

The Science of Impulsive Behaviour

What is meant by impulsive behaviour?

People who are impulsive tend to act before thinking. There are many varieties of impulsivity from the premature expression of behaviour before sufficient information is gathered ('reflection impulsivity') to the tendency of accepting small immediate or likely rewards as opposed to larger but delayed or unlikely rewards ('choice' impulsivity). It is also on occasion associated with aggression. In conceptual terms it is helpful to categorise impulsivity into 'stopping' and 'waiting' subtypes. In the former case this is assessed by the inhibition or cancellation of a response that has already been started. This is different from 'waiting' impulsivity which is best described as a dislike or intolerance of delayed rewards.

Why is it important to study this?

Impulsivity is part of everyday normal life and indeed it is often an advantage to make decisions without first weighing up every conceivable possibility! However, impulsivity can be severe and persistent in some individuals particularly those suffering from attention-deficit hyperactivity disorder (ADHD), substance abuse and addiction, mania and anti-social behaviour. Understanding the cause of deficient impulse control in such individuals, therefore, may shed new light on underlying brain mechanisms and thereby facilitate the development of new therapies. For many years the mainstream treatment for ADHD has been stimulant drugs such as amphetamine and methylphenidate (or Ritalin[®]). However, despite intensive research we are still unclear how these drugs work to alleviate impulsivity. The same is true for newer non-stimulant based medications such as atomoxetine (Strattera[®]). By deciphering the brain mechanisms responsible for causing ADHD it is hoped that effective treatments can be developed to target the different subtypes of impulsivity as well as preventing the emergence of co-occurring brain disorders such as addiction.

What has research discovered in this area?

ADHD is a common developmental brain disorder that manifests early in life and is characterised by inattentiveness, hyperactivity and impulsivity. The prevalence of ADHD is in the range of 2-5% and the disorder has a strong genetic basis. About two thirds of children with ADHD continue to experience symptoms as adults. In the last few years researchers have generally concluded that ADHD is a highly variable clinical disorder that can fluctuate in intensity over relatively short time periods in affected individuals. This inherent variability has hampered the search for a core biological mechanism. Nevertheless, there has been a remarkable convergence of findings from studies using modern

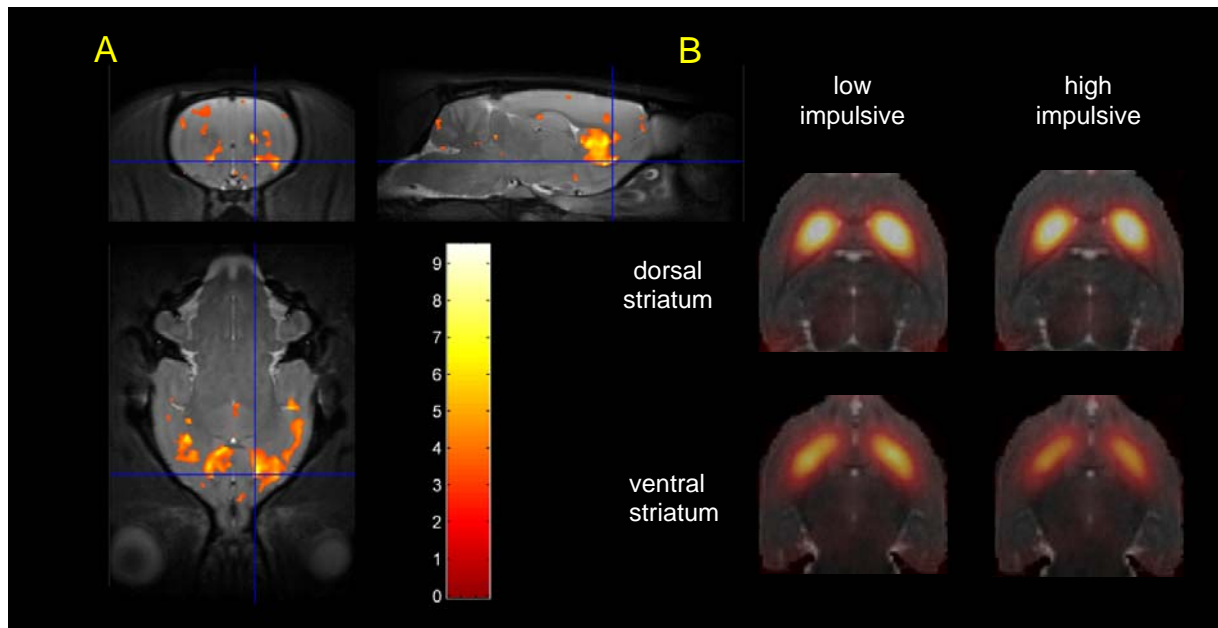
brain imaging techniques such as functional magnetic resonance imaging (MRI) and positron emission tomography (PET). The main conclusions from this work indicate smaller volumes and reduced activation of the cerebellum and fronto-striatal systems, including especially the prefrontal cortex and caudate. The dramatic effectiveness of stimulant drugs in ADHD, which increase levels of the brain chemicals dopamine and noradrenaline, suggests that the underlying pathology in ADHD could involve problems with their function. However, the precise nature of this impairment remains the focus of current research.

