Full length article

Psychosocial and neural indicators of resilience among youth with a family history of substance use disorder

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ABSTRACT

Background: Little is known regarding the combined influence of psychosocial and neural protective mechanisms against substance use. The present study examined the extent to which neuroimaging measures of disinhibition predicted resilience against binge drinking and marijuana use among youth with a family history of substance use disorder (SUD; FH+), accounting for psychosocial measures of behavioral control.
Methods: Participants were 57 FH+ youth from the Michigan Longitudinal Study categorized into resilient and high-risk groups based on patterns of weekly binge drinking and monthly marijuana use during early adulthood. Psychosocial measures of behavioral control (reactive control and externalizing behavior during early and late adolescence) and neural measures of disinhibition (Go/No-Go task and Monetary Incentive Delay Task (MIDT) measured through functional magnetic resonance imaging (fMRI)) were entered sequentially in hierarchical logistic regression models to predict resilient versus high-risk groups.
Results: Greater activation in the right dorsolateral prefrontal cortex (DLPFC) during correctly inhibited trials on the Go/No-Go task was a significant predictor of resilience (OR = 2.46, $p < 0.05$), over and above greater reactive control in early adolescence (OR = 4.96, $p < 0.05$) and lower externalizing behavior in late adolescence (OR = 0.64, $p < 0.05$). Neural activation in the ventral striatum associated with reward anticipation during the MIDT was not a significant predictor of resilience.
Conclusions: Brain function in the right DLPFC associated with inhibitory control may be a neural indicator of resilience against elevated substance use among FH+ youth, even after accounting for psychosocial measures of behavioral control.

1. Introduction

Youth with a family history of substance use disorder (SUD; FH+) are vulnerable to drug and alcohol problems (Zucker, 2014), including recurrent patterns of disordered use, impaired functioning, and greater mental health service utilization through adulthood (Milne et al., 2009). Multiple, often complex, factors confer risk for FH+ youth to develop substance use problems, such as conflict and chaos in the home environment and negative parent-child interactions (Arria et al., 2012; Smith and Wilson, 2016). In addition, deficits in self-regulation displayed by heightened impulsivity and externalizing behavior are believed to be an inherited behavioral phenotype that predisposes FH+ youth for later substance use (Dougherty et al., 2015). Yet, certain FH+ youth are resilient. Resilience has been defined as the ability to avoid a pathological outcome, or achieve a successful one, despite experiences of adversity (e.g., Hurd and Zimmerman, 2016; Masten et al., 1990;

Windle and Zucker, 2010). Despite genetic and environmental risks, subgroups of FH+ youth have been found to display low or developmentally limited rates of substance use from adolescence through early adulthood (Chassin et al., 2002; Jester et al., 2015; Park and Schepp, 2015; Warner et al., 2007), an age period typically coinciding with escalating substance use and SUD onset (Schulenberg et al., 2017; Substance Abuse and Mental Health Services Administration (SAMHSA), 2015, respectively). Thus, a pattern of low substance use through the transition to adulthood is a useful measure of resilience among FH+ youth.

Factors within individual, familial, and other social domains have been found to be protective against heavy substance use among FH+ youth (Hurd and Zimmerman, 2016; Park and Schepp, 2015). For example, individual level protective factors include greater self-regulation, temperament characteristics of being flexible and optimistic, and positive affect (Martel et al., 2007; Pearson et al., 2011). Family level

factors associated with resilience are having one versus both parents with a SUD (Hussong et al., 2007) and greater family cohesion and parental monitoring (Shorey et al., 2013). Additional protective factors within the social domain are positive adult role models and non-substance using peers (e.g., Moe et al., 2007).

The few studies that have examined neural processes involved in resilience among FH+ youth have focused on differences between FH + and FH- youth rather than within the ostensibly vulnerable FH+ group. No studies to-date have specifically examined how neural function is associated with resilience among FH+ youth over and above other sociodemographic and psychosocial factors. Such information would add uniquely to understanding the constellation of protective factors related to resilience among FH+ youth. Indeed, investigating neural mechanisms associated with resilience has been cited as an important direction for research on factors impacting substance use outcomes among FH+ youth (Cservenka, 2016).

To study the complex, multi-level mechanisms involved in resilience against substance use problems, it is beneficial to employ a developmental psychopathology framework (Hussong et al., 2011). This theoretical framework posits that resilience should be considered in addition to risk, that both psychological and neurobiological components are essential to examine in predicting behavioral outcomes such as substance use, and that the cascading influence of distal and proximal developmental factors should be considered (Cicchetti and Rogosch, 1999; Cox et al., 2010). In line with a developmental psychopathology framework, and given that an externalizing behavioral phenotype has been linked to familial risk for substance dependence, the under-control/disinhibition pathway to SUDs (Zucker et al., 2011) may be a useful target to identify psychosocial and neural mechanisms underlying resilience. Behavioral under-control and disinhibition are related constructs, with the prior describing psychosocial function and the latter characterized by the neural function associated with self-regulation.

