Neurocognitive correlates of the variance common and unique to externalising disorders and substance misuse in adolescence and the efficacy of preventative interventions targeting these profiles.

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High rates of comorbidity between adult substance use and antisocial personality disorders on the one hand and childhood conduct disorder, oppositional defiant disorder, attention deficit hyperactivity disorder (ADHD), and substance misuse on the other suggest a shared etiology across externalizing problems. The current study aims to reformulate psychopathological diagnostic categories from a dimensional and neuroscience perspective in order to identify new targets for prevention and treatment.

Objective: Data from the IMAGEN study are used to model the unique and common variance across conduct disorder, substance misuse, and attention deficit hyperactivity disorder (ADHD) and to investigate the neurocognitive factors that relate generally or uniquely to externalizing problems in adolescence.

Method: Personality and behavioral measures and functional imaging responses to reward sensitivity and response inhibition tasks were assessed in 1,778 European adolescents at age 14 and, using structural equation modeling, were related to the unique and common variance across externalizing problems assessed and modeled at ages 14 and 16.

Results: Externalizing problems at 14 and 16 years of age best fit a general-specific model made up by a specific factor representing ADHD and conduct disorder symptoms, a specific factor representing substance misuse symptoms, and a common externalizing factor representing the variance shared among all symptoms. Common variance across externalizing problems was associated with high impulsivity and delay discounting as well as low blood-oxygen-level-dependent (BOLD) response in the substantia nigra and subthalamic nucleus but high BOLD response in the presupplementary motor area and precentral gyrus during successful inhibition. Unique variance for ADHD/conduct disorder was associated with impulsivity, poor response inhibition, and high delay discounting, as well as low BOLD response in frontal brain areas bilaterally during failed inhibition. In contrast, unique variance for substance misuse was associated with high sensation seeking and delay discounting, as well as differential brain response to reward anticipation: high BOLD response in the left orbitofrontal cortex but low BOLD response in the left inferior frontal gyrus. Findings will be put into context with respect to the potential to inform new intervention strategies for reducing concurrent mental health and addictive behaviours in youth at risk. The author will present data from the Adventure personality targeted prevention trial, which targets at least two of the three neurophenotypes revealed in the current study and shows significant effects on substance use and behavioural outcomes.

Conclusions: Personality, behavioral, and fMRI findings suggest that abnormalities in response inhibition, error processing, and reward processing are differentially implicated in underlying vulnerability specific to ADHD/conduct disorder and substance misuse and general to externalizing problems. Similarly, from prevention trials targeting these endophenotypes suggests that these risk factors can be targeted in psychosocial interventions to reduce risk for substance misuse and externalizing problems more generally.

Acknowledgements:
The other authors report no financial relationships with commercial interests.
Funding for this research was provided from European Union-funded FP6 Integrated Project IMAGEN (Reinforcement- Related Behaviour in Normal Brain Function and Psychopathology; LSHM-CT- 2007-037286), the FP7 project IMAGEMEND (Imaging Genetics for Mental Disorders) and the Innovative Medicine Initiative Project EU-AIMS (115300-2), the Medical Research Council Programme Grant “Developmental Pathways Into Adolescent Substance Abuse” (93558), and the Swedish funding agency FORMAS. Further support was provided by the Bundesministerium für Bildung und Forschung (BMBF grants 01GS08152 and 01EV0711), the Deutsche Forschungsgemeinschaft (DFG) Reinhart-Koselleck Award (SP 383/5-1), and DFG grants SM80/5-2, SM 80/7-1, SFB 940/1. This research was also supported by the German Ministry of Education and Research (grant 01EV0711). Dr. Castellanos-Ryan’s and Dr. Conrod’s salaries are awarded from the Fonds de Recherche du Québec–Santé and the Adventure Trial was funded by Action on Addiction, UK.