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Abnormal time course of low beta modulation in non-fluent preschool children: A magnetoencephalographic study of rhythm tracking

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ABSTRACT

Stuttering is a disorder of speech affecting millions of people around the world. Whilst the exact aetiology of stuttering remains unknown, it has been hypothesised that it is a disorder of the neural mechanisms that support speech timing. In this article, we used magnetoencephalography (MEG) to examine activity from auditory regions of the brain in stuttering and non-stuttering children aged 3–9 years. For typically developing children, we found that MEG oscillations in the beta band responded to rhythmic sounds with a peak near the time of stimulus onset. In contrast, stuttering children showed an opposite phase of beta band envelope, with a trough of activity at stimulus onset. These results suggest that stuttering may result from abnormalities in predictive brain responses which are reflected in abnormal entrainment of the beta band envelope to rhythmic sounds.

Introduction

Stuttering is a neurodevelopmental disorder characterised by speech dysfluencies in the form of repetitions, prolongations and blocks (World Health Organisation, 2010). It has a peak onset age of 3–5 years. It is estimated that anywhere from 32% (Johnson and Associates, 1959) to 80% (Yairi and Ambrose, 1999) of the children who begin to stutter will spontaneously recover, whilst the rest will continue to stutter into adulthood. In the last century, significant resources have been devoted to elucidating the cause of stuttering and numerous explanations have been proposed. It has been suggested that stuttering results from dryness of the tongue, adverse parental reactions to normal childhood dysfluencies or that it is a psychogenic disorder (for review see Büchel and Sommer, 2004). None of these explanations have received overwhelming support. More recently, investigations have shifted focus to compare patterns of brain activity in people who stutter (PWS) and people who do not stutter (PWDS). These studies have documented an array of anomalies in the structure and function of both cortical and subcortical regions in stuttering and have produced a variety of explanations regarding the brain basis of stuttering (see Brown et al., 2005; Belyk et al., 2014; Budde et al., 2014; Neef et al., 2015 for meta analyses). Investigations into the neurological underpinnings of stuttering via electrophysiological and brain-imaging studies may bring us closer to understanding its cause.

A great deal of progress has been made in elucidating differences in brain structure and function activity between PWS and PWDS. For example, there are significant differences in the haemodynamic response in auditory and motor regions when speaking (Toyomura et al., 2011) at rest (Xuan et al., 2012) and in the structural connectivity between auditory and motor areas (Cai et al., 2014; Kronfeld-Duenias et al., 2014) of the brain. Despite this, there remains significant uncertainty about the cause of the disorder. This is partly because most studies have focused on adults who stutter (AWS), making it hard to determine whether the observations of structural and functional anomalies are causally related to stuttering or the result of compensatory neuroplastic reorganisation (Chang and Zhu, 2013; Fox et al., 1996; Etchell et al., 2014a,b). Unlike AWS who have adapted to stuttering over time, such compensatory neural reorganisation either not evident or much less extensive in children who stutter (CWS Chang et al., 2008; Chang and Zhu, 2013; Beal et al., 2013). Studies of CWS are therefore crucial for isolating the neural origin or source of dysfluency. However, researchers face considerable difficulties in studying young children because of their inability to maintain sustained attention for the length of time necessary for the successful completion of even behavioural experiments. Recording neural activity during such experiments adds a further layer of complexity. Because neuroimaging studies place significant demands on young children by requiring them to remain as still as possible for extended periods of time, or are conducted in an environment that is noisy or confined and not well tolerated by this population, the

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majority have focused on AWS. Notably however, a number of studies have examined the brains of CWS (see G. Chang et al., 2015; Sato et al., 2011; Sowman et al., 2014; Usler and Weber-Fox, 2015). These methodological challenges perhaps explain why there are so few behavioural or neuroimaging studies of CWS.

Studies examining the behavioural performance of CWS provide valuable insight as to what might be causing the disorder. By and large they converge on the idea that stuttering is a disorder associated with temporal processing (see Etchell et al., 2014b, for a review). For example, Olander et al. (2010) found that the variability of paced and unpaced clapping in CWS was significantly greater than in children who do not stutter (CWDS) and that this variability was bimodally distributed. Specifically, the variability of 60% of the CWS overlapped with the variability of the CWDS, but 40% of the CWS exhibited variability that was worse than the poorest performing CWDS. Interestingly, these numbers closely corresponded to the number of children aged 4–6 years old (65%) who generally recover from stuttering (Yairi and Ambrose, 1992) and those who do not. The researchers took their findings to suggest that timing performance (as defined by the ability to clap to a beat) amongst that cohort was predictive of recovery from stuttering. It could be argued that a time processing disorder is potentially a cause of stuttering. Falk et al. (2015) compared the behavioural performance of children and adolescents who did and did not stutter in synchronising finger taps to simple and complex musical beats. At various inter-stimulus rates (450, 600 ms and 750 ms) CWS exhibited poorer behavioural performance (both in accuracy and variability) as compared to CWDS. Whereas the performance of CWDS improved with age, the performance of CWS did not. Furthermore, the analysis of behavioural performance revealed that low synchronisation accuracy was associated with increased stuttering severity, leading the authors to conclude that developmental stuttering could be linked with a more generalised deficit in timing (Falk et al., 2015).

