Fractionating the impulsivity construct in adolescence

Robert Whelan[1] and Hugh Garavan[1]

Correspondence can be addressed to RW (robert.whelan@uvm.edu) or HG (hugh.garavan@uvm.edu)

[1]Department of Psychiatry and Department of Psychology,

University of Vermont,

1 S Prospect St.

Burlington

VT 05401,

USA

The teenage years are often associated with 'impulsive' behavior; that is, behavior with diminished regard to potential negative consequences. Adolescent impulsivity, while often adaptive, can manifest itself in a number of different sub-optimal behaviors, including use of nicotine, alcohol, or illicit substances, symptoms associated with attention deficit hyperactivity disorder (ADHD), or poorer performance on laboratory assays of impulse control. Although these maladaptive behaviors are often co-morbid, the correlation among them is not perfect. It is therefore increasingly recognized that impulsivity is a multi-dimensional construct, with some predicting that "what is generally denoted as impulsivity will be fractionated into distinct forms that may, however, often coexist in the same individual" (Dalley *et al*, 2011, p. 691).

Fractionating impulsivity is challenging, however, not least because of the large sample size needed to ensure an adequate number of participants in each phenotypic group, although recently the "population neuroscience" (Paus, 2010) approach has provided these large samples. Data from the IMAGEN (Schumann *et al*, 2010) project permitted the data-driven identification of impulsivity subtypes by Whelan *et al* (2012). Nearly 1,900 14-year-olds completed a test of motor inhibition – the Stop Signal Task (SST) – while undergoing functional magnetic resonance imaging (fMRI). In contrast to the mass-univariate approach typically employed in fMRI studies, the large sample size allowed functional brain activity to be decomposed into a smaller number of distinct networks using factor analysis (a data-reduction method). Next, these networks were tested for relationships with various phenotypes. Adolescents who had experimented with either alcohol, cigarettes or illicit substances showed reduced activity in an orbitofrontal cortex network on successful stop trials, even for those adolescents with only 1-4 total lifetime alcohol uses. For adolescents who had used illicit substances, there was hyperactivity in a right frontal network (inferior frontal gyrus, cingulate and insula), an effect that remained even after

controlling for nicotine and alcohol effects. In contrast, ADHD symptoms were associated with bilateral frontal (inferior frontal gyri, anterior cingulate, and anterior insula) and basal ganglia networks only on unsuccessful stop trials. Individual differences in the speed of the inhibition process on the SST were associated with activity in the right frontal network, and with activity in the basal ganglia. Finally, the right frontal network was also associated with allelic variation in a single nucleotide polymorphism located in the SLC6A2 gene, which codes for the norepinephrine transporter (see summary figure).

Understanding the neural correlates of impulsivity subtypes is important because it yields insights into the etiology of maladaptive impulsive behaviors. Disentangling the biological basis of substance misuse and ADHD symptoms has proven difficult previously because, for example, adults who misuse substances are more likely to retrospectively endorse childhood ADHD symptoms (Ivanov *et al*, 2008). However, Whelan *et al*.'s (2012) results suggest that ADHD symptoms and adolescent substance misuse can be separated, at least in terms of brain activity during a test of inhibitory control. A goal of future research will be to shed more light on the structural, functional, neurochemical, and genetic underpinnings of the various impulsivity brain networks.

References

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Figure caption: The impulsivity networks and associated phenotypes described in Whelan *et al* (2012), for both trials on which subjects successfully inhibited an already initiated motor response (Stop Success) and trials on which subjects failed to inhibit (Stop Fail). A: anterior; ADHD; attention deficit hyperactivity disorder; OFC: orbitofrontal cortex; NET: norepinephrine transporter.

