Supplementary Materials

Cognitive dysfunction and anxious-impulsive personality traits are endophenotypes for drug dependence

Karen D. Ersche, Abigail J. Turton, Samuel R. Chamberlain, Ulrich Müller,
Edward T. Bullmore and Trevor W. Robbins

Supplementary Methods

Study sample

Consistent with previous research (25, 26, 112), a considerable number of drug-dependent individuals also met criteria for major depression (44%) and/or anxiety disorder (42%). Two drug-dependent individuals (4%) satisfied the diagnostic criteria for obsessive-compulsive disorder and one drug user was HIV positive. There were correspondingly higher levels of concomitant medication prescribed to the drugs users and their siblings than to the healthy volunteers. Thus, four drug-dependent individuals (8%) were prescribed d-amphetamine and twenty-three drug-dependent individuals (46%) received methadone on prescription. Further concomitant mediation in the drug user group was as followed: antidepressants (serotonin-reuptake inhibitors: 16%, tricyclic antidepressants: 10%), benzodiazepines (diazepam 8%), mediation for hypertension (telmisartan 2%, propanolol 2%) or pain relief (gabapentin 4%), and agents for the treatment of asthma (beclomethhasone 4%), HIV (abacavir/lamivudine 2%), or heartburn (omeprazole 2%).

Affective disorders were also present in the sibling group: three siblings had a current diagnosis of major depressive disorder (6%) and 12 had an anxiety disorder (24%). Two siblings were currently prescribed antibiotics (4%), another two were taken mediation against heartburn (4%). There were no axis I disorders in the control group; one control volunteer received treatment for asthma (beclomethhasone), another was receiving medication for heartburn (omeprazole), and one control volunteer was receiving antibiotics for the treatment of acne. We deliberately specified the eligibility criteria to be minimally exclusive because minor psychopathology in relatives or co-morbidity in drug-dependent individuals may be clinical markers of genetic risk and the identification of endophenotypes will not benefit from exclusion of high-risk individuals.

During the assessment session, all participants were asked whether anyone (or anyone else) in their family uses drugs or drinks heavily. If this was the case, participants were asked whether the use was problematic and why. The sibling pairs were assessed simultaneously but separately from each other and their reports about parental drug use concurred in all 50 pairs.

Some individuals in the sibling or volunteer groups were tobacco smokers (siblings: 54% current, 38% past tobacco smokers; volunteers: 12% current, 46% past tobacco smokers) and reported recreational use of cannabis (siblings: 10% current, 66% past; volunteers: 22% past). All urine screens provided by siblings and healthy volunteers were negative for drugs of abuse

Figure S1: Recruitment process: Stimulant-dependent individuals with a biological sibling were either referred by treatment services or self-referred to the study. The two most common reasons for the exclusion of the stimulant-dependent individuals were a non-biological sibling or a co-morbid psychotic disorder. Only stimulant-dependent individuals, who passed the screening process with regard to inclusion/exclusion criteria, were asked to contact one sibling to consider participation. The most common reason for exclusion for siblings was alcohol abuse. Healthy control volunteers were recruited through local advertisements also underwent a careful screening process. The two most common reasons for exclusion were current treatment with antidepressants or a family history of mental health problems. Healthy volunteers were matched as closely as possible to the sib-pairs with regard to age, gender and education level.

