Selected reference - Trevor Robbins

Ersche, K. D., Williams, G. B., Robbins, T. W., & Bullmore, E. T. (2013). Meta-analysis of structural brain abnormalities associated with stimulant drug dependence and neuroimaging of addiction vulnerability and resilience. *Current Opinion in Neurobiology, 23,* 615-624.
Notes: Since the first study in stimulant-dependent individuals using structural MRI was published fifteen years ago, much evidence has accumulated on brain abnormalities associated with stimulant drug dependence. Here we conducted a voxel-based morphometry meta-analysis of published MRI data in stimulant-dependent individuals to clarify the most robust abnormalities underlying the disorder. We found that neuroimaging studies in stimulant-dependent individuals consistently report a gray matter decline in the prefrontal cortex regions associated with self-regulation and self-awareness. One of the next key questions that neuroimaging research today needs to address is the question of causality, namely to what extent these brain abnormalities are caused by the toxic effects of drug exposure, or the possibility that these may have predated drug-taking and even predisposed individuals for the development of drug dependence. Although the question of causality has not yet been answered completely, there has been significant progress made to date
University of Cambridge, Behavioural and Clinical Neuroscience Institute, Cambridge, UK. Electronic address: ke220@cam.ac.uk

Smith, D. G. & Robbins, T. W. (2013). The neurobiological underpinnings of obesity and binge eating: a rationale for adopting the food addiction model. *Biological Psychiatry, 73,* 804-810.
Notes: The food addiction model of overeating has been proposed to help explain the widespread advancement of obesity over the last 30 years. Parallels in neural substrates and neurochemistry, as well as corresponding motivational and behavioral traits, are increasingly coming to light; however, there are still key differences between the two disorders that must be acknowledged. We critically examine these common and divergent characteristics using the theoretical framework of prominent drug addiction models, investigating the neurobiological underpinnings of both behaviors in an attempt to justify whether classification of obesity and binge eating as an addictive disorder is merited
Behavioural and Clinical Neuroscience Institute and Department of Psychology, University of Cambridge, Cambridge, United Kingdom. ds555@cam.ac.uk

Blakemore, S. J. & Robbins, T. W. (2012). Decision-making in the adolescent brain. *Nature Neuroscience, 15,* 1184-1191.
Notes: Adolescence is characterized by making risky decisions. Early lesion and neuroimaging studies in adults pointed to the ventromedial prefrontal cortex and related structures as having a key role in decision-making. More recent studies have fractionated decision-making processes into its various components, including the representation of value, response selection (including inter-temporal choice and cognitive control), associative learning, and affective and social aspects. These different aspects of decision-making have been the focus of investigation in recent studies of the adolescent brain. Evidence points to a dissociation between the relatively slow, linear development of impulse control and response inhibition during adolescence versus the nonlinear

development of the reward system, which is often hyper-responsive to rewards in adolescence. This suggests that decision-making in adolescence may be particularly modulated by emotion and social factors, for example, when adolescents are with peers or in other affective ('hot') contexts
Institute of Cognitive Neuroscience, University College London, London, UK

Ersche, K. D., Turton, A. J., Chamberlain, S. R., Muller, U., Bullmore, E. T., & Robbins, T. W. (2012). Cognitive dysfunction and anxious-impulsive personality traits are endophenotypes for drug dependence. *American Journal of Psychiatry, 169*, 926-936.
Notes: OBJECTIVE Not everyone who takes drugs becomes addicted, but the likelihood of developing drug addiction is greater in people with a family history of drug or alcohol dependence. Relatively little is known about how genetic risk mediates the development of drug dependence. By comparing the phenotypic profile of individuals with and without a family history of addiction, the authors sought to clarify the extent to which cognitive dysfunction and personality traits are shared by family members-and therefore likely to have predated drug dependence-and which aspects are specific to drug-dependent individuals. METHOD The authors assessed cognitive function and personality traits associated with drug dependence in stimulant-dependent individuals (N=50), their biological siblings without a history of drug dependence (N=50), and unrelated healthy volunteers (N=50). RESULTS Cognitive function was significantly impaired in the stimulant-dependent individuals across a range of domains. Deficits in executive function and response control were identified in both the stimulant-dependent individuals and in their non-drug-dependent siblings. Drug-dependent individuals and their siblings also exhibited elevated anxious-impulsive personality traits relative to healthy comparison volunteers. CONCLUSIONS Deficits in executive function and response regulation as well as anxious-impulsive personality traits may represent endophenotypes associated with the risk of developing cocaine or amphetamine dependence. The identification of addiction endophenotypes may be useful in facilitating the rational development of therapeutic and preventive strategies

