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Defining the phenotype of young adults with family histories of alcohol and other substance use disorders: Studies from the family health patterns project

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HIGHLIGHTS

- Measures affected by family history of substance use disorders were compared.
- From these measures three principal components were identified.
- An externalizing behaviors and adversity component best predicted family history.
- This same component also best predicted substance use disorders.

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ABSTRACT

Individuals with a family history of alcohol and other drug use disorders (FH +) are at increased risk for developing substance use disorders themselves relative to those with no such histories (FH −). Here we sought to identify key characteristics associated with FH + status and alcohol and other drug use disorder status in a large cohort of FH + and FH − young adults.

We conducted principal component analyses on demographic, temperament, and cognitive measures differentiating 506 FH + and 528 FH − young adults. Three principal components were identified, and these component scores were then used to predict the odds of being FH + and the odds of having an alcohol or other drug use disorder. Component 1 consisted of measures indexing internalizing traits, with higher component scores indicating greater depressive, anxious, and emotional instability tendencies. Component 2 consisted of measures of externalizing traits as well as exposure to early life adversity (ELA), with higher scores indicating less impulse control, more antisocial behavior, and greater ELA exposure. Component 3 consisted of estimated intelligence, delay discounting, and demographic characteristics, with higher scores indicating lower estimated intelligence, greater discounting of delayed rewards, less education, and lower childhood socioeconomic status. For each 1-point increase in the Component 1, 2, and 3 scores, the odds of being classified FH + increased by 2%, 8%, and 4%, respectively. Similar findings were observed when individuals with alcohol or other drug use disorders were removed from the analyses. Finally, greater Component 2 scores were also associated with increased odds of having an alcohol or other drug use disorder. Collectively, these findings provide a more comprehensive understanding of the FH + phenotype in young adults and help form a basis for further studies on biological mechanisms underlying risk for substance use disorders. The present findings also provide further support for a prominent role of ELA in promoting risk for problem alcohol and other drug use.

1. Introduction

Abuse of alcohol and other drugs results in substantial public harm, with alcohol misuse alone accounting for approximately 25% of deaths in young adults (WHO, 2014). The best-known risk factor for alcohol and other drug use disorders is having a positive family history (FH +) of substance use disorders relative to persons with no such histories (FH −; Cotton, 1979, Cloninger, Bohman, & Sigvardsson, 1981a). FH + persons display a complex phenotypic pattern variously termed "behavioral undercontrol" or "neurobehavioral disinhibition,"

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characterized by biases in decision-making and cognition, variability in behavior and unstable mood regulation (Sher, Grekin, & Williams, 2004; Sher & Trull, 1994; Tarter et al., 2003). As much of this work has been done in youths, we developed the Family Health Patterns (FHP) project to extensively characterize and contrast nonabusing FH + and FH − young adults. Our work allows us to study the FH + phenotype in individuals with mature cognitive, temperament, and personality development while still minimizing confounding influences of excessive substance use.

Through the FHP project, we have shown that FH + young adults have alterations in temperament and personality (Lovallo, Yechiam, Sorocco, Vincent, & Collins, 2006; Saunders et al., 2008), altered decision-making and cognitive functioning (Acheson, Vincent, Sorocco, & Lovallo, 2011; Lovallo et al., 2006), and increased exposure to early life adversity (ELA) (Lovallo et al., 2013; Sorocco, Carnes, Cohoon, Vincent, & Lovallo, 2015). One of our most robust findings is that FH + young adults in the FHP cohort have increased antisocial tendencies as indexed by low scores on the Socialization scale of Gough's California Psychological Inventory (CPI-So) (Gough, 1994a; Vincent, Sorocco, Carnes, Cohoon, & Lovallo, 2017). We were also the first to demonstrate that FH + persons have clear increases in discounting of delayed rewards (Acheson et al., 2011), similar to findings in individuals with substance use disorders (see MacKillop, 2013, Gray & MacKillop, 2015 for reviews). Finally, another notable finding is the increased ELA exposure in FH + is directly linked to differences observed on many measures including their increased anti-social tendencies and increased discounting of delayed rewards (Lovallo et al., 2013; Sorocco et al., 2015), consistent with findings demonstrating both a genetic contribution to the elevated risk in FH + (Cloninger, Bohman, & Sigvardsson, 1981b; Merikangas, 1990; Reich et al., 1998; Slutske et al., 2002) and a strong role for early childhood trauma and adversity (Kendler et al., 2012; Svingen et al., 2016).

