Functional brain correlates of response time variability in children.

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Objective: In tasks of response inhibition, intra-subject response time (RT) variability, a measure of motor response preparation, has been found to correlate with errors of commission. Increased RT variability is also a consistent finding in attention-deficit/hyperactivity disorder (ADHD), in which response inhibition is implicated as a core deficit. Neural correlates of RT variability have thus far been examined in a single fMRI study of adults performing a Go/Nogo task with a high cognitive load (Bellgrove et al., 2004 *Neuropsychologia*); higher RT variability correlated with increased activation in prefrontal and subcortical regions, but there were no observed neural correlates of lower RT variability. We hypothesized that lower RT variability during performance of a simplified Go/No-go task (Mostofsky et al., 2003 *Cog Brain Res*) with minimal cognitive demands would be associated with Nogo activation in premotor regions important for motor response preparation, while higher variability would be associated with prefrontal and subcortical regions important for higher-order cognitive control; this was examined in children, allowing for a wider range of performance.

Methods: Thirty typically developing children, ages 8-12 years, completed a simple Go/Nogo task in which cognitive demands were minimized using well-ingrained stimulus-response associations (green=go, red=nogo). Stimuli were presented for 300ms with an ISI of 1500ms. The ratio of Go:Nogo stimuli was 3:1, allowing for effective jittering of No-go stimuli. FMRI data were acquired on a 1.5T Philips scanner and analyzed using SPM99. Individual voxel-wise contrast maps were created for Go and Nogo conditions. Correlations of Go and No-go activation with intra-individual RT variability were examined using intra-individual coefficient of variability (ICV) [(standard deviation of RT) / (mean RT)] (Stuss et al., 2003 *Brain*).

Results & Discussion: ICV correlated with rate of commission errors ($r=.46$, $p=.006$). FMRI correlational analyses revealed that lower ICV was association with Go activation (Fig. 1A) in the anterior cerebellum (culmen), an area associated with timing/coordination of motor responding, and with Nogo activation (Fig. 1B) in the supplementary motor area (BA6), important for motor response preparation, as well as ipsilateral (right) sensorimotor cortex (BA3/4) and contralateral (left) anterior cerebellum (culmen). Higher ICV was associated with both Go (Figure 3) and Nogo (Figure 4) activation in the right middle frontal gyrus (BA9/10) and the caudate, regions associated with higher-order cognitive control. The results from correlation between higher ICV and Nogo activation are consistent with previous findings in adults (Bellgrove et al., 2004).

Fig. 1: Regions showing a negative correlation between ICV and (A) Go and (B) Nogo activation

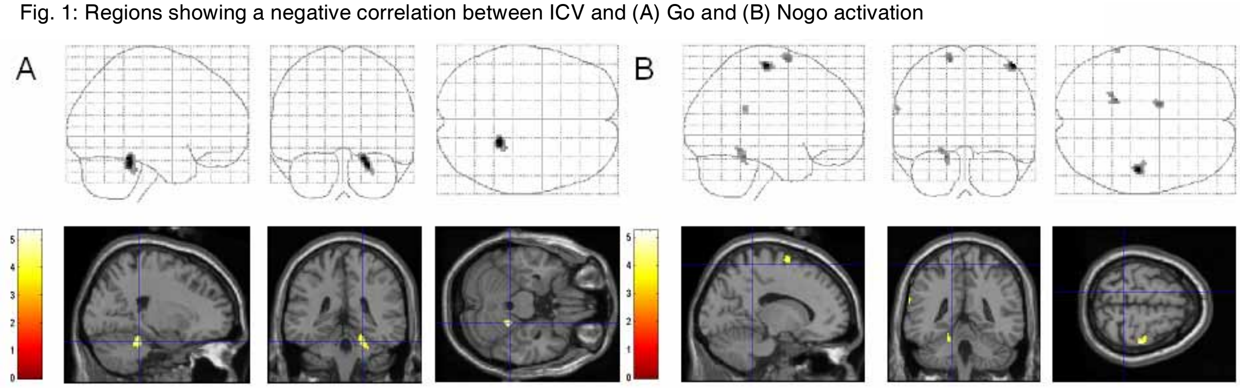
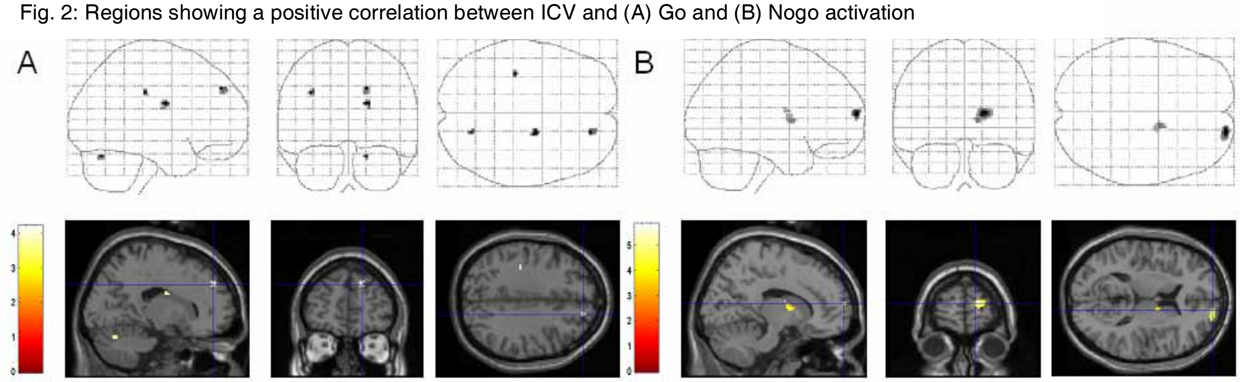


Fig. 2: Regions showing a positive correlation between ICV and (A) Go and (B) Nogo activation



Conclusions: These findings suggest that the neural basis of RT variability has a significant effect on the functional correlates of motor response selection and inhibition. The results revealed that lower RT variability was associated with both Go and Nogo activation in premotor circuits, while higher variability was associated with both Go and Nogo activation in prefrontal circuits, suggesting that children who perform the Go/Nogo task efficiently principally utilize automatic premotor circuits important for motor response selection (including selecting not to respond), while those who cannot perform the task efficiently must instead rely on less automatic prefrontal circuits involved in higher-order cognitive control. These findings have implications for ADHD, in which both motor response selection and inhibition are found to be impaired, which may reflect abnormalities in medial premotor and cerebellar regions.