesis has been confirmed by neuroimaging findings (see Brown et al., 2005), even if it is more likely that these neural correlates are related to compensatory attempts rather than to causal relationships with stuttering (see below). In fact, fluency-shaping techniques may help to restore aberrant neural activity in DS (see Neumann et al., 2003; Preibisch et al., 2003; Toyomura et al., 2011, 2015).

One of the principal aims of the present article is to provide a collection of experimental evidence as a basis for targeting future Transcranial Magnetic Stimulation (TMS) research in DS, with two objectives: (i) to obtain new understanding in the field of DS neurophysiology and neuropathology and (ii) to obtain new and more effective suggestions for more focused DS treatments.

The use of non-invasive, neurophysiologic evaluation tools such as TMS, provides an interesting possibility to shed further light on DS physiopathology, with particular attention to the functioning of the motor system and its balance of excitation and inhibition, in both speech- and non speech-related contexts. Unfortunately, and quite surprisingly, the potential of TMS has been underestimated in stuttering. A web-based research in PubMED, performed in March 2017, using "transcranial stimulation" and "stuttering" as keywords, gave an output of only 16 reports, which is very few compared to other basal ganglia related disturbances such as Parkinson's Disease (443 results), Tourette's Syndrome (57 results), and dystonia (302 results). Of these reports, six were not really focused on original and/or novel TMS and DS research (Cai et al., 2012; Chesters et al. 2016; Ingham, 2001; Neef et al. 2015a; Sandyk, 1997; Stewart et al., 2001).

In the present review, we will consider this evidence in the field of TMS and stuttering also with respect to neuroimaging, neurophysiologic, and behavioral research related to DS. We will critically review the current literature to provide useful information to stimulate critical thinking about the promising possibilities of non-invasive methods of brain stimulation in DS.

2. Models of DS speech production and related neurophysiology

Evidence suggests that DS is a general motor disorder, which is most evident during speech because of the high neural demand that is required for motor programming and coordination. However, theories have been proposed that also suggest psycholinguistic origins of dysfluencies, where the deficit is especially evident before motor preparation and/or execution of speech. Some examples are reported in the following paragraphs. Perkins et al. (1991) propose that stuttering may result from speech components that are not properly synchronized, also because of time pressure. Similarly, the Covert Repair Hypothesis (Postma and Kolk, 1993) suggests that stuttering may be the result of a series of errors that are present before, after, or during word execution. This theory, suggests that stuttering comes from the repetition of the repaired speech programs before motor execution and the lack of the ability to generate error-free speech programs. Another example is the Execution and Planning (EXPLAN) model that proposes planning of the next speech component as processed in the same moment of the motor execution of the current speech component. As a consequence, planning difficulties caused by phonetic/lexical complexities may arise, which ultimately result in stuttering (Howell,