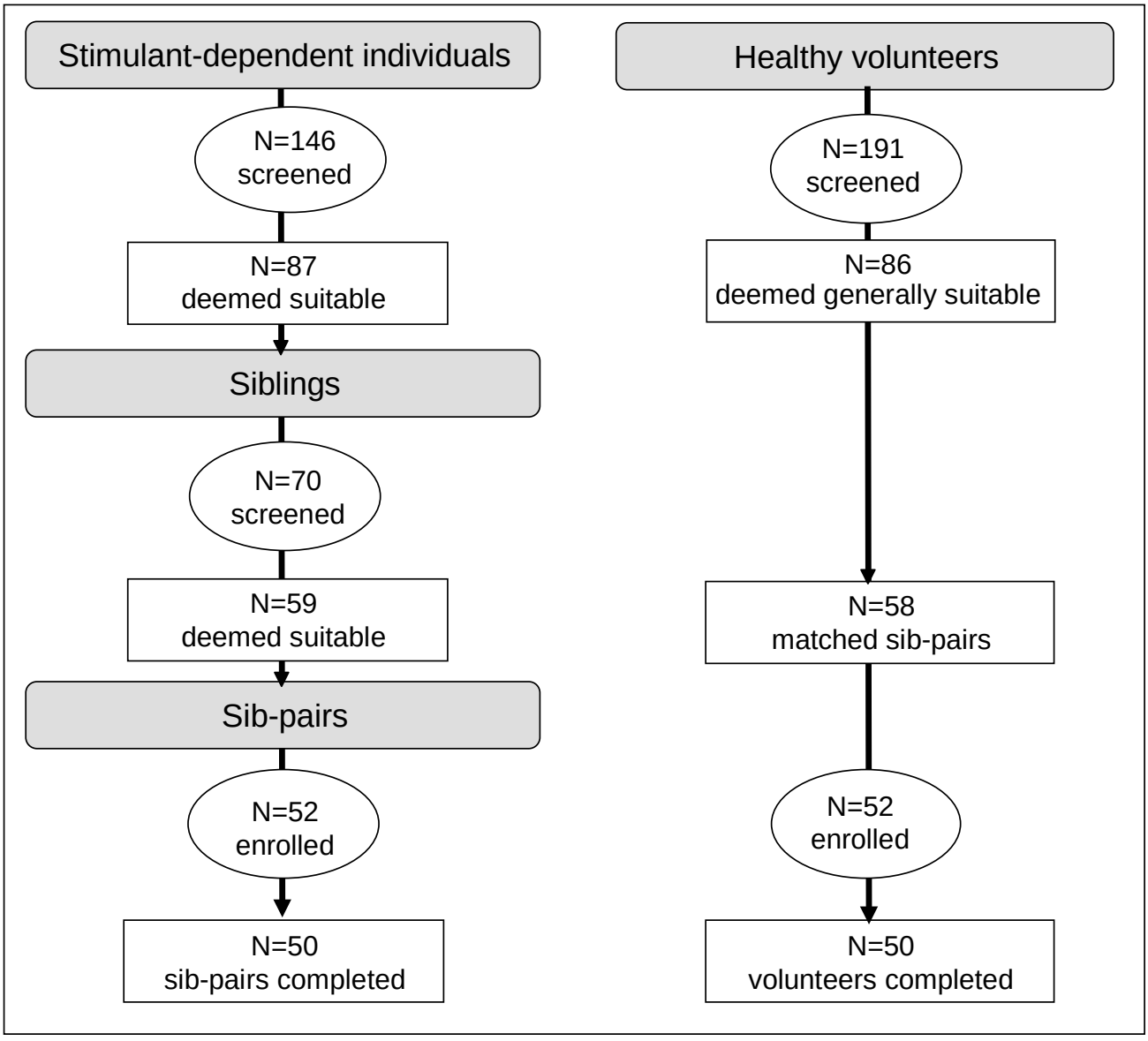

Table S1: Correlation Matrix

		Executive function	Visual memory	Attention	Response control	Emotional functioning	Psychosocial functioning	Impulsive-Compulsive	Self-evaluation traits
Executive function	Pearson *r*	1.000	0.108	0.143	0.319	0.416	0.313	-0.341	0.236
	P		0.190	0.085	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.004**
Visual memory	Pearson *r*	0.108	1.000	-0.007	0.055	0.114	-0.025	-0.077	0.120
	P	0.190		0.937	0.505	0.165	0.766	0.348	0.145
Attention	Pearson *r*	0.143	-0.007	1.000	0.315	0.040	0.052	0.035	0.173
	P	0.085	0.937		**<0.001**	0.630	0.530	0.677	**0.037**
Response control	Pearson *r*	0.319	0.055	0.315	1.000	0.240	0.169	-0.128	0.193
	P	**<0.001**	0.505	**<0.001**		**0.003**	**0.040**	0.121	**0.018**
Emotional functioning	Pearson *r*	0.416	0.114	0.040	0.240	1.000	0.507	-0.479	0.585
	P	**<0.001**	0.165	0.630	**0.003**		**<0.001**	**<0.001**	**<0.001**
Psychosocial functioning	Pearson *r*	0.313	-0.025	0.052	0.169	0.507	1.000	-0.171	0.421
	P	**<0.001**	0.766	0.530	**0.040**	**<0.001**		**0.036**	**<0.001**
Impulsive-compulsive traits	Pearson *r*	-0.341	-0.077	0.035	-0.128	-0.479	-0.171	1.000	-0.331
	P	**<0.001**	0.348	0.677	0.121	**<0.001**	**0.036**		**<0.001**
Self-Evaluation traits	Pearson *r*	0.236	0.120	0.173	0.193	0.585	0.421	-0.331	1.000
	P	**0.004**	0.145	**0.037**	**0.018**	**<0.001**	**<0.001**	**<0.001**	

TABLE S2. Summary of the Neuropsychological Tests Used for the Cognitive Assessment

