Children who stutter show reduced action-related activity in the rostral cingulate zone

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ABSTRACT

Previous studies have indicated that children who stutter show not only speech-related problems, but also wider difficulties in self-control. In this study we test the novel hypothesis that children who stutter may experience difficulties with inhibitory control over voluntary actions. We used functional MRI to compare brain activity between children who stutter and children who do not stutter in a task that captures key cognitive aspects of voluntary action control. Participants performed a rolling marble task, in which they were instructed to press a key to stop a rolling marble from crashing on some of the trials (instructed action condition). They were also asked to choose voluntarily whether to execute or inhibit this prepotent response in other trials (volition condition). Children who stutter reported less motor and cognitive impulsivity and had shorter stop-signal reaction times when controlled for IQ, consistent with greater inhibition, compared to children who do not stutter. At the neural level, children who stutter showed decreased activation in the rostral cingulate zone during voluntary action selection compared to children who do not stutter. This effect was more pronounced for children who were rated as showing more stuttered syllables in the stutter screening, and was furthermore correlated with stop-signal reaction times and impulsivity ratings. These findings suggest that stuttering in childhood could reflect wider difficulties in self-control, also in the non-verbal domain. Understanding these neural mechanisms could potentially lead to more focused treatments of stuttering.

1. Introduction

Stuttering is a speech problem characterized by blocks, repetitions, or prolongations of speech segments (WHO, 2007). One percent of all adults suffer from developmental stuttering, which is defined as stuttering that develops during childhood without obvious neurological origin (Bloodstein and Ratner, 2008). Stuttering has negative emotional, psychological and social consequences for preschool children, as reported by their parents (Langvin et al., 2010). Quality of life is reduced when stuttering persists after preschool into adolescence and adulthood (Davis et al., 2002; Koedoot et al., 2011; Yaruss, 2010). Thus, this developmental disorder has severe consequences for daily life functioning, but the underlying cognitive and neural mechanisms remain poorly understood.

Recently, it was found that children who stutter (CWS) show abnormalities not only in speaking, but also in self-control more generally. These studies reported that CWS showed less attentional control compared to children who do not stutter (CWNS) (Eggers et al., 2009, 2012; Kaganovich et al., 2010). Parents and teachers also reported more attentional problems in CWS than in CWNS (Eggers et al., 2009, 2010; Felsenfeld et al., 2010; Karrass et al., 2006; Schwenk et al., 2009, 2010; Felsenfeld et al., 2010; Karrass et al., 2006; Schwenk et al., 2009, 2010). Furthermore, CWS had more difficulty with inhibitory control than CWNS based on parent-report questionnaires (Eggers et al., 2009, 2010), and performance on the Go/NoGo task (Eggers et al., 2013). Other studies, however, failed to find differences between CWS and CWNS in parent-rated attentional focusing, impulsivity and inhibitory control (Anderson and Wagovich, 2010). Taken together, self-control may be a key dimension in understanding the underlying mechanisms of stuttering, but prior studies report inconsistent findings and a comprehensive study on self-control in relation to stuttering is lacking.

Self-control is often studied by focusing on inhibition in response to external cues, for example in the stop-signal reaction time task (Band et al., 2003; Logan and Cowan, 1984). However, self-control in daily life is mostly internally triggered, suggesting an important role for voluntary action control. This can be further subdivided into voluntary
action selection (choosing what action to make), action initiation, and voluntary inhibition (choosing, at given moment, to suppress action, rather than acting). Previous studies in adults have shown that voluntary action selection was related to activity in the rostral cingulate zone (RCZ) (Brass and Haggard, 2008; Brass et al., 2013; Demanet et al., 2013). Voluntary control of inhibition remains a controversial idea, but has been linked to an internal decision to inhibit an action that has already been prepared. Several studies linked this form of inhibition to activation of the dorso-frontal median cortex (dFMC) (Brass and Haggard, 2008; Brass et al., 2013; Filevich et al., 2012).

Thus, these studies suggest that two important regions in the medial frontal cortex, the RCZ and the dFMC, are critically involved in voluntary action selection and voluntary inhibition, respectively. Regions in the lateral prefrontal cortex have also been implicated in self-control. An fMRI study showed that 10–12-year-old typically developing children recruited the right inferior frontal gyrus (IFG) more during voluntary inhibition than adults (Schel et al., 2014b). Consistent with this finding, studies of stimulus-driven inhibition demonstrated ongoing changes in the same network (Casey et al., 2002; Crone and Dahl, 2012; Durston et al., 2006; Luna et al., 2010).

One might hypothesize that developmental stuttering could be related to protracted or deviant development of the brain. Most studies have revealed that stuttering is related to increased activation in certain brain regions, often interpreted as compensatory activity. For instance, during speech perception, adults who stutter (AWS) showed increased activity in the right IFG and left Heschl’s gyrus (Halag-Milo et al., 2016) and left anterior insula (Lu et al., 2016), but decreased activity in several motor regions and angular gyrus (Chang et al., 2009) compared to adults who do not stutter (AWNS). During speech production, increased activity was found in primary motor and auditory regions (Chang et al., 2009). A conjunction analysis that focused on both speech perception and speech production revealed coincident activity in speech motor areas (Lu et al., 2016). CWS showed increased activity in the anterior insula and cingulate sulcus during speech production (Watkins et al., 2008). The latter region may be closely related to the RCZ, given that both are located in the medial frontal cortex. Prior research has also related stuttering symptoms to a non-speech related executive function task, the Simon spatial incompatibility task. CWS and AWS showed more activity in frontostriatal regions when resolving conflict, but less activity in the dorsolateral prefrontal cortex (dLPFC) when adapting to changes in conflict compared to AWNS and AWNS.

