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Research report

Motor excitability evaluation in developmental stuttering: A transcranial magnetic stimulation study

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ABSTRACT

Introduction: Developmental stuttering (DS) is viewed as a motor speech-specific disorder, although several lines of research suggest that DS is a symptom of a broader motor disorder. We investigated corticospinal excitability in adult DS and normal speakers.
Methods: Transcranial magnetic stimulation (TMS) was administered over left/right hand representation of the motor cortex while recording motor evoked potentials (MEPs) from the contralateral first dorsal interosseous (FDI) muscle. Resting, active motor thresholds, silent period threshold and duration were measured. A stimulus–response curve at resting was also obtained to evaluate MEP amplitudes.
Results: Lower corticospinal responses in the left hemisphere of DS were found, as indicated by a reduction of peak-to-peak MEP amplitudes compared to normal speakers.
Conclusions: This provides further evidence that DS may be a general motor deficit that also involves motor non-speech-related structures. Moreover, our results confirm that DS may be related to left hemisphere hypoactivation and/or lower left hemisphere dominance. The present data and protocol may be useful for diagnosis of subtypes of DS that may benefit from pharmacological treatment by targeting the general level of cortical excitability.

1. Introduction

Stuttering is defined as a disruption of the rhythm of speech and language articulation, where the subject knows what he/she wants to say, but is unable to utter the intended word or phrase fluently (World Health Organization, 1977). Developmental stuttering (DS) is the most common form of stuttering, and appears during childhood. A percentage of children recover from DS, while others remain persistent stutterers in adulthood even if DS may spontaneously disappear years after its onset (Kell et al., 2009). The principal symptoms of DS are blocks and/or repetitions at the beginning of phrases and/or words (Bloodstein, 1995). It is usually accompanied by evident movements and spasms, especially of the oro-facial muscular

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districts, in order to overcome disfluencies (Mulligan et al., 2003; Riva-Posse et al., 2008). DS is considered as a complex and multi-factorial disorder (Ambrose et al., 1993; Ambrose et al., 1997; Ludlow and Loucks, 2003; Maguire et al., 2002; Yairi et al., 1996). Orton (1928) and Travis (1978) theorized that DS was the result of an incomplete left language lateralization in the brain, followed by over-activation of the right one, resulting in a conflict for the execution of speech motor tasks. Recent functional magnetic resonance imaging (fMRI) studies have confirmed this hypothesis (Blomgren et al., 2003; Braun et al., 1997; Chang et al., 2009; De Nil et al., 2000; Fox et al., 2000, 1996; Ingham et al., 2004; Kell et al., 2009; Neumann et al., 2003; Preibisch et al., 2003; Sommer et al., 2002).

Anatomically, the stuttering brain also shows differences compared with that of fluent subjects. For example, stutterers fail to show the normal hemispheric asymmetries that are present in prefrontal and occipital lobes (Foundas et al., 2003) or in the frontal operculum and planum temporale (Foundas et al., 2001). Thus, it has been suggested that stutterers may have a different pattern of neural connections compared to fluent speakers (Cykowski et al., 2010; Ludlow and Loucks, 2003; Lu et al., 2010b, 2009; Salmelin et al., 2000; Sommer et al., 2002; Watkins et al., 2008).

It is not clear if these abnormalities are a prerequisite for the appearance of stuttering, or if they are the result of long-term stuttering in adults. However, it can be suggested that overt disfluencies are not needed to differentiate the stuttering brain from that of fluent individuals. In fact, it appears that the brain in stutterers is characterized by dopamine-related abnormalities (Wu et al., 1997, 1995). In this regard, it is clear that stuttering deficits remit after administration of anti-dopaminergic and/or serotoninergic drugs (Boldrini et al., 2003; Busan et al., 2009; Kumar and Balan, 2007; Maguire et al., 2004, 2000; Murray et al., 1977). However, although the chemical equilibrium in the brain may be an important factor in stuttering (Schreiber and Pick, 1997), contrasting reports (Guthrie and Grunhaus, 1990; Lee et al., 2001; Linazasoro and Van Blercom, 2007) suggest that different subgroups of stutterers may exist (Alm, 2004). This is especially true if it is considered that both dopamine and serotonin are important for the modulation of motor output (Cantello et al., 2002; Loubinoux et al., 2002, 1999; Pariente et al., 2001).