Domain	Task[a]	Description	Behavioral Variables	Evidence for Impairment Associated With Stimulant Abuse
CANTAB executive function battery	Spatial Working Memory	A self-ordered search task involving a search through a spatial array of colored boxes for tokens, without returning to a box which had already contained a token (76); duration: 8 minutes	Strategy score (a high strategy score reflects an inefficient strategy); total errors; token-search time (ms)	Preclinical (77); clinical (16;18)
	One-Touch Stockings of Cambridge	A spatial planning test involving planning a sequence of move s to achieve a goal arrangement of colored balls without moving the balls (78); duration: 10–15 minutes	Mean attempts to solve planning problems at varying levels of difficulty (easy solutions require 1–2 moves, medium solutions require 2–4 moves, hard solutions require 5–6 moves of mental planning)	Preclinical (79); clinical (15;16)
CANTAB visual memory battery	Pattern Recognition Memory	A two-choice test of abstract visual pattern recognition memory (80); duration: 5 minutes plus 25-minute delay	Percentage correct; response time (ms)	Preclinical (79); clinical (15)
	Paired Associates Learning	A test of episodic memory which involves the learning of spatial locations of geometric visual patterns (81); duration: 10–15 minutes	First trial memory score (sum of patterns correctly located after first presentation); total trials needed to learn the paired associates; total errors made to learn the paired associates	Preclinical (82); clinical (15;18)
CANTAB attentional battery	Reaction Time	A reaction time task which uses a procedure to separate response latency from movement time (83); duration: 5 minutes	Accuracy score; premature responses; response time (ms)	Preclinical (84;85); clinical (86)
	Rapid Visual Information Processing	A test of sustained attention in which infrequent 3-digit sequences have to be detected from among serially presented digits (87); duration: 8 minutes	A' (target sensitivity, a measure of discriminability between signal and noise; scores range from –1 to 1, with 0.5 equal to chance; higher A' indicate better target discrimination); B" (response bias, a measure of an individual's response strategy (liberal versus conservative); scores range from –1 to 1); commission errors (incorrectly identified targets); omission errors (missed targets); response time (ms)	Preclinical (88); clinical (18;21)
Response Control	Stop-Signal Task	A test of response inhibition which uses staircase functions to generate an estimate of stop signal reaction time. Stop signals are presented such that the probability of successful inhibition is approximately 50% (89;90); duration: 20 minutes	Percent of successful stop trials; reaction time on successful go trials (ms); reaction time following stop trials (ms); SSRT (measure of response inhibition)	Preclinical (91;92); clinical (21;93-95)

[a] The tasks were administered to all participants approximately 2 hours after their arrival in the following order: Pattern Recognition Memory (immediate), Rapid Visual Information Processing, Spatial Working Memory; Reaction Time, Pattern Recognition Memory (delay), Paired Associates Learning, and One-Touch Stockings of Cambridge; the Stop-Signal Task was administered approximately 2 hours later.

TABLE 3. Summary of the Measures of Clinical, Emotional, Psychosocial, and Personality Assessment in a Study of Endophenotypes for Drug Dependence[a]

Clinical Assessment	Abbreviation	Description
Structured Clinical Interview for DSM-IV-TR (42)	SCID	Diagnostic examination used to determine DSM-IV axis I and axis II disorders.
Drug Abuse Screening Test (44)	DAST-20	A quantitative index of whether a person's drug use is harmful or not. A cutoff score greater than 5 indicates probable drug abuse.
Alcohol Use Disorders Identification Test (45)	AUDIT	A quantitative index of whether a person's alcohol consumption is harmful. A cutoff score greater than 8 indicates probably alcohol abuse.
National Adult Reading Test (96)	NART	Estimation of premorbid intelligence levels of English-speaking individuals.
Childhood Trauma Questionnaire (97)	CTQ	Assessment of childhood maltreatment with regard to sexual, physical, and emotional abuse; emotional and physical neglect. The cutoff scores for the three abuse subscales are: for emotional abuse ≥13, for physical abuse ≥10, and for sexual abuse ≥8.
Emotional Functioning		
Beck Depression Inventory-II (98)	BDI-II	Index of depression severity; cut off scores for mild (14–19), moderate (20–28) severe depression (29–63)
Snaith-Hamilton Pleasure Scale (99)	SHAPS	A quantitative index of the presence and severity of anhedonia; cut-off score: ≥ 3
Spielberger Anxiety Inventory (100)	STAI	A quantitative index of the general propensity to be anxious (STAI-T) and a temporary state of feeling anxious (STAI-S). Cut-off score for clinically-relevant anxiety: >40
Perceived Stress Scale (101)	PSS-14	A quantitative index of the degree to which situations are appraised as stressful. Higher scores reflect higher levels of stress.
Psychosocial Functioning		
Community Integration Questionnaire (102)	CIQ	A quantitative index of an individual's integration into home and family life, social activity, and productive activity. Higher scores reflect better integration.
Impulsive and Compulsive Traits		
Barratt Impulsiveness Scale, Version 11 (103)	BIS-11	A quantitative index of trait-impulsivity. Scores are summed to yield one total score of the subscales for attention, motor behavior, nonplanning. Higher scores reflect greater levels of impulsivity.
Sensation-Seeking Scale, Form V (104)	SSS-V	A quantitative index of sensation-seeking. Scores are summed to yield one total score of the subscales for thrill and adventure seeking, experience seeking, disinhibition, boredom susceptibility. Higher scores reflect greater levels of sensation-seeking traits.
Behavioral-Approach/Behavioral Inhibition Scale (105)	BIS/BAS	The BIS items assess behavioral tendencies in the anticipation of punishment and the BAS items assess behavior in the anticipation of rewarding outcomes.
Padua Inventory for Obsessive-Compulsive Symptoms (106)	PI-WSUR	A quantitative index of common obsessional and compulsive behaviors. Scores are summed to yield one total score of the subscales for thoughts of harming self/others, impulses to harm self/others, contamination / washing, checking compulsions, and dressing/grooming. Higher scores reflect higher symptom levels.
Self-Evaluation traits		
General Self-Efficacy Scale (107)	GES	A quantitative index of a person's optimistic self-beliefs to cope with daily hassles and life events. Higher scores reflect higher levels of self-efficacy.
Social Comparison Rating Scale (108)	SCRS	A measure that uses the semantic-differential approach to assess how individuals evaluate themselves in relation to others. Higher scores reflect a better assimilation / more similarities with others.

