Basal Perfusion in Adolescents at Risk for Alcohol Use Disorders

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Introduction: The purpose of this study was to investigate alterations in baseline cerebral blood flow (CBF) in adolescents at risk for alcohol use disorder (AUD). Our previous research indicates that adolescents with high familial loading for depression have a significantly increased risk for developing AUD during adolescence. Since prior investigations have shown that the peak period for developing depression or AUD occurs between the ages of 15-20 years [1], we targeted the initial assessment of adolescents to occur prior to entering this peak risk period. It is anticipated that identifying group differences in CBF at baseline may identify trait markers for the future development of both depression and AUD.

Methods: Subjects were adolescents aged 12 to 15 years who were randomly recruited from the greater San Antonio area. A family history interview was conducted with the adolescent's parent(s) to determine lifetime psychiatric disorders in first- (parents, brothers, sisters) and second (grandparents, aunts, uncles, ½ sibs) -degree relatives of the adolescents. Based on our preliminary work, adolescents were identified as being at high risk for alcohol use disorders if at least one first- and one second-degree relative had either recurrent or childhood onset depression. Low-risk adolescents were required to have no first-degree and less than 20% of their second-degree relatives with a life time history of depression. Adolescents were excluded if they had a learning disability or had a lifetime externalizing disorder including conduct disorder, attention deficit disorder, or oppositional defiant disorder. Imaging acquisition and analysis: A pulsed arterial spin labeling (PASL) sequence was used to measure resting CBF [2] with an eight-channel phase array coil on a 3T Siemens Trio platform. Interleaved images with and without labeling were acquired using an EPI sequence (FOV= 24 cm, matrix size = 64× 64, TR/TE = 2440/19 ms, delay time (TI_1) = 700 ms, label time (TI_2) = 1000 ms, flip angle = 90°, 13 slices (7.5 mm thickness with 1.5 mm gap)) acquired in sequential order from inferior to superior. The resting perfusion scanning protocol lasted 4 minutes (NEX=100). The equilibrium brain tissue magnetization (M_0) was measured using similar parameters as described above but TR/TI_1/TI_2 = 8000/5000/6000 ms and NEX = 4. Raw ASL images (ΔM) were obtained by subtracting the labeled and unlabeled images. The quantitative CBF was then obtained by the following equation [2]:

$$CBF(mL/100g/\min) = \frac{\lambda \Delta M}{2\alpha M_0 TI_1 \exp(-TI_2/T_{1a})}$$

λ: the blood/tissue water partition coefficient, T_{1a} : the longitudinal relaxation time of blood, α : the inversion efficiency.

Results and Discussion: Figure 1 shows the whole brain basal perfusion in low- (N=19) and high- (N=9) risk groups. No statistical difference was observed between global CBF magnitude across the two groups (63.5 ± 5.7and 68.7 ± 4.4 mL/100g/min for low- and high- risk groups, respectively, p>0.5). Direct group comparisons focused on corticolimbic circuits mediating emotional reactivity and implicated in the pathophysiology of both depression and AUD revealed relatively increased CBF in bilateral amygdala and ventromedial prefrontal cortex and relatively decreased CBF in bilateral insula, right dorsal anterior cingulate cortex (ACC) and occipital lobe cuneus of high-risk adolescents (Figures 2a and 2b). These preliminary findings suggest that adolescents at relatively high-risk for AUD exhibit altered patterns of resting CBF in distributed corticolimbic regions supporting emotional behaviors. We hypothesize that relatively increased amygdala and ventromedial prefrontal CBF may contribute to increased emotional reactivity and sensitivity to environmental stressors in these individuals while diminished insula/occipital cuneus and dorsal ACC CBF may lead to poor integration of visceral and sensory changes accompanying such emotional stress responses and top-down regulation of amygdale, reactivity. These hypotheses will be evaluated in larger samples using behavioral, clinical and BOLD fMRI measures being collected as part of our ongoing longitudinal protocol.

References: [1] Weissman MM et al., (2006) *Am J Psychiatry* 163:1001-1008. [2] Wang JJ et al., (2003) *Magn Reson Med* 49:796-802. Grant support: NIAAA R01AA016274 (Williamson)

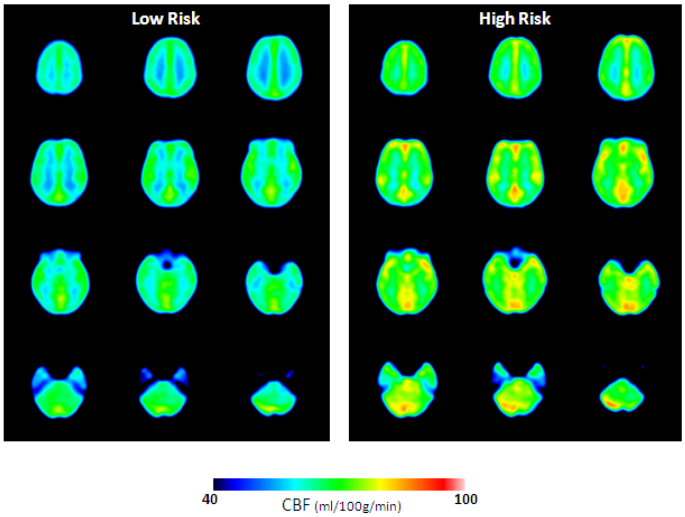

Fig.1 The whole brain basal CBF in low and high risk groups

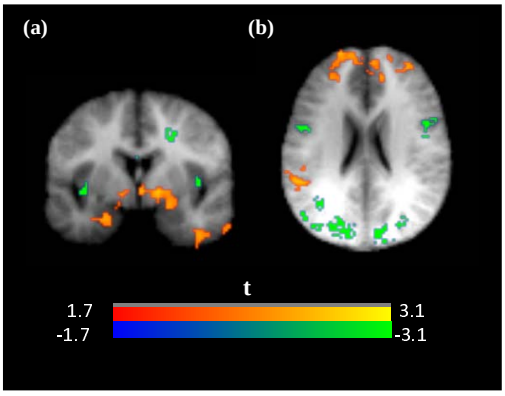

Fig.2 Compare to the low risk group, the high risk group shows (a) greater basal CBF in bilateral amygdale but less CBF in bilateral insula and ACC (b) greater basal CBF in ventromedial prefrontal cortex but less CBF in occipital cortex cuneus