These differences were interpreted as suggesting failure to recruit control-related regions in some task conditions, and possibly a compensatory mechanism for other task conditions (Liu et al., 2014). Interestingly, this study showed that activity in the ACC was negatively correlated with the severity of stuttering symptoms, possibly reflecting a failure to recruit conflict related regions to resolve stuttering (Liu et al., 2014).

Even though almost no studies examined functional brain activation in children who stutter, some hypotheses can be derived from studies that related stuttering in children to structural brain measures. Structural brain imaging studies reported that CWS and children who recovered from stuttering showed reduced grey matter volume in the left IFG and bilateral temporal brain areas, areas that are related to speech (Chang et al., 2008), as well as the auditory areas, supplementary motor area (SMA) and putamen (Chang, 2014). The latter two regions are possibly related to initiation and timing of speech motor control (Chang, 2014). Taken together, prior studies show some differences in brain activity during several aspects of cognitive control in CWS and AWS (Liu et al., 2014), and structural brain development studies indicate differences in neural trajectories in CWS (Chang, 2014; Chang et al., 2008), but it is currently unknown how difficulties in self-control in CWS are related to differences in brain activity.

The goal of the present study was therefore to compare neural responses between CWS and CWNS during voluntary action control. We used an adapted version of the marble task (Schel et al., 2013) to measure brain activity during voluntary action control in CWS and CWNS between the ages of 9 and 14 years. In this task, participants could choose to execute (voluntary action selection) or inhibit (voluntary inhibition) a key press to stop a marble from rolling down the ramp (Kühn et al., 2009; Schel et al., 2014a). These choice trials were interleaved with trials in which a stimulus instructed participants to stop the marble. The speed of the marble required rapid responding in instructed trials. As a result the action response became prepotent, and the voluntary inhibition response became, in turn, an exercise of self-control over a prepotent action tendency. Our first hypothesis was that CWS would show impaired voluntary action selection, based on behavioral studies that show that CWS have poorer attentional control (Eggers et al., 2009, 2012; Kaganovich et al., 2010; Karras et al., 2006; Schwenk et al., 2007). We expected that this would be accompanied by aberrant activation of the RCZ (Brass and Haggard, 2008; Brass et al., 2013; Demanet et al., 2013). Our second hypothesis was that CWS would show specific deficits in voluntary inhibition based on behavioral studies showing less inhibitory control in CWS (Eggers et al., 2009, 2010, 2013). We expected that this would be accompanied by differential activation in the inhibition network including the dFMC, IFG/pre-SMA and the putamen (Brass and Haggard, 2008; Brass et al., 2013; Filevich et al., 2012; Schel et al., 2014b).

All participants also performed a stop-signal task (Logan and Cowan, 1984) to obtain a behavioral measure of stimulus-driven inhibition and to further test for difficulties in self-control. In addition, all participants filled out the Barrett Impulsiveness Scale (Patton et al., 1995), to test whether CWS and CWNS differed in impulsivity.

2. Material and methods

2.1. Participants

Seventeen CWS and nineteen CWNS between the ages of 9 and 14 years participated in this study. Care was taken to recruit a similar number of boys and girls in this study. CWS were diagnosed and referred to us by speech therapists1 and CWNS were recruited from schools in the local area and through recruitment websites. The control group data was published previously in a study about developmental effects in voluntary action control (Schel et al., 2014b). All children were right-handed, had normal or corrected-to-normal vision, and none of the children had a current or past neurological or psychiatric disorder. Table 1 displays the means and standard deviations of CWS and CWNS across several background variables. CWS and CWNS did not differ in age, $F(1, 34)=0.44, p=0.51$, and the distribution of gender was the same in both groups, $X^2(1)=0.47, p=0.53$. Informed consent was signed by parents for children under 12 years, and by both parents and participants for children over 12 years. The study was approved by the Internal Review board at Leiden University Medical Center.

To check for differences in cognitive functioning, all participants performed two subtests of the Wechsler Intelligence Scale for Children (WISC) (Wechsler, 1991). Estimated IQ scores were within the normal range. However, estimated IQ was lower in CWS than in CWNS, $F(1, 34)=10.83, p=0.002$. Therefore, we performed all analyses also with IQ added as a covariate and we report the results of both analyses.

All children were screened for stuttering. We collected two speech samples of 300 syllables per child, while reading aloud a story and while having a conversation with the experimenter. Two independent trained analysts scored these speech samples. CWS stuttered significantly more syllables (range 1.07–14.32) than CWNS (range 0.16 – 1.47) across the two speech samples, $F(1, 34)=18.58, p<0.001$. The interanalyst reliability was computed using a Pearson correlation of the average percentage of stuttered syllables across the two speech samples.

1 It should be noted that no speech-language tests were conducted, so the children may have other disorders.
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