A large-sample fMRI study (n = 1,252) of individual differences in inhibitory control

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Introduction

Adolescents tend to engage in more risky behavior than either children or adults. Poor inhibitory control is a risk factor for problematic substance experimentation in early adolescence and is also a feature of Attention-Deficit Hyperactivity Disorder (ADHD). However, impulsivity and impulse control are multi-faceted constructs measured in numerous ways that very often correlate poorly with one another in non-clinical samples. This raises the possibility of the involvement of numerous distinct brain networks contributing to the cognitive, clinical and behavioral elements of impulsivity. The stop-signal reaction-time task (SST) is a test of inhibitory control that requires the participant to withhold responding to an already initiated motor response. The time required to stop a response in this way – the stop signal reaction time (SSRT) – is extensively used as a clinical index of inhibitory control. Slower SSRTs have been observed in subjects with lesions in the prefrontal cortex (Aron et al., 2003) or the basal ganglia (Eagle & Robbins, 2003). Neurochemically, norepinephrine (NE) plays an important role in successful inhibition. The work described here had two major objectives: 1) to determine the neural correlates of inhibitory control in early adolescence and 2) to describe individual differences in inhibitory control for SSRT, ADHD symptoms, drug use, and genetic factors.

Methods

Imaging data were acquired from 1,252 adolescents tested as part of the multi-site IMAGEN project (Schumann et al., 2010) (mean age = 14.51 years, standard deviation (SD) = 0.855 years; 52.1% female; 89.03% right-handed; verbal IQ = 108.26, SD = 14.37; performance IQ = 107.32, SD = 14.42). During fMRI scanning, participants performed the SST which consisted of 400 go trials and 80 variable delay stop trials. In order to reduce the dimensionality of the data and to identify networks of correlated regions, we used factor analysis, a method that utilizes the interdependencies between observed variables to generate a smaller number of underlying

factors. Measures of drug use and attention deficit hyperactivity disorder (ADHD) were also obtained.

Results

The factor analysis results for Stop Success identified seven networks and six networks for Stop Failure. The factors were largely bilateral and separated the activated regions into distinct subcortical, frontal, parietal and motor networks. We divided SSRT into upper and lower quartiles. There were significant differences for Stop Success in Factors 1 (bilateral subcortical regions, $F(1, 259) = 12.85$) and 6 (right frontal cortex, $F(1,260) = 13.91$) and for Stop Fail Factor 1 (bilateral insula, ACC and IFG, $F(1,258) = 15.96$) with higher brain activity for subjects with faster SSRTs. Those adolescents with most drug use showed reduced inhibition-related activity for Stop Success Factors 3 (bilateral dorsal and orbitofrontal cortex, $F(1, 328) = 7.387$, $p = .007$) and 7 (bilateral precentral gyri and pre-SMA, $F(1,324) = 6.653$, $p=.01$). We identified 74 participants with subclinical features of ADHD and matched each of them with a control participant with no ADHD symptoms. There were significant differences for Stop Fail trials for Factors 1, (bilateral insula, ACC and IFG, $t(139) = 3.21$) and 6 (bilateral putamen, pallidum and caudate, $t (139) = 2.99$), with reduced activity in participants with subclinical features of ADHD. We obtained genetic data on 645 participants and found that the NE receptor gene, ADRA2B, was associated with Stop Success Factor 6 (right lateralized IFG, insula and ACC; $p=0.0005$).

Conclusions

The inter-individual variation in different networks was shown to relate to different aspects of impulsive behavior ranging from the speed of inhibitory control, subclinical ADHD features and drug-use. This fractionation may reflect the multidimensionality of inhibitory control which can have many related yet distinct and often uncorrelated characteristics.

References

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