Internal-External Scale (109)	I-E	A quantitative index of the degree to which a person feels that rewards in life are contingent on his/her own behavior or are controlled by external forces[a]. Higher scores reflect more external control beliefs.

[a] The three items of the Internal-External Scale referring to situations at school have been found inappropriate for adults(110;111) and were therefore removed from the scale.

References

1. Nutt DJ, Robbins TW, Stimson GV, Ince M, Jackson ARW: Drugs and the Future: Brain Science, Addiction and Society. Oxford, UK, Elsevier, 2006

2. Nutt D, King LA, Saulsbury W, Blakemore C: Development of a rational scale to assess the harm of drugs of potential misuse. Lancet 2007; 369:1047–1053 PubMed

3. Merikangas KR, Stolar M, Stevens DE, Goulet J, Preisig MA, Fenton B, Zhang HP, O'Malley SS, Rounsaville BJ: Familial transmission of substance use disorders. Arch Gen Psychiatry 1998; 55:973–979 PubMed

4. Kendler KS, Jacobson KC, Prescott CA, Neale MC: Specificity of genetic and environmental risk factors for use and abuse/dependence of cannabis, cocaine, hallucinogens, sedatives, stimulants, and opiates in male twins. Am J Psychiatry 2003; 160:687–695 PubMed

5. Tyrfingsson T, Thorgeirsson TE, Geller F, Runarsdottir V, Hansdottir I, Bjornsdottir G, Wiste AK, Jonsdottir GA, Stefansson H, Gulcher JR, Oskarsson H, Gudbjartsson D, Stefansson K: Addictions and their familiality in Iceland. Ann N Y Acad Sci 2010; 1187: 208–217

6. Zucker RA: The developmental behavior genetics of drug involvement: overview and comments. Behav Genet 2006; 36:616–625 PubMed

7. Vanyukov MM, Kirisci L, Moss L, Tarter RE, Reynolds MD, Maher BS, Kirillova GP, Ridenour T, Clark DB: Measurement of the risk for substance use disorders: phenotypic and genetic analysis of an index of common liability. Behav Genet 2009; 39:233–244 PubMed

8. Tsuang MT, Lyons MJ, Meyer JM, Doyle T, Eisen SA, Goldberg J, True W, Lin N, Toomey R, Eaves L: Co-occurrence of abuse of different drugs in men: the role of drug-specific and shared vulnerabilities. Arch Gen Psychiatry 1998; 55:967–972 PubMed

9. Bierut LJ: Genetic vulnerability and susceptibility to substance dependence. Neuron 2011; 69:618–627 PubMed

10. Gottesman II, Gould TD: The endophenotype concept in psychiatry: etymology and strategic intentions. Am J Psychiatry 2003; 160:636–645 PubMed
11. Dalley JW, Cardinal RN, Robbins TW: Prefrontal executive and cognitive functions in rodents: neural and neurochemical substrates. Neurosci Biobehav Rev 2004; 28:771–784 PubMed
12. Goldstein RZ, Volkow ND: Drug addiction and its underlying neurobiological basis: neuroimaging evidence for the involvement of the frontal cortex. Am J Psychiatry 2002; 159:1642–1652 PubMed
13. Fillmore MT, Rush CR: Impaired inhibitory control of behavior in chronic cocaine users. Drug Alcohol Depend 2002; 66:265–273 PubMed
14. Monterosso JR, Aron AR, Cordova X, Xu J, London ED: Deficits in response inhibition associated with chronic methamphetamine abuse. Drug Alcohol Depend 2005; 79:273–277 PubMed
15. Ersche KD, Clark L, London M, Robbins TW, Sahakian BJ: Profile of executive and memory function associated with amphetamine and opiate dependence. Neuropsychopharmacology 2006; 31:1036–1047 PubMed
16. Ornstein TJ, Iddon JL, Baldacchino AM, Sahakian BJ, London M, Everitt BJ, Robbins TW: Profiles of cognitive dysfunction in chronic amphetamine and heroin abusers. Neuropsychopharmacology 2000; 23:113–126 PubMed
17. Tomasi D, Goldstein RZ, Telang F, Maloney T, Alia-Klein N, Caparelli EC, Volkow ND: Widespread disruption in brain activation patterns to a working memory task during cocaine abstinence. Brain Res 2007; 1171:83–92
18. Ersche KD, Roiser JP, Lucas M, Domenici E, Robbins TW, Bullmore ET: Peripheral biomarkers of cognitive response to dopamine receptor agonist treatment. Psychopharmacology (Berl) 2011; 214:779–789 PubMed
19. Fernández-Serrano MJ, Pérez-García M, Schmidt Río-Valle J, Verdejo-García A: Neuropsychological consequences of alcohol and drug abuse on different components of executive functions. J Psychopharmacol 2010; 24:1317–1332 PubMed