As part of screening for the FHP project, we have accumulated a large dataset from a cohort of 506 FH + and 528 FH − young adults with and without alcohol and other drug use disorders on a battery of measures including demographics, estimated intelligence, ELA, measures of temperament and personality, and delay discounting. While our earlier reports have identified specific variables affected by FH status in non-abusing young adults, this dataset allows us to much more comprehensively compare these affected variables and extend our findings to individuals with substance use disorders. Here we first use this dataset to determine which variables are most robustly affected by FH status in young adults and how these variables relate to each other. Finally, we examined how these variables predicted both FH status and number of parents and grandparents with alcohol and other drug use disorders (a key risk index) as well as the presence of alcohol and other drug use disorders in the individuals themselves.

2. Method

2.1. Participants

We examined data from 1031 healthy young adults recruited from the local community who were 18–30 years of age and were screened for potential inclusion in the FHP study and had complete data for relevant study variables (77% of the full sample of screened participants). All participants signed consent forms approved by the Institutional Review Boards at the University of Oklahoma Health Sciences Center and the Veterans Affairs Medical Center in Oklahoma City, OK and at the University of Texas Health Sciences Center, San Antonio, TX and were paid for their participation. Privacy was further protected by a Certificate of Confidentiality from the U.S. Department of Health and Human Services.

2.2. Screening, inclusion and exclusion criteria

Subjects were recruited using advertisement in local newspapers, flyers posted in locations frequented by persons of the desired age range including college campuses, direct contact via campus job fairs and student activities, and electronic media including Craig's List and campus list servers directed to students and staff. This multipronged approach to subject recruitment is preferable to a single source of volunteers, such as students or campus employees, and is superior to random telephone dialing in terms of attracting the needed numbers of volunteers (Sorocco, Vincent, Collins, Johnson, & Lovallo, 2006). Subjects were screened by telephone to ensure general conformity with entrance criteria followed by a laboratory visit for further evaluation. Physical health was assessed through a medical history checklist and self-report of current good health. Psychiatric history was assessed using the computerized version of the Diagnostic Interview Schedule updated for DSM-IV diagnoses (C-DIS-IV) (Blouin, Perez, & Blouin, 1988) administered by a trained interviewer working under the direction of a licensed clinical psychologist.

2.2.1. Inclusion criteria

To qualify, participants were required to have current good health and no use of CNS-acting medications, and no history of neurological impairment or diabetes mellitus. They were also required to have normal intelligence based on Shipley Institute of Living verbal scale score ≥ 20 (John & Rattan, 1992), have been raised by at least one biological parent and be in contact with them, and be between 18 and 30 years old.

2.2.2. Exclusions

Participants were not allowed to participate if they had suspected maternal alcoholism during subject's gestation, or were unable to provide credible report of family alcohol use patterns for two generations.

2.2.3. Family history of alcohol and other drug use disorders

FH classification was established using Family History Research Diagnostic Criteria (FH-RDC), which have a high degree of inter-rater reliability for reports of substance use disorders (Andreasen, Endicott, Spitzer, & Winokur, 1977). Inclusion criteria required that each proband be raised by at least one biological parent, be in touch with that parent, and adoptees were excluded from consideration. Persons were considered FH + if either biological parent met FH-RDC criteria for alcohol or other drug use disorder. FH − were those reporting an absence of SUD in their biological parents and grandparents. The reliability of proband FH-RDC reports was verified by parent interview in 52% of the cases participating in the full study protocol, and these yielded 90% agreement between the two sources. In cases of disagreement between parent and proband reports, the subject's data were excluded from analysis if parent reports did not allow a clear FH group assignment (8.8% of cases), and in the remaining cases the parent report was given precedence and the subject's assignment was changed accordingly. FH– were coded 0 and FH + were coded 1. A family history density score (FH density) was calculated by counting the number of biological parents and grandparents meeting criteria for any substance use disorder (including abuse, dependence, and/or withdrawal). Scores ranged from 0 (FH– participants) to a possible 6 (FH + participants with both parents and all grandparents affected).

2.3. Analytic variables

Variables selected for inclusion in this analysis were determined from preliminary analyses examining differences between FH groups in the full screening sample (Table 2). Only those variables shown to differ between the FH groups (using independent *t*-tests) with a Cohen's *d* effect size ≥ 0.2 were included in the current analyses. These variables are detailed below and consisted of demographic measures, estimated