Robbins, T. W., Gillan, C. M., Smith, D. G., de Wit, S., & Ersche, K. D. (2012). Neurocognitive endophenotypes of impulsivity and compulsivity: towards dimensional psychiatry. *Trends in Cognitive Sciences, 16*, 81-91.
Notes: A key criticism of the main diagnostic tool in psychiatry, the Diagnostic and Statistical Manual of Mental Health Disorders (DSM-IV), is that it lacks a biological footing. In this article, we argue for a biological approach to psychiatry based on 'neurocognitive endophenotypes', whereby changes in behavioural or cognitive processes are associated with discrete deficits in defined neural systems. We focus on the constructs of impulsivity and compulsivity as key examples of the approach and discuss their possible cross-diagnostic significance, applying them to co-morbidities and commonalities across a range of disorders (attention-deficit/hyperactivity disorder, substance dependence, obsessive-compulsive disorder and eating disorders). We argue that this approach has important implications for the future classification of psychiatric disorders, genetics and therapeutics
Behavioural and Clinical Neuroscience Institute, University of Cambridge, Cambridge CB2 3EB, UK. twr2@cam.ac.uk

Dalley, J. W., Everitt, B. J., & Robbins, T. W. (2011). Impulsivity, compulsivity, and top-down cognitive control. *Neuron, 69,* 680-694.
Notes: Impulsivity is the tendency to act prematurely without foresight. Behavioral and neurobiological analysis of this construct, with evidence from both animal and human studies, defines several dissociable forms depending on distinct cortico-striatal substrates. One form of impulsivity depends on the temporal discounting of reward, another on motor or response disinhibition. Impulsivity is commonly associated with addiction to drugs from different pharmacological classes, but its causal role in human addiction is unclear. We characterize in neurobehavioral and neurochemical terms a rodent model of impulsivity based on premature responding in an attentional task. Evidence is surveyed that high impulsivity on this task precedes the escalation subsequently of cocaine self-administration behavior, and also a tendency toward compulsive cocaine-seeking and to relapse. These results indicate that the vulnerability to stimulant addiction may depend on an impulsivity endophenotype. Implications of these findings for the etiology, development, and treatment of drug addiction are considered
Behavioural and Clinical Neuroscience Institute, University of Cambridge, Downing Street, Cambridge CB2 3EB, UK; Department of Experimental Psychology, University of Cambridge, Downing Street, Cambridge CB2 3EB, UK; Department of Psychiatry, University of Cambridge, Addenbrooke's Hospital, Hills Road, Cambridge CB2 2QQ, UK

Robbins, T. W. & Crockett, M. J. (2010). Role of central serotonin in impulsivity and compulsivity: Comparative studies in experimental animals and humans. In C.P.Müller & B. L. Jacobs (Eds.), *Handbook of the behavioral neurobiology of serotonin* pp. 415-427). Amsterdam: Elsevier.
Notes: Handbook of behavioral neuroscience, Vol.21

Robbins, T. W., Everitt, B. J., & Nutt, D. J. (2010). Introduction: The neurobiology of drug addiction - new vistas. In T.W.Robbins, B. J. Everitt, & D. J. Nutt (Eds.), *The neurobiology of addiction: New vistas* (pp. 1-4). Oxford: Oxford University Press.

Robbins, T. W. & Arnsten, A. F. (2009). The neuropsychopharmacology of fronto-executive function: monoaminergic modulation. *Annual Review of Neuroscience, 32,* 267-287.
Notes: We review the modulatory effects of the catecholamine neurotransmitters noradrenaline and dopamine on prefrontal cortical function. The effects of pharmacologic manipulations of these systems, sometimes in comparison with the indoleamine serotonin (5-HT), on performance on a variety of tasks that tap working memory, attentional-set formation and shifting, reversal learning, and response inhibition are compared in rodents, nonhuman primates, and humans using, in a behavioral context, several techniques ranging from microiontophoresis and single-cell electrophysiological recording to pharmacologic functional magnetic resonance imaging. Dissociable effects of drugs and neurotoxins affecting these monoamine systems suggest new ways of conceptualizing state-dependent fronto-executive functions, with implications for understanding the molecular genetic basis of mental illness and its treatment

Department of Experimental Psychology, and Behavioral and Clinical Neuroscience Institute, University of Cambridge, Cambridge CB23EB, UK. twr2@cam.ac.uk