20. Gooding DC, Burroughs S, Boutros NN: Attentional deficits in cocaine-dependent patients: converging behavioral and electrophysiological evidence. Psychiatry Res 2008; 160:145–154 PubMed
21. Ersche KD, Barnes A, Jones PS, Morein-Zamir S, Robbins TW, Bullmore ET: Abnormal structure of frontostriatal brain systems is associated with aspects of impulsivity and compulsivity in cocaine dependence. Brain 2011; 134:2013–2024 PubMed
22. London ED, Berman SM, Voytek B, Simon SL, Mandelkern MA, Monterosso J, Thompson PM, Brody AL, Geaga JA, Hong MS, Hayashi KM, Rawson RA, Ling W: Cerebral metabolic dysfunction and impaired vigilance in recently abstinent methamphetamine abusers. Biol Psychiatry 2005; 58:770–778 PubMed
23. Beveridge TJR, Smith HR, Daunais JB, Nader MA, Porrino LJ: Chronic cocaine self-administration is associated with altered functional activity in the temporal lobes of non human primates. Eur J Neurosci 2006; 23:3109–3118 PubMed
24. Beveridge TJR, Gill KE, Hanlon CA, Porrino LJ: Parallel studies of cocaine-related neural and cognitive impairment in humans and monkeys. Philos Trans R Soc Lond B Biol Sci 2008; 363:3257–3266
25. Regier DA, Farmer ME, Rae DS, Locke BZ, Keith SJ, Judd LL, Goodwin FK: Comorbidity of mental disorders with alcohol and other drug abuse: results from the Epidemiologic Catchment Area (ECA) study. JAMA 1990; 264:2511–2518 PubMed
26. Merikangas KR, Mehta RL, Molnar BE, Walters EE, Swendsen JD, Aguilar-Gaziola S, Bijl R, Borges G, Caraveo-Anduaga JJ, Dewit DJ, Kolody B, Vega WA, Wittchen HU, Kessler RC: Comorbidity of substance use disorders with mood and anxiety disorders: results of the International Consortium in Psychiatric Epidemiology. Addict Behav 1998; 23:893–907
27. Merikangas KR, Dierker LC, Szatmari P: Psychopathology among offspring of parents with substance abuse and/or anxiety disorders: a high-risk study. J Child Psychol Psychiatry 1998; 39:711–720 PubMed
28. Volkow ND: The reality of comorbidity: depression and drug abuse. Biol Psychiatry 2004; 56:714–717 PubMed

29. Kosten TR, Markou A, Koob GF: Depression and stimulant dependence: neurobiology and pharmacotherapy. J Nerv Ment Dis 1998; 186:737–745 PubMed

30. Markou A, Kosten TR, Koob GF: Neurobiological similarities in depression and drug dependence: a self-medication hypothesis. Neuropsychopharmacology 1998; 18:135–174 PubMed

31. Hawkins JD, Catalano RF, Miller JY: Risk and protective factors for alcohol and other drug problems in adolescence and early adulthood: implications for substance abuse prevention. Psychol Bull 1992; 112:64–105 PubMed

32. Fisher M, Crome I, Macleod J, Bloor R, Hickman M: Predictive factors for illicit drug use among young people: a literature review. Probation Journal 2007; 54:278–279

33. de Wit H: Impulsivity as a determinant and consequence of drug use: a review of underlying processes. Addict Biol 2009; 14:22–31 PubMed

34. Meda SA, Stevens MC, Potenza MN, Pittman B, Gueorguieva R, Andrews MM, Thomas AD, Muska C, Hylton JL, Pearlson GD: Investigating the behavioral and self-report constructs of impulsivity domains using principal component analysis. Behav Pharmacol 2009; 20:390–399 PubMed

35. Stephenson MT, Helme DW: Authoritative parenting and sensation seeking as predictors of adolescent cigarette and marijuana use. J Drug Educ 2006; 36:247–270 PubMed

36. Lawrance L, Rubinson L: Self-efficacy as a predictor of smoking behavior in young adolescents. Addict Behav 1986; 11:367–382 PubMed

37. Barkin SL, Smith KS, DuRant RH: Social skills and attitudes associated with substance use behaviors among young adolescents. J Adolesc Health 2002; 30:448–454 PubMed

38. Newcomb MD, Harlow LL: Life events and substance use among adolescents: mediating effects of perceived loss of control and meaninglessness in life. J Pers Soc Psychol 1986; 51:564–577 PubMed

39. Ersche KD, Turton AJ, Croudace T, Stochl J: Who do you think is in control in addiction? a pilot study on drug-related locus of control beliefs. Addict Disord Their Treatment (Epub ahead of print, Jan 15, 2012)

40. Dielman TE, Campanelli PC, Shope JT, Butchart AT: Susceptibility to peer pressure, self-esteem, and health locus of control as correlates of adolescent substance abuse. Health Educ Q 1987; 14:207–221 PubMed

41. Goldman D, Oroszi G, Ducci F: The genetics of addictions: uncovering the genes. Nat Rev Genet 2005; 6:521–532 PubMed

42. First MB, Spitzer RL, Gibbon M, Williams JBW: Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Non-Patient Edition (SCID-I/NP). New York, New York State Psychiatric Institute, Biometrics Research, 2002