Other lines of research have investigated the controversial relationship between impulsivity and drug addiction. Although impulsivity may be a pre-existing personality trait that pre-disposes individuals to addiction, one of the consequences of taking drugs may be the development of impulsivity. *A key question, therefore, is resolving how impulsivity contributes causally to the development of addiction.* Work in our laboratory has begun to address this issue using animal models in which the genetic background and behavioural profile of the animal can be assessed, prior to any controlled exposure to drugs of abuse. This research has led to the discovery that naturally impulsive rats (they can't wait for future rewards!) lose control over their intake of cocaine and gradually develop a compulsive habit.

By bingeing on cocaine the impulsive rats reduce their naturally impulsive behavioural tendencies, an outcome that is clearly analogous to the beneficial effects of stimulant drugs in ADHD. In other research we have investigated the biological basis of impulsivity in rats using MRI and PET (see below). Key findings include the demonstration that high impulsive rats show (1) a reduction in the uptake of the dopamine $D_{2/3}$ receptor ligand 18F-fallypride in the ventral striatum (an index of the level of dopamine receptors) (2) a significant loss of grey matter in the core sub-region of the nucleus accumbens (a region within the ventral striatum) along with reductions in markers of function for the brain chemical known as GABA.

Where might this research lead?

The results of this research indicate pre-existing structural and chemical abnormalities in a region of the forebrain known as the nucleus accumbens core, which may be involved in the expression of impulsivity and drug addiction. A risk factor for both disorders appears to involve a reduced level of dopamine $D_{2/3}$ receptors in the striatum. The additional detection of abnormalities in GABA-ergic function in impulsive rats suggests this may be promising early biomarker for disorders of impulse control, including drug addiction.



Structural MRI and PET brain imaging in rats: the images on the left (A) are examples of voxel-based morphometry (VBM) used to detect changes in the density of grey matter in the brain; the images on the right (B) show uptake of the selective dopamine $D_{2/3}$ receptor antagonist ^{18}F -fallypride in the dorsal and ventral striatum of low and high impulsive rats. Note the reduced uptake of ^{18}F -fallypride in the ventral striatum of high impulsive rats.

Jeff Dalley^{1,2,3}, Daniele Caprioli^{1,2}, Trevor Robbins^{1,2}, Barry Everitt^{1,2},
 Tim Fryer^{1,4}, Franklin Aigbirhio^{1,4}, Adrian Carpenter⁴, Steve Sawiak^{1,4}

University of Cambridge

Behavioural and Clinical Neuroscience Institute¹
 Department of Experimental Psychology²
 Department of Psychiatry³
 Wolfson Brain Imaging Centre⁴

For more information contact Dr Jeff Dalley (jwd20@cam.ac.uk). This research was funded by the UK Medical Research Council and Wellcome Trust.