



MRI-based cortical thickness and volumetric abnormalities in cocaine dependence



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Introduction: Cocaine dependence has been associated with structural alterations in brain networks influencing cognitive and affective behavior (Breiter et al., 2006). Volumetric studies in cocaine dependence identify abnormalities in cortical and subcortical regions. We previously found an absence of right-left asymmetry due to an unequal reduction in amygdala volumes in subjects with cocaine dependence. Based on these findings we proposed that altered amygdala morphology is a vulnerability marker for or early consequence of cocaine use. Thickness and surface area are additional indicators of cortical architectonic integrity. To expand upon our earlier results and further refine the regions of structural abnormality, we hypothesized that the neural networks and cortical centers underlying the processing of reward information, the executive oversight of this processing and its use for behavioral planning, and attention functions (EF) would be most affected.

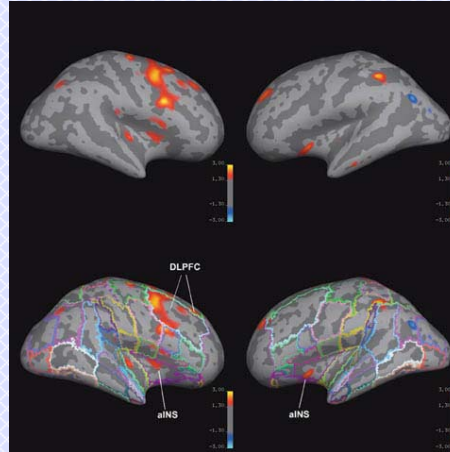


Figure 1: Cortical thickness group differences. Red indicates cortical thinning in cocaine dependants ($p < 0.05$)
Abbreviations: DLPPFC - Dorsolateral prefrontal cortex, aINS - Anterior Insula

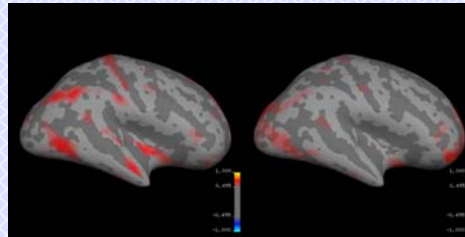


Figure 2: Standard deviation of cortical thickness maps show controls on the left and cocaine users (with lower s.d.) on the right.

Methods: 3D MP-RAGE sequences were used with a 1.5 T Siemens Avanto system at the MGH Martinos Center in a sample of adults with cocaine dependence ($n = 20$) and their matched controls ($n = 20$). Volumetric analyses were done using segmentation procedures and cortical thickness differences were mapped using semi-automated procedures (Filipek et al., 1994; Makris et al., 1999; Makris et al., 2006)

Results: Compared to healthy adults, adults with cocaine dependence showed a significant overall bilateral reduction of the cerebral cortex volume and selective thinning of the dorsolateral prefrontal cortex, the anterior insular lobule, orbitofrontal, paracingulate and cingulate cortices (Figure 1). These cortical processors are key components of the networks sub-serving executive function and the processing of reward information.

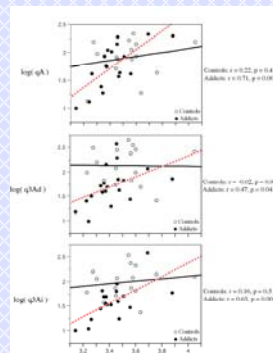


Figure 3: Correlations between cortical thickness with three attentional tasks. The tasks tested selective, sustained and divided attention. There are significant differences between the correlations of thickness and performance on the tasks between the groups.

Discussion: This study is the first to demonstrate that cocaine dependence affects the structures of the neural systems sub-serving reward and executive function, and centers mediating fronto-limbic interactions. These centers are critical for cue or stimulus associations to reward and for evaluation of reinforcing stimuli. To a large extent it is through these associations that sensory inputs are processed and transformed to powerful motivational and emotional representations.

Summary of findings:

1. Thinning of cortex (Figure 1) and reduced volume (~50cc), primarily in the prefrontal cortex such as dorsolateral prefrontal cortex and orbitofrontal cortex. These regions help regulate executive oversight of motivated behavior and with the inhibition of impulses that might optimize short-term gain, but produce long-term negative consequences.
2. Cortical regions within the paralimbic cortex, involved with the assessment and planning of behavior around reward and aversion show reduced thickness. The cortical thinning of the anterior cingulate for example, correlates with years of cocaine use but not with the age of starting to use cocaine. This suggests the structural abnormalities are drug induced.
3. Cocaine dependent subjects show less heterogeneity in the thickness (lower standard deviation) than normal matched controls (Figure 2). Typically, acquired disease increases heterogeneity (increased standard deviation). Thus our results suggest a genetic link to a predisposition to addictive drug use.
4. There is a significant difference in the correlation between cortical thickness and attention for addicts and controls (Figure 3). The attention tasks tested selective attention, sustained attention and divided attention. Additionally, the correlation between cortical thickness and how well an individual controlled the range of their responses in a reward task was altered in addicts compared to controls.

References:

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