43. Franken IHA, Hendriksa VM, van den Brink W: Initial validation of two opiate craving questionnaires the Obsessive Compulsive Drug Use Scale and the Desires for Drug Questionnaire. Addict Behav 2002; 27:675–685 PubMed

44. Gavin DR, Ross HE, Skinner HA: Diagnostic validity of the Drug Abuse Screening Test in the assessment of DSM-III drug disorders. Br J Addict 1989; 84:301–307 PubMed

45. Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M: Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption—II. Addiction 1993; 88:791–804 PubMed

46. Menzies L, Achard S, Chamberlain SR, Fineberg N, Chen CH, del Campo N, Sahakian BJ, Robbins TW, Bullmore E: Neurocognitive endophenotypes of obsessive-compulsive disorder. Brain 2007; 130:3223–3236 PubMed

47. Hartlage S, Alloy LB, Vázquez C, Dykman B: Automatic and effortful processing in depression. Psychol Bull 1993; 113:247–278 PubMed

48. Howell DC: Statistical Methods for Psychology. London, Duxbury Press, 1997

49. Bradley RG, Binder EB, Epstein MP, Tang Y, Nair HP, Liu W, Gillespie CF, Berg T, Evces M, Newport DJ, Stowe ZN, Heim CM, Nemeroff CB, Schwartz A, Cubells JF, Ressler KJ: Influence of child abuse

on adult depression: moderation by the corticotropin-releasing hormone receptor gene. Arch Gen Psychiatry 2008; 65:190–200 PubMed

50. Acheson A, Richard DM, Mathias CW, Dougherty DM: Adults with a family history of alcohol related problems are more impulsive on measures of response initiation and response inhibition. Drug Alcohol Depend 2011; 117:198–203 PubMed
51. Tarter RE, Kirisci L, Mezzich A, Cornelius JR, Pajer K, Vanyukov M, Gardner W, Blackson T, Clark D: Neurobehavioral disinhibition in childhood predicts early age at onset of substance use disorder. Am J Psychiatry 2003; 160:1078–1085 PubMed
52. Dawes MA, Tarter RE, Kirisci L: Behavioral self-regulation: correlates and 2-year follow-ups for boys at risk for substance abuse. Drug Alcohol Depend 1997; 45:165–176 PubMed
53. Nigg JT, Wong MM, Martel MM, Jester JM, Puttler LI, Glass JM, Adams KM, Fitzgerald HE, Zucker RA: Poor response inhibition as a predictor of problem drinking and illicit drug use in adolescents at risk for alcoholism and other substance use disorders. J Am Acad Child Adolesc Psychiatry 2006; 45:468–475 PubMed
54. Chambers RA, Taylor JR, Potenza MN: Developmental neurocircuitry of motivation in adolescence: a critical period of addiction vulnerability. Am J Psychiatry 2003; 160:1041–1052 PubMed
55. Kalivas PW, Volkow ND: The neural basis of addiction: a pathology of motivation and choice. Am J Psychiatry 2005; 162:1403–1413 PubMed
56. Ersche KD, Jones PS, Williams GB, Turton AJ, Robbins TW, Bullmore ET: Abnormal brain structure implicated in stimulant drug addiction. Science 2012; 335:601–604 PubMed
57. Ersche KD, Turton AJ, Pradhan S, Bullmore ET, Robbins TW: Drug addiction endophenotypes: impulsive versus sensation-seeking personality traits. Biol Psychiatry 2010; 68:770–773 PubMed
58. Newman JP, Wallace JF: Diverse pathways to deficient self-regulation: implications for disinhibitory psychopathology in children. Clin Psychol Rev 1993; 13:699–720

59. Whiteside SP, Lynam DR: The Five Factor Model and impulsivity: using a structural model of personality to understand impulsivity. Pers Individ Dif 2001; 30:669–689
60. Casey BJ, Jones RM, Hare TA: The adolescent brain. Ann NY Acad Sci 2008; 1124:111–126 PubMed
61. Steinberg L: Cognitive and affective development in adolescence. Trends Cogn Sci 2005; 9:69–74 PubMed
62. Lewis MD, Todd RM: The self-regulating brain: cortical-subcortical feedback and the development of intelligent action. Cogn Dev 2007; 22:406–430
63. Ernst M, Romeo RD, Andersen SL: Neurobiology of the development of motivated behaviors in adolescence: a window into a neural systems model. Pharmacol Biochem Behav 2009; 93:199–211 PubMed
64. Mann M, Hosman CMH, Schaalma HP, de Vries NK: Self-esteem in a broad-spectrum approach for mental health promotion. Health Educ Res 2004; 19:357–372 PubMed
65. DiClimente CC: Self-efficacy and the addictive behaviours. J Soc Clin Psychol 1986; 4:302–315
66. Narvaez JCM, Magalhaes PVS, Trindade EK, Vieira DC, Kauer-Sant'Anna M, Gama CS, von Diemen L, Kapczinski NS, Kapczinski F: Childhood trauma, impulsivity, and executive functioning in crack cocaine users. Compr Psychiatry 2012; 53:238–244 PubMed
67. Brodsky BS, Oquendo M, Ellis SP, Haas GL, Malone KM, Mann JJ: The relationship of childhood abuse to impulsivity and suicidal behavior in adults with major depression. Am J Psychiatry 2001; 158:1871–1877 PubMed
68. Roy A: Childhood trauma and impulsivity: possible relevance to suicidal behavior. Arch Suicide Res 2005; 9:147–151 PubMed
69. Pechtel P, Pizzagalli DA: Effects of early life stress on cognitive and affective function: an integrated review of human literature. Psychopharmacology (Berl) 2011; 214:55–70 PubMed

