Alcohol adolescent substance use disorder and the “with limited prosocial emotions” specifier: brain activation during decision associated with increasing other harm and self-benefit
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INTRODUCTION:
- Adolescent SUD is common and predicts increased risk of drug abuse, other behavioral problems and worse health outcomes in adulthood (SAMHSA. 2017 NSDUH Annual National Report 2017; Nelson SE et al., 2015).
- DSM-5 also describes a “with limited prosocial emotions” (LPE) specifier identifying individuals who display high callous-unemotional traits, as these adolescents may be at even greater risk of substance misuse (Baskin-Sommers AR et al., 2015).
- The neuroscience of social cognition is often conspicuously absent from biological models of addiction; the available literature suggests that SUD is associated with deficits in social cognition (Uakerrman J, 2018).
- Adolescent prosocial behaviors and empathy have a negative association to adolescent substance use over time (Carlo G et al., 2011; Winters DE et al., 2020).
- Problem Statement: Very limited work has examined the association of social cognition and prosocial decision making with adolescent SUD/extending behavior problems in the MRI environment.
- Project Aim: We sought to better understand brain structures engaged during decisions which may be beneficial to others and increasingly beneficial to self, and to identify group differences in brain activation patterns.
- Hypothesis: We hypothesize that all three groups will have measurable differences in the pattern of brain activation depending on whether the subject is behaving in a manner that is beneficial to versus harmful to others.

METHODS:
Groups studied: (1) male patients with SUD+LPE, (2) male patients with SUD but without LPE and (3) male controls.

Inclusion:
- Adolescents 15-18 years old
- Male
- No history of IQ <80
- No history of DSM diagnosis of major depressive illness or other psychiatric disorder, or substance use disorder (regardless of LPE) and what may be more specifically related to LPE.
- Right-handed

Exclusion:
- Current dangerousness
- Red Green color blindness
- Psychosocial biopsychosocial disorder
- Callowhitecnic withdrawal
- withdrawal from use 12 hours prior to scan
- Volunteered left from
- Red Cross
- Standard MRI exclusion

Sample:
- Patients recruited from a University based treatment program for youth with substance and conduct problems (all had at least one non-nicotine substance use disorder).
- Controls recruited from same neighborhoods as patients and excluded for prior convictions (minor traffic and curfew violations permitted) or for history of substance related treatment/exposure/triposition
- 66 adolescents (21 SUD patients with LPE; 21 without LPE and 24 controls) imaged in 3T MRI while playing Alka’s game.
- (The Colorado Multiple Institutional Review Board approved the study (COMIRB protocol 12-0111). For adolescents under the age of 18, parents gave consent and patients assent. Participants 18 years of age given written consent to participation.

Imaging Parameters:
- We obtained functional brain images with Blood Oxygen Level Dependent (BOLD) contrast using a T2*-weighted gradient-echo planar imaging (EPI) technique over a 64×64 matrix (TE/TR/TI (in milliseconds): 26/2000/70; Flip angle: 70°; FOV: 200×200 mm in axial acquisition.

RESULTS:
- Figure 1. What brain areas are engaged (more and less) as other harm increases (selecting high-you-gain amounts 16, 32, 64 and examining changes between -3.4. -4.16 and -20.04)

Panel A. Analyses within 24 male control adolescents.

Panel B. Three-group ANCOVA: How do groups differ when other harm changes?
- Significant P<0.05 in bilateral insula and inferior parietal gyrus, right inferior parietal, and orbitofrontal cortex, among other areas (13 clusters; 174 voxels)

Panel C. Two-group analyses: How do groups differ when other harm increases?

SUD patients with LPE-Controls

- Regions engaged in controls include: 1 premotor cortex (PMd) and supplementary motor area (SMA), premotor cortex (M1), and supplementary motor area (SMA)
- Group differences are primarily between controls and SUD patients and show differences in regions implicated in:
  - Theory of Mind (temporal-parietal junction; Tunche et al., 2016)
  - Executive control (superior frontal)
  - Frontal involvement (increased prefrontal connectivity; Dalwani et al., 2014)
  - Facial recognition and social contextual awareness (fusiform, parahippocampal, Chavies & Insausti, 2017)

All OTHER HARM INCREASES:
- Regions engaged in controls include:
  - Superior frontal gyrus, orbitofrontal, inferior parietal, and superior temporal gyrus

AS YOU GAIN INCREASES
- Regions engaged in controls include:
  - Right inferior parietal, superior parietal, superior frontal, middle temporal, and cerebellum

AS OTHER HARM INCREASES
- Regions engaged in controls include:
  - Right inferior parietal, superior parietal, superior frontal, middle temporal, and cerebellum

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DISCUSSION/CONCLUSION:
- Our methods allow modeling of engagement of brain regions based on trial content (e.g., as there is increasing harm to a beneficent other, what brain regions become more active during decision).
- The three-group design allows examination of what differences are related to SUD patient status (regardless of LPE) and what may be more specifically related to LPE.