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Atypical brain activation in children who stutter in a visual Go/Nogo task: An ERP study

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HIGHLIGHTS

- Children who stutter (CWS) show atypical brain activation compared to typically developing children (TDC) in a visual Go/Nogo task especially in the right frontal area.
- CWS had prolonged N2 in both conditions while the Nogo P3 component was diminished compared to TDC.
- Stimulus classification and/or inhibitory control may operate abnormally in the CWS.

ABSTRACT

Objective: The aim of the study was to investigate inhibitory control by evaluating possible differences in the strength and distribution of the brain activity in a visual Go/Nogo task in children who stutter (CWS) compared to typically developing children (TDC).
Methods: Eleven CWS and 19 TDC participated. Event related potentials (ERP) were recorded using a 64-channel EEG-cap during an equiprobable visual Go/Nogo task. The global field power (GFP) as well as the mean amplitudes in the P3 time frame were compared between groups. Additionally, the potential maps of the groups were investigated visually in the N2 and P3 time windows.
Results: The groups differed significantly in the right frontal area especially in the Nogo condition ($p < 0.001$) with CWS showing smaller (less positive) mean amplitudes, most likely due to a prolonged and asymmetrical N2 component. Also the fronto-central Nogo P3 component was rather indistinct in CWS, but easily recognizable in TDC in the potential maps.
Conclusions: The CWS show atypical brain activation compared to the TDC in a Go/Nogo task as indexed by the excessive N2-related activity in both conditions and reduced P3-related activity in Nogo condition.
Significance: These findings indicate atypical stimulus evaluation and response inhibition processes in CWS.

1. Introduction

The ability to communicate is an essential part of our everyday lives and any problem in this area can have a harmful effect on the quality of life. In developmental stuttering, speech is characterized with repetitions, prolongations and blocks that make the speech dysfluent thus affecting communication negatively. According to current theories stuttering may arise from neurobiological and neurophysiological differences in brain areas related to speech and auditory processing (Giraud et al., 2008; Jansson-Verkasalo et al., 2014; Watkins et al., 2008; for an overview, see review by Alm, 2004).

An increasing number of studies have shown structural and functional brain abnormalities both in adults (Beal et al., 2007; Salmelin et al., 2000; Sommer et al., 2002; Watkins et al., 2008)

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and in children who stutter (CWS) (Beal et al., 2013; Chang et al., 2008; Chang and Zhu, 2013). In an interesting study using magnetoencephalography (MEG), Salmelin et al. (2000) discovered a reversed sequence of activation in a delayed reading paradigm. Contrary to the fluent speakers, the left lateral central sulcus and dorsal premotor cortex were activated first and then followed by activation in the left inferior frontal cortex in the stutterers, indicating delayed articulatory programming versus motor preparation. The authors also suggested impaired functional connectivity between the left frontal cortex and the right motor/premotor cortex. Imaging studies have indicated decreased white matter integrity and thus reduced connectivity of left laryngeal and tongue representation areas in the sensorimotor cortex (Sommer et al., 2002), but also clusters of increased grey or white matter density in areas relevant to speech, for example the superior temporal gyri and especially the right primary auditory cortex (Beal et al., 2007). By using functional imaging Watkins et al. (2008) found over-activity bilaterally in the anterior insula, cerebellum and midbrain as well as the basal ganglia in persons who stutter when compared to fluent persons. On the other hand, persons with stuttering showed under-activity in areas essential for planning and execution of speech; bilateral ventral premotor cortex, Rolandic operculum, sensorimotor cortex and Heschl's gyrus on the left and in the premotor and motor cortices related to articulation and speech production. In addition, Watkins et al. found reduced white matter integrity in the detected under-active areas in the ventral premotor cortex.

Studies on children are scarce, but recently, Chang and Zhu (2013) showed that stuttering children aged 3–9 years had attenuated connections between both auditory-motor and cortical – basal ganglia areas on the left side compared to controls. Earlier Chang et al. (2008) found reduced grey matter volume (GMV) in left inferior frontal gyrus and bilateral temporal regions and reduced white matter integrity in the tracts below motor regions for face and larynx. Beal et al. (2013) also found abnormalities in grey and white matter volume in CWS compared to fluently speaking children, more specifically reduced GMV in the bilateral inferior frontal gyri and left putamen, increased GMV in right Rolandic operculum and superior temporal gyrus and reduced white matter volume (WMV) bilaterally in the corpus callosum. These irregularities are only partially similar in stuttering children and adults implicating some plastic reorganization of the brain by age. Although more studies on young children are needed, these findings suggest reduced GMV and WMV mostly in the left hemisphere and decreased connectivity within left hemisphere or between hemispheres. Thus the over-activity or increased grey and white matter volume on the right might partially result from compensation of left-sided defects.