70. Verdejo-García A, Pérez-García M: Profile of executive deficits in cocaine and heroin polysubstance users: common and differential effects on separate executive components. Psychopharmacology (Berl) 2007; 190:517–530 PubMed

71. Pace-Schott EF, Morgan PT, Malison RT, Hart CL, Edgar C, Walker M, Stickgold R: Cocaine users differ from normals on cognitive tasks which show poorer performance during drug abstinence. Am J Drug Alcohol Abuse 2008; 34:109–121 PubMed

72. Woicik PA, Moeller SJ, Alia-Klein N, Maloney T, Lukasik TM, Yeliosof O, Wang GJ, Volkow ND, Goldstein RZ: The neuropsychology of cocaine addiction: recent cocaine use masks impairment. Neuropsychopharmacology 2008; 34:1112–1122

73. Kreek MJ, Koob GF: Drug dependence: stress and dysregulation of brain reward pathways. Drug Alcohol Depend 1998; 51:23–47 PubMed

74. Sinha R: How does stress increase risk of drug abuse and relapse? Psychopharmacology (Berl) 2001; 158:343–359 PubMed

75. Lee ACH, Owen AM, Rogers RD, Sahakian BJ, Robbins TW: Utility of CANTAB in Functional Neuroimaging, in Functional Neuroimaging in Child Psychology. Edited by Ernst M, Rumsey J. Cambridge, UK, Cambridge University Press, 2000, pp 366–377

76. Owen AM, Downes JJ, Sahakian BJ, Polkey CE, Robbins TW: Planning and spatial working memory following frontal lobe lesions in man. Neuropsychologia 1990; 28:1021–1034 PubMed

77. Chudasama Y, Robbins TW: Dopaminergic modulation of visual attention and working memory in the rodent prefrontal cortex. Neuropsychopharmacology 2004; 29:1628–1636 PubMed

78. Owen AM, Sahakian BJ, Semple J, Polkey CE, Robbins TW: Visuo-spatial short-term recognition memory and learning after temporal lobe excisions, frontal lobe excisions or amygdalo-hippocampectomy in man. Neuropsychologia 1995; 33:1–24 PubMed

79. Chudasama Y: Animal models of prefrontal-executive function. Behav Neurosci 2011; 125:327–343 PubMed

80. Mehta MA, Sahakian BJ, McKenna PJ, Robbins TW: Systemic sulpiride in young adult volunteers simulates the profile of cognitive deficits in Parkinson's disease. Psychopharmacology (Berl) 1999; 146:162–174 PubMed

81. Sahakian BJ, Morris RG, Evenden JL, Heald A, Levy R, Philpot M, Robbins TW: A comparative study of visuospatial memory and learning in Alzheimer-type dementia and Parkinson's disease. Brain 1988; 111:695–718 PubMed

82. Talpos JC, Winters BD, Dias R, Saksida LM, Bussey TJ: A novel touchscreen-automated paired-associate learning (PAL) task sensitive to pharmacological manipulation of the hippocampus: a translational rodent model of cognitive impairments in neurodegenerative disease. Psychopharmacology (Berl) 2009; 205:157–168 PubMed

83. Sahakian BJ, Owen AM, Morant NJ, Eagger SA, Boddington S, Crayton L, Crockford HA, Crooks M, Hill K, Levy R: Further analysis of the cognitive effects of tetrahydroaminoacridine (THA) in Alzheimer's disease: assessment of attentional and mnemonic function using CANTAB. Psychopharmacology (Berl) 1993; 110:395–401 PubMed

84. Robbins TW: The 5-choice serial reaction time task: behavioural pharmacology and functional neurochemistry. Psychopharmacology (Berl) 2002; 163:362–380 PubMed

85. Dalley JW, Fryer TD, Brichard L, Robinson ESJ, Theobald DEH, Lääne K, Peña Y, Murphy ER, Shah Y, Probst K, Abakumova I, Aigbirhio FI, Richards HK, Hong Y, Baron JC, Everitt BJ, Robbins TW: Nucleus accumbens D2/3 receptors predict trait impulsivity and cocaine reinforcement. Science 2007; 315:1267–1270 PubMed

86. Comer SD, Haney M, Foltin RW, Fischman MW: Amphetamine self-administration by humans: modulation by contingencies associated with task performance. Psychopharmacology (Berl) 1996; 127:39–46 PubMed

87. Park SB, Coull JT, McShane RH, Young AH, Sahakian BJ, Robbins TW, Cowen PJ: Tryptophan depletion in normal volunteers produces selective impairments in learning and memory. Neuropharmacology 1994; 33:575–588 PubMed

88. Gendle MH, Strawderman MS, Mactutus CF, Booze RM, Levitsky DA, Strupp BJ: Impaired sustained attention and altered reactivity to errors in an animal model of prenatal cocaine exposure. Brain Res Dev Brain Res 2003; 147:85–96 PubMed