One current neurophysiological explanation for stuttering is that it is a disorder of the internal timing network (comprised of the basal ganglia and the supplementary motor area) and that these temporal processing deficits can be compensated for by an external timing network [comprised of the cerebellum, premotor cortex and right inferior frontal gyrus (IFG)]. This explanation derives from the fact that there is a great degree of overlap in the neural structures underpinning rhythmic timing and speech production/perception (see Fujii and Wan, 2014). This contention is further supported by a host of neuroimaging studies linking deficits in this network to stuttering. For example, Beal et al. (2013) used structural MRI to compare grey and white matter volumes between CWS and CWDS. They found decreased grey matter volume in the left putamen of CWS which they suggested was particularly interesting in light of emerging evidence for difficulties in speech motor sequence learning in PWS and the recognised role of the left putamen in motor sequence learning (Beal et al., 2013). Beal et al. (2013) concluded that abnormalities in the neurodevelopmental trajectory of regions such as the left putamen, bilateral IFG and supplementary and premotor cortex may result in the breakdown of accurate speech motor learning and control. Similarly, Chang and Zhu (2013) examined functional resting state activity and used diffusion tensor imaging (DTI) to investigate differences in the structural connections of the brains of CWS and CWDS. The authors found attenuated functional activity (as measured by correlations between the left putamen and the right posterior superior temporal gyrus, left SMA and left insula) and structural connectivity (between the left putamen and the left inferior frontal gyrus and the middle temporal gyrus as measured by white matter tractography) in CWS as compared to CWDS. Chang and Zhu (2013) concluded that CWS have attenuated connectivity in neural networks that support timing of self-paced movement control. The young participants were included in Chang and Zhu's study very soon after the onset of their stuttering symptoms. Hence, it is likely that subcortical regions like the putamen are causally related to the onset of stuttering. Whilst there are relatively well-established abnormalities in the structure and function of cortical regions in stuttering, far fewer studies have examined whether there might be abnormalities in oscillatory neural dynamics within these cortical regions and whether or not such differences can be related to putative temporal processing deficits in stuttering.

Neural oscillations refer to rhythmic fluctuations in the excitation and inhibition of large populations of neurons that can be recorded using tools like magnetoencephalography (MEG) or electroencephalography (EEG) and are most probably caused by changes in large scale synchronous transmembrane currents (Thut et al., 2012). These oscillations are characterised according to the frequency at which they occur and can each be linked to different cognitive functions. For example, the delta band is prevalent during the sleep cycle and the gamma band is associated with memory. The beta band is modulated prior to and during the execution, observation and imagination of movement (Burianová et al., 2013, 2014; Kilavik et al., 2013). Specifically, beta band activity drops (desynchronises) immediately prior to and during movement before increasing (resynchronising) once the movement becomes stable. There are many theories about the function of neural oscillations in the brain. One such theory posits that the function of oscillatory activity is to predictively focus attention at salient events by (for example), entraining the brain to auditory stimuli (Large and Jones, 1999). According to this view, neural oscillations are crucial for processing temporal information because of their inherent regularity (Arnal and Giraud, 2012; Zanto et al., 2006; Fujioka et al., 2009). A less well known characteristic of the beta band is that it may be particularly important for temporal processing. Recent data indicates that passively listening to isochronous sounds modulates beta band activity in the auditory cortices at the rate of the pacing stimulus (Fujioka et al., 2012). In Fujioka et al.'s study, participants passively listened to trains of isochronous sounds of either 390, 585 or 780 ms, or to sounds whose period varied randomly between 390 and 780 ms. Time–frequency analysis of auditory cortex virtual sensor data derived from magnetoencephalographic recordings revealed a decrease in beta band power 200 ms after stimulus onset that was identical across both the rhythmic and random conditions. However, the rising slope of the beta band activity (also known as the beta rebound) was modulated according to the rate of isochrony. Whereas the beta rebound peaked before the next expected stimulus in the rhythmic condition, in the random condition, the rebound was much less steep. Based on these data, the authors suggest that beta rebound may be a neural mechanism for predictive timing. More recently, Cirelli et al. (2014) replicated Fujioka et al.'s (2012) paradigm in an EEG experiment on children. Cirelli and colleagues demonstrated that children as young as 7 years of age exhibit a similar pattern of activity to adults for the slower, but not faster tempos in the auditory cortex. This finding demonstrates that typically developing school-aged children and adults exhibit comparable beta band responses to rhythmic and less rhythmic sounds.

Only four published reports exist that describe beta band dynamics in PWS, and none have examined them in the context of temporal processing. Rastatter et al. (1998) investigated the effects of delayed auditory feedback on oscillatory activity of adults who stuttered. The authors showed that this fluency-inducing technique markedly reduced hyperactivity of the beta band in adults who stuttered relative to a baseline resting condition. Salmelin et al. (2000) used MEG to compare the sequences of cortical beta band activation during single word reading in stuttering and non-stuttering adults. Whilst the overt behavioural performance of the two groups was identical, there were marked differences in the sequence of beta band responses. In contrast to the adults who did not stutter (AWDS), the adults who stuttered (AWS) had significantly weaker beta band modulation in the hand and mouth areas of the motor cortex during speech production. Additionally, whilst the fluent adults displayed salient time-locked responses in the mouth area of the motor cortex, no such response was evident in the AWS, suggesting that whilst the rolandic operculum was active, the responses in this region were not properly synchronised. A later study by Özge