Cools, R., Roberts, A. C., & Robbins, T. W. (2008). Serotoninergic regulation of emotional and behavioural control processes. *Trends in Cognitive Sciences, 12,* 31-40.
Notes: F. C. Donders Centre for Cognitive Neuroimaging, Radboud University Nijmegen, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands. roshan.cools@fcdonders.ru.nl
5-Hydroxytryptamine (5-HT, serotonin) has long been implicated in a wide variety of emotional, cognitive and behavioural control processes. However, its precise contribution is still not well understood. Depletion of 5-HT enhances behavioural and brain responsiveness to punishment or other aversive signals, while disinhibiting previously rewarded but now punished behaviours. Findings suggest that 5-HT modulates the impact of punishment-related signals on learning and emotion (aversion), but also promotes response inhibition. Exaggerated aversive processing and deficient response inhibition could underlie distinct symptoms of a range of affective disorders, namely stress- or threat-vulnerability and compulsive behaviour, respectively. We review evidence from studies with human volunteers and experimental animals that begins to elucidate the neurobiological systems underlying these different effects
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Dalley, J. W., Mar, A. C., Economidou, D., & Robbins, T. W. (2008). Neurobehavioral mechanisms of impulsivity: fronto-striatal systems and functional neurochemistry. *Pharmacology,Biochemistry,and Behavior, 90,* 250-260.
Notes: Impulsive acts and decisions are a part of everyday normal behavior. However, in its pathological forms, impulsivity can be a debilitating disorder often associated with a number of neuropsychiatric disorders, including attention-deficit hyperactivity disorder (ADHD). This article reviews recent progress in our understanding of the neurobiology of impulsivity using examples from recent investigations in experimental animals. Evidence is reviewed from several well-established paradigms with putative utility in assessing distinct forms of impulsive behavior in rodents, including the 5-choice serial reaction time (5CSRT) task and the delay discounting paradigm. We discuss, in particular, recent psychopharmacological and in-vivo neurochemical data in task-performing rats showing functional heterogeneity of the forebrain dopamine (DA), noradrenaline (NA), serotonin (5-HT) and acetylcholine (ACh) systems and identify how these systems normally function to facilitate flexible goal-directed behavior in situations that tax basic attentional functions and inhibitory response control mechanisms. We also discuss future research needs in terms of understanding the functional diversity of different sub-regions of prefrontal cortex (PFC) and how these systems normally interact with the striatum and main nuclei of origin of DA and NA neurons. Finally, we argue in line with others that animal paradigms are unlikely to model all aspects of complex psychiatric conditions such as ADHD but components of such syndromes may be amenable to investigation using sophisticated animal models based on highly-defined psychiatric endophenotypes
Behavioral and Clinical Neuroscience Institute, University of Cambridge, Downing St, Cambridge, CB2 3EB, UK. jwd20@cam.ac.uk

Everitt, B. J., Belin, D., Economidou, D., Pelloux, Y., Dalley, J. W., & Robbins, T. W. (2008). Review. Neural mechanisms underlying the vulnerability to develop compulsive drug-seeking habits and addiction. *Philosophical Transactions of the Royal Society.B: Biolological Sciences, 363,* 3125-3135.
Notes: We hypothesize that drug addiction can be viewed as the endpoint of a series of transitions from initial voluntary drug use through the loss of control over this behaviour, such that it becomes habitual and ultimately compulsive. We describe evidence that the switch from controlled to compulsive drug seeking represents a transition at the neural level from prefrontal cortical to striatal control over drug-seeking and drug-taking behaviours as well as a progression from ventral to more dorsal domains of the striatum, mediated by its serially interconnecting dopaminergic circuitry. These neural transitions depend upon the neuroplasticity induced by chronic self-administration of drugs in both cortical and striatal structures, including long-lasting changes that are the consequence of toxic drug effects. We further summarize evidence showing that impulsivity, a spontaneously occurring behavioural tendency in outbred rats that is associated with low dopamine D2/3 receptors in the nucleus accumbens, predicts both the propensity to escalate cocaine intake and the switch to compulsive drug seeking and addiction
Department of Experimental Psychology, Behavioural and Clinical Neuroscience Institute, University of Cambridge, Downing Street, Cambridge, UK. bje10@cam.ac.uk

Robbins, T. W., Everitt, B. J., & Nutt, D. J. (2008). Introduction. The neurobiology of drug addiction: new vistas. *Philosophical Transactions of the Royal Society.B: Biolological Sciences, 363,* 3109-3111.
Notes: Experimental Psychology and Behavioural and Clinical Neuroscience Institute, University of Cambridge, Cambridge, UK. twr2@cam.ac.uk