

## ***Substance Use in the Philadelphia Neurodevelopmental Cohort***

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**Background:** Substance use in youth is increasing and occurs at a critical period of brain maturation and vulnerability. Multiple factors - environmental, social, psychopathology, genetics – contribute to and modulate substance use in youth. Studies have applied complementary strategies to examine commonly help-seeking individuals. The Philadelphia Neurodevelopmental Cohort (PNC) provides an opportunity to evaluate a community-based sample that was not help seeking. We sought to examine substance use and association with psychopathology and brain-behavior measures in this cohort.

**Methods:** The PNC is a large-scale, community-based study of approximately 9,500 youths age 8-21 from the greater Philadelphia area. Participants were selected at random, after stratification by sex, age, and ethnicity, from a large pool of youths who had been recruited and genotyped by the Center for Applied Genomics at the Children's Hospital of Philadelphia (CHOP) and had provided written consent to be re-contacted for future studies. Participants were assessed for psychopathology as well as substance use. A computerized neurocognitive battery was administered measuring accuracy and speed of performance in major neurobehavioral domains and a random subsample of about 1600 underwent multi-modal neuroimaging on a single Siemens 3T scanner. Substance use was dimensionalized from 0= denied ever using substance, 1=endorsed ever using, 2=subthreshold, 3=threshold (reports at least one adverse effect of using substance)

**Results:** The PNC provides data on an ethnically diverse and equally distributed sample of males and females. No substance use was reported before age 11 and less than 1% reported substance use for ages 12-14. For the entire sample, 62% reported no substance use, 3% provided no data and 35% reported using: tobacco (44%); marijuana (43%); alcohol (42%); over the counter (22%); inhalants (9%); tranquilizers (7%); opiates, psychedelic, stimulants, steroids and downers (4%); cocaine (3%). Among the users, 44% reported use of one substance, 23% two substances, 21% three substances and 12% four or more. Focusing on the two major substances use, marijuana and alcohol, 5% reported above threshold use for marijuana while 14% reported such use for alcohol with 18% overlap. Psychopathology was co-morbid with substance use. Neurocognitive measures indicated that frequent marijuana users had lower than average performance on executive functions and higher than average performance on spatial memory and social cognition measures. Neuroimaging data indicated greater gray matter density in the reward network for marijuana users compared to non-users and increased activation for a working memory task with poorer performance.

**Discussion:** Substance use is common in adolescents and young adults and affects daily functioning in a substantial group. It is associated with significant comorbid psychopathology as well as deficits in neurocognitive performance related to frontotemporal functioning. The better than average performance for marijuana users on spatial memory and social cognition may indicate that youths with such abilities are

more likely to be drawn to substance use or to have the social network associated with use. To determine whether these abnormalities, as well as the abnormalities in brain structure and function, are consequences or predisposing factors requires longitudinal studies.

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