1.1. Behavioral under-control

Behavioral under-control, defined as the inability, unwillingness, or failure to inhibit behaviors despite experiencing negative consequences of those behaviors, is associated with two related yet distinct psychosocial constructs—reactive control and externalizing behavior (Wong et al., 2006; Zucker et al., 2011). Reactive control is characterized by the capability to inhibit impulsive responding to immediate rewards (Eisenberg, 2015). Individuals with low reactive control are sensitive to immediate gratification and rewarding stimuli, and therefore, at heightened risk for substance use problems (Martel et al., 2009; Wong et al., 2006). Externalizing behavior, including aggression and delinquency, is also an important component of behavioral under-control (Zucker et al., 2011). Reactive control and externalizing behavior have an impact across the spectrum of risk and resilience (Park and Schepp, 2015). Thus, higher levels of reactive control and lower levels of externalizing behavior may be associated with resilience against heavy substance use among FH+ youth.

1.2. Disinhibition

Inhibitory control and reward responsivity are two key neural functions involved in disinhibition, which are related more broadly to dual-systems models of risk-taking (Zucker et al., 2011). These models posit that heightened risk behaviors during adolescence and early adulthood, such as substance use, are attributable to a developmental mismatch between two brain systems—a bottom-up subcortical brain system involved in reward responsivity that develops in early adolescence and a later maturing top-down prefrontal brain system associated with inhibitory control (Casey et al., 2008; Shulman et al., 2016). While a useful heuristic, dual-systems models of risk-taking often fail to account for heterogeneity in risk outcomes even among the putatively

homogeneous high or low-risk groups (Pfeifer and Allen, 2012). This is particularly relevant to FH+ youth, who are believed to share an underlying vulnerability to SUDs but in fact display variation in their levels of substance use (Heitzeg et al., 2008).

1.3. Present study

Examining both psychosocial and neural measures of behavioral control/under-control and disinhibition may not only predict resilience versus risk among FH+ youth but may also demonstrate the incremental predictive utility of neural function measures beyond psychosocial measures of the same underlying construct. Toward this aim, the present longitudinal study investigated the extent to which neural function involved in disinhibition (inhibitory control measured by a Go/No-Go task and reward responsivity measured by a Monetary Incentive Delay Task (MIDT)) predicted resilience in terms of low substance use across the transition to adulthood among FH+ youth, over and above the psychosocial influence of behavioral control (reactive control and externalizing behavior). Resilient and high-risk FH+ groups were categorized based on 1) binge drinking and marijuana use trajectory classes through the transition to adulthood (ages 17–26); and 2) more conservative groupings based on heavy past-year binge drinking (i.e., weekly) and/or marijuana use (i.e., monthly) reported during two or more time points from ages 17 to 26. Findings from prior literature were used to determine heavy binge drinking (Hasin and Beseler, 2009; Schulenberg et al., 1996) and marijuana use (Harper et al., 2012; Hides et al., 2009; Schulenberg et al., 2005) thresholds. This latter step was taken to improve the face validity of characterization of resilient and high-risk groups estimated through trajectory classes. As the most commonly used drugs of abuse among youth during the transition to adulthood (Schulenberg et al., 2017), developmental patterns of alcohol and marijuana use during early adulthood were used to determine resilient and high-risk groups. To account for other substance use, cigarette and any other drug use within the age range of 17–26 were controlled for in the regression analyses predicting resilient versus high-risk groups. Since earlier experiences often have downstream effects on later functioning (Dodge et al., 2009; Schulenberg and Maggs, 2008), reactive control and externalizing behavior were assessed both in early adolescence (ages 12–14) when substance use tends to begin (SAMHSA, 2015) and also in late adolescence (ages of 17–18) when substance use begins to peak (Schulenberg et al., 2017) and disordered use begins to emerge (Windle and Zucker, 2010). Neuroimaging data were collected during early adulthood (approximately age 20).

The resilient group was hypothesized to have greater reactive control and less externalizing behavior both in early adolescence and late adolescence compared to the high-risk group. Compared to the high-risk group, resilient youth were hypothesized to have greater activation in prefrontal brain regions during the Go/No-Go task and lower activation in subcortical brain regions during the MIDT task measuring reward responsivity. Greater activation associated with inhibitory control and lower activation associated with reward responsivity were hypothesized to predict resilient versus high-risk group membership after accounting for sociodemographic characteristics, cigarette and other illicit drug use, and both early and late adolescent psychosocial functioning involving reactive control and externalizing behavior.

2. Methods

2.1. Participants

Two hundred and thirty-five youth (75.32% male; 96.60% White) followed annually from ages 12 to 26 from the Michigan Longitudinal Study (MLS), a prospective study of community-recruited youth from families at high risk for SUD (Zucker et al., 2000), were included in initial analyses to determine resilient and high-risk groups through