Developmental Cognitive Neuroscience 16 (2015) 191

Contents lists available at ScienceDirect

Developmental Cognitive Neuroscience

journal homepage: http://www.elsevier.com/locate/dcn

Commentary

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The composite studies of this edition of *Developmental Cognitive Neuroscience* give further impetus to the recent national efforts designed to evaluate the effects of adolescent substance use on the developing brain (see http://addictionresearch.nih.go/adolescent-brain-cognitive-development-study).

Collectively, these studies highlight the value of addiction science in understanding neurodevelopment in the adolescent years. Alcohol, tobacco and cannabis use are among the prevalent emergent behaviors of concern during the adolescent years. Many other health and mental health disorders can be understood only when considered in concert with these co-occurring behaviors.

Adolescent neurodevelopment is multi-systemic and nonlinear. Thus, examination of morphologic, functional and neural connectivity precursors and consequences of substance exposure contribute uniquely to understanding the dynamics of substance use onset, progression and offset. Several studies highlight the value of determination of pre-existing neurobiological characteristics associated with use vulnerabilities (e.g., Becker et al., Peeters et al.) Peeters and colleagues, which represents the largest cohort study of youth, suggests that distinctive features of executive function, particularly working memory, predict early use and progression, whereas response inhibition may play a less salient role. Distinguishing salient risks for transition into each stage of substance use progression is a critical next step for science.

The means by which several previously identified risks and vulnerabilities operate to potentially influence initial use decisions or other processes promoting substance use progression are being uncovered. The altered prefrontal cortex and neurochemical profile differences linked to family history of substance abuse reported by Cohen-Gilbert and colleagues as well as childhood negative emotions and resiliency (Heitzeg et al.) demonstrate the heterogeneity and consequent complexity of the matrix of developmental risk for adolescent substance use and disorders.

As patterns of individual and multiple substance exposure effects become clearer, the types of research needed to clarify developmental processes and use-related cascades will become more evident to the field. For example, animal research of Saalfield and Spear demonstrates that early behavioral patterns of high dose substance use persist into adulthood, as does insensitivity to alcohol effects. As evident in prior research, some studies find that early adolescent substance use onset is associated with poor neurocognitive performance and differential neural activation patterns compared to late adolescent substance use onset (Sagar et al.). Others do not find such distinctive patterns.

Longitudinal investigations considering independent and joint use of substances may be most helpful in this regard, such as the examinations by Karoly et al. and Jacobus et al. For example, Jacobus and colleagues evaluated joint use of cannabis and alcohol over a three-year period demonstrating altered neural tissue development and apparent interference with neuromaturation as measured by level of cortical thickness change in frontal and parietal regions.

Longer term study holds considerable promise in clarifying neurodevelopmental processes that are linked to behavioral changes expected with maturation. For example, intrinsic neural network strength (resting state functional connectivity) independent of task demands can explicate the linkage of early reward processing differences to more mature cognitive control needed for self-regulatory behavior of young adulthood (Weissman et al.). When linked to differences in rates of morphologic change (e.g. Filbey et al.), the impact of substance use on structure and neurodevelopmental processes can more directly be applied to behavioral science of substance use disorders.

Of particular note, the size and scope of most neuroimaging studies prohibit evaluation of comprehensive models of the impact of substance use in the developing brain. Use of large scale longitudinal cohort and accelerated longitudinal designs, coupled with twin and genetically informed designs will be particularly useful given the heterogeneity of risks for adolescent substance use disorders.

The utility of adolescent substance use neurodevelopmental research is not limited to articulation of progression into use and disorders. Outcome and treatment process studies focusing on treated and untreated youth (e.g. Chung et al.), are critical to understanding both rate and process of return to healthy brain functioning. Such resiliency studies will play a critical role in the development of the personalized medicine approach for addictive disorders.

http://dx.doi.org/10.1016/j.dcn.2015.11.001