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Basal ganglia network

Faster inhibition

Right frontal network

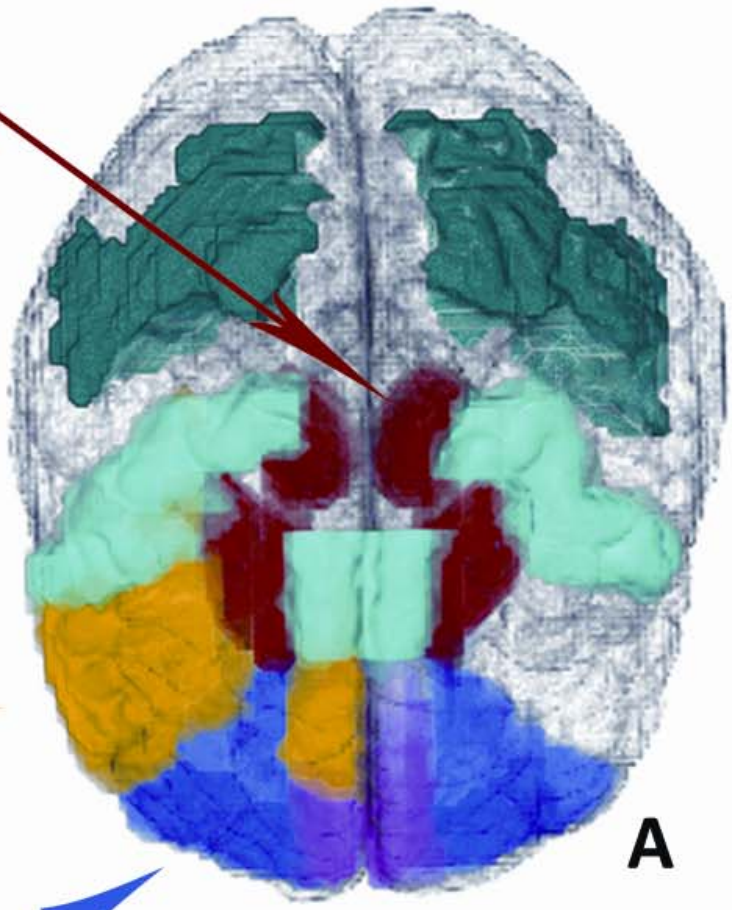
Faster inhibtion

Illicit substance misuse

Allelic variation in NET gene

OFC network

Alcohol, nicotine or illicit substance misuse



Stop Success

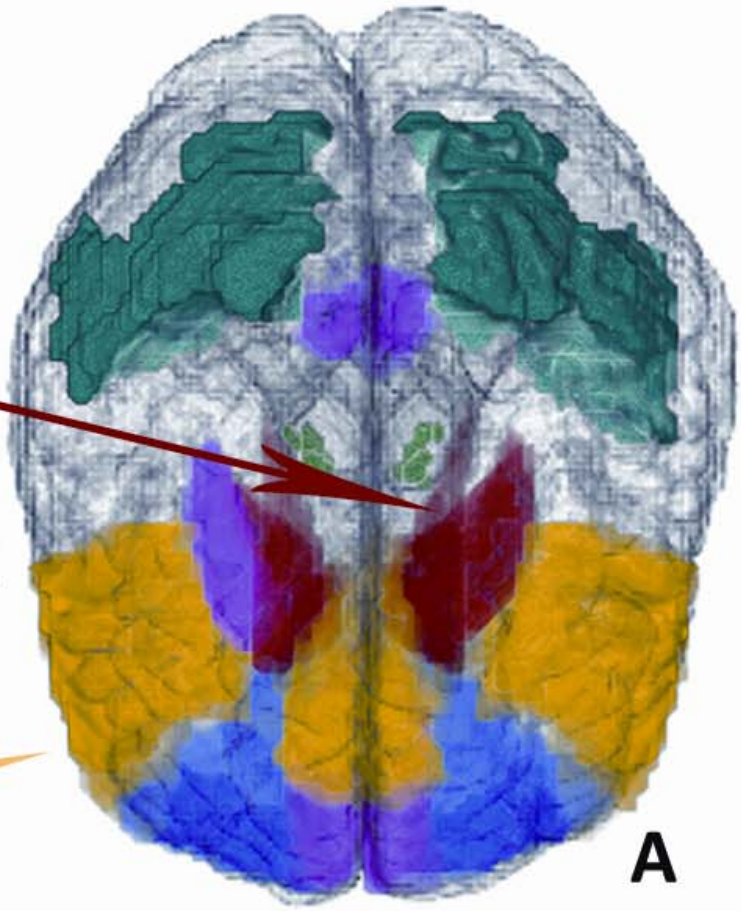
Basal ganglia network

ADHD symptoms

Bilateral frontal network

Faster inhibtion

ADHD symptoms



Stop Fail