Also temperamental factors such as emotional reactivity have been proposed to affect the severity of stuttering (Conture et al., 2006; Bloodstein and Bernstein-Ratner, 2008). These theories suggest that an intense reaction to a moment of dysfluency may increase speech disruption. However, questionnaires on temperament traits in CWS have not shown a higher level of anxiety or shyness (see review by Alm, 2014). Instead, some CWS showed traits typical of ADHD, such as inattention and impulsivity or hyperactivity. In recent studies using a questionnaire and a flanker task, the CWS showed poorer inhibitory control (Eggers et al., 2010) as well as atypical attentional orienting (Eggers et al., 2012), respectively. Inhibitory control is essential for attention and regulation of impulsivity. Basically it means the ability to prevent an inappropriate response when needed or, on the other hand, to perform a response when appropriate (Rothbart, 1989) or to ignore irrelevant information (Rothbart and Posner, 1985. Without sufficient inhibitory control, focusing on a complex task or processing information would be compromised.

The Go/Nogo paradigm is an inhibitory control related task. In this task the Go-signal requires a response, but to the Nogo-signal the response has to be withheld. In a recent study using the Go/Nogo subtest of the Amsterdam Neuropsychological Tasks (ANT) with equiprobable Go/Nogo stimuli, CWS had more false alarms, premature responses and difficulties in adapting their response style after errors (Eggers et al., 2013) indicating abnormal inhibitory control in CWS. However, behavioral indices as errors and reaction time are quite robust measures and do not give detailed information on the underlying processes. For this reason, the Go/Nogo paradigm has commonly been combined with event-related potential (ERP) measurements in the study of inhibitory control (Johnstone et al., 2009, 2005; Jonkman, 2006; Jonkman et al., 2003; Piispala et al., 2016; Spronk et al., 2008). Compared to for example MRI, EEG- and ERP-measures have good temporal resolution and are therefore good methods to investigate fast cognitive processes.

In the Go/Nogo paradigm the negative N2 and positive P3 responses are the main ERP components modified by the paradigm. They are most distinguishable at 200–400 ms (N2) and 250–650 ms (P3) time windows depending on the stimulus and the paradigm (Jonkman et al., 2003; Jonkman, 2006; Johnstone et al., 2007). The N2 and P3 are both usually enhanced in the Nogo condition compared to the Go-condition (the Nogo effect) (Donkers and Van Boxtel, 2004; Falkenstein et al., 1999; Jonkman et al., 2003; Jonkman, 2006). In addition to the task parameters, age affects the ERPs (Brydges et al., 2013; Johnstone et al., 2005; also see review Huster et al., 2013). The Nogo effect on the N2 component is more distinct in children compared to adults. However, the Nogo P3 may be vague up to the age of 9 years (Johnstone et al., 2007; Jonkman, 2006; Spronk et al., 2008).

The N2 component is maximal fronto-centrally. It has been connected to inhibitory processes (Falkenstein et al., 1999; Pliszka et al., 2000) but also to conflict monitoring (Donkers and Van Boxtel, 2004; Enriquez-Geppert et al., 2010; Randall and Smith, 2011; Smith, 2011; see review by Van Veen and Carter, 2002) and novelty effect (Albert et al., 2013). The N2 component most likely consists of subcomponents that are activated differently when the task parameters are manipulated to increase either visual mismatch, conflict within the task or response inhibition demands, thus explaining the diverse results (Kropotov et al., 2011; for an overview, see also Folstein and Van Petten, 2008).

The P3 component has different topography in Go and Nogo conditions. Therefore the Go P3 and Nogo P3 components are probably produced by separate neural generators (Bokura et al., 2001; Gajewski and Falkenstein, 2011; Kropotov et al., 2011; Tekok-Kilic et al., 2001). The P3 seen in Go condition is maximal in centro-parietal regions both in adults (Barry and De Blasio, 2013; Bokura et al., 2001; Tekok-Kilic et al., 2001) and children (Barry et al., 2014). It is believed to represent stimulus evaluation and classification similarly to the P3b in the oddball paradigm (Barry and Rushby, 2006; also see reviews by Polich, 2007 and Linden, 2005). The Nogo P3, on the other hand, is maximal fronto-centrally (Bokura et al., 2001; Tekok-Kilic et al., 2001; Johnstone et al., 2007; Jonkman, 2006; Smith, 2011). It may be specific to the inhibition process, as suggested by an increasing number of studies (Albert et al., 2013; Donkers and Van Boxtel, 2004; Smith et al., 2006, 2013).

Recently we performed a visual Go/Nogo task with simultaneous EEG-recording on 7–9 year old CWS and typically developed children (TDC) (Piispala et al., 2016). In this first Go/Nogo-ERP study on CWS we examined the N2 and P3 components in both Go and Nogo condition over 9 electrodes (F3,Fz,F4, C3,Cz,C4, P3, Pz,P4) along with behavioral measures. We found significantly delayed N2 component in the Go condition in CWS, indicating possibly atypical stimulus evaluation and/or response preparation. In contrast, there was no significant latency difference in the Nogo condition. No significant peak amplitude differences were seen