89. Aron AR, Fletcher PC, Bullmore ET, Sahakian BJ, Robbins TW: Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. Nat Neurosci 2003; 6:115–116 PubMed

90. Logan GD, Schachar RJ, Tannock R: Impulsivity and inhibitory control. Psychol Sci 1997; 8:60–64

91. Eagle DM, Bari A, Robbins TW: The neuropsychopharmacology of action inhibition: cross-species translation of the stop-signal and go/no-go tasks. Psychopharmacology (Berl) 2008; 199:439–456 PubMed

92. Eagle DM, Baunez C, Hutcheson DM, Lehmann O, Shah AP, Robbins TW: Stop-signal reaction-time task performance: role of prefrontal cortex and subthalamic nucleus. Cereb Cortex 2008; 18:178–188 PubMed

93. Monterosso JR, Aron AR, Cordova X, Xu J, London ED: Deficits in response inhibition associated with chronic methamphetamine abuse. Drug Alcohol Depend 2005; 79:273–277 PubMed

94. Li CSR, Morgan PT, Matuskey D, Abdelghany O, Luo X, Chang JLK, Rounsaville BJ, Ding YS, Malison RT: Biological markers of the effects of intravenous methylphenidate on improving inhibitory control in cocaine-dependent patients. Proc Natl Acad Sci USA 2010; 107:14455–14459 PubMed

95. Li CS, Milivojevic V, Kemp K, Hong K, Sinha R: Performance monitoring and stop signal inhibition in abstinent patients with cocaine dependence. Drug Alcohol Depend 2006; 85:205–212 PubMed

96. Nelson HE: National Adult Reading Test Manual. Windsor, UK, NFER-Nelson, 1982

97. Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, Stokes J, Handelsman L, Medrano M, Desmond D, Zule W: Development and validation of a brief screening version of the Childhood Trauma Questionnaire. Child Abuse Negl 2003; 27:169–190 PubMed

98. Beck AT, Steer RA, Brown GK: Manual for Beck Depression Inventory-II. San Antonio, Tex, Psychological Corporation, 1996

99. Snaith RP, Hamilton M, Morley S, Humayan A, Hargreaves D, Trigwell P: A scale for the assessment of hedonic tone: the Snaith-Hamilton Pleasure Scale. Br J Psychiatry 1995; 167:99–103 PubMed

100. Spielberger C, Gorsuch R, Lushene R: STAI manual for the State-Trait Anxiety Inventory. Palo Alto, Calif, Consulting Psychologists Press, 1983

101. Cohen S, Kamarck T, Mermelstein R: A global measure of perceived stress. J Health Soc Behav 1983; 24:385–396 PubMed

102. Willer B, Ottenbacher KJ, Coad ML: The community integration questionnaire: a comparative examination. Am J Phys Med Rehabil 1994; 73:103–111 PubMed

103. Patton JH, Stanford MS, Barratt ES: Factor structure of the Barratt Impulsiveness Scale. J Clin Psychol 1995; 51:768–774 PubMed

104. Zuckerman M, Eysenck S, Eysenck HJ: Sensation seeking in England and America: cross-cultural, age, and sex comparisons. J Consult Clin Psychol 1978; 46:139–149 PubMed

105. Carver CS, White TL: Behavioral-inhibition, behavioral activation, and affective responses to impending reward and punishment: the BIS/BAS Scales. J Pers Soc Psychol 1994; 67:319–333

106. Burns GL, Keortge SG, Formea GM, Sternberger LG: Revision of the Padua Inventory of Obsessive Compulsive Disorder Symptoms: distinctions between worry, obsessions, and compulsions. Behav Res Ther 1996; 34:163–173 PubMed

107. Schwarzer R, Jerusalem M: Generalised Self-Efficacy Scale, in Measures in Health Psychology: A Users' Portfolio: Causal and Control Beliefs. Edited by Weiman J, Wright S, Johnston M. Windsor, UK, NFER-Nelson, 1995, pp 35–37

108. Allan S, Gilbert P: A social comparison scale: psychometric properties and relationship to psychopathology. Pers Individ Dif 1995; 19:293–299

109. Rotter JB: Generalized expectancies for internal versus external control of reinforcement. Psychol Monogr 1966; 80:1–28 PubMed

110. Chamberlain SR, Fineberg NA, Menzies LA, Blackwell AD, Bullmore ET, Robbins TW, Sahakian BJ: Impaired cognitive flexibility and motor inhibition in unaffected first-degree relatives of patients with obsessive-compulsive disorder. Am J Psychiatry 2007; 164:335–338 PubMed

111. Menzies L, Achard S, Chamberlain SR, Fineberg NA, Chen C-H, del Campo N, Sahakian BJ, Robbins TW, Bullmore ET: Neurocognitive endophenotypes of obsessive-compulsive disorder. Brain 2007; 130:3223–3236

112. Goodwin RD, Stayner DA, Chinman MJ, Wu P, Tebes JK, Davidson L: The relationship between anxiety and substance use disorders among individuals with severe affective disorders. Comprehensive Psychiatry 2002; 43(4):245-252