Taken together, these studies suggest that DS is an incompletely understood neurological problem, wherein disfluency is only one symptom of a more complex and subtle motor syndrome (Büchel and Sommer, 2004; Saltuklaroglu et al., 2009). This has been confirmed by recent investigations (Chang et al., 2009) demonstrating that stutterers show less BOLD signal change than control subjects during motor planning for both speech- and non-speech-related tasks.

In agreement with such a non-speech specific origin of DS, investigations have been conducted on general motor skills in stutterers (Webster, 1990a, 1990b, 1989) which have shown that stutterers may have difficulties in motor skills that are unrelated to speech (Brown et al., 1990; Forster and Webster, 2001; Jones et al., 2002; Smits-Bandstra and De Nil, 2007; Smits-Bandstra et al., 2006; Starkweather et al., 1984; Vaughn and Webster, 1989; Webster, 1990a, 1990b, 1989, 1986; Zelaznik et al., 1997).

As a consequence, we postulated that DS might also show some secondary indexes of motor abnormalities, as measured by transcranial magnetic stimulation (TMS; Cantello et al., 2002). Specifically, we investigated if DS might affect non-speech specific motor representations (e.g., hand muscle representation). Herein, we studied hand muscle representations allowing a direct comparison with previous publications (Busan et al., 2009; Sommer et al., 2009, 2003). Earlier studies showed that resting and active motor thresholds (AMTs) are increased in stuttering, suggesting the presence of a more widespread general motor cortical inhibition in DS with respect to normal speakers (Sommer et al., 2003). However, inter-hemispheric inhibition, intra-cortical inhibition (ICI) and facilitation (ICF) appear to be normal in DS when considering hand representation (Sommer et al., 2009, 2003). Weaker inhibition (in the right hemisphere) and a reduced facilitation (bilaterally) may be evident in the tongue motor representation of stutterers, accompanied by a steeper stimulus–response curve during muscular activation of the same districts (Neef et al., 2011b). Furthermore, a previous study (Busan et al., 2009) showed that the cortical silent period (believed to be an index of intra-cortical inhibition) was significantly reduced in a group of adult DS after the administration of paroxetine.

In the present study, we measured several indices of corticospinal excitability, some of which were not previously evaluated in DS subjects. Specifically, we measured bilateral resting and AMTs, cortical silent period threshold and duration and a resting motor evoked potential (MEP) stimulus–response curve. These measures were obtained from bilateral motor hand representations to directly investigate whether: (i) stuttering is a wider motor disorder and not exclusively a motor speech-related abnormality; (ii) stuttering is characterized by abnormal left hemisphere corticospinal activation.

2. Materials and methods

2.1. Subjects

A total of 40 subjects were recruited: 17 were developmental stutterers from childhood [6 females, age range: 19–46 years, mean: 26.5, standard deviation (SD): 6.9, 16 with right hand preference, 6 smokers], while 23 were sex-, age- and handedness-matched normal speakers (6 females, age range: 20–43 years, mean: 26.3, SD: 6.2, 21 with right hand preference, 7 smokers). Recruitment was conducted at two different centres (Ferrara and Trieste; Table 1) to obtain a sufficient number of stuttering subjects. Experimental groups were matched for similar characteristics, with particular attention to maintain a good balance between groups in their totality (stutterers *vs* normal speakers), considering mean age, handedness scores and gender, as in previous studies on stuttering (Braun et al., 1997; Cykowski et al., 2008). This led to

Table 1 – Subdivision of recruited subjects for each group and centre.

Subjects/centres	Ferrara	Trieste
Stutterers	5 males/4 females	6 males/2 females
Normal speakers	7 males/5 females	10 males/1 female