CORTICAL THICKNESS IN COCAINE USERS: RELATIONSHIP TO RESTING FUNCTIONAL CONNECTIVITY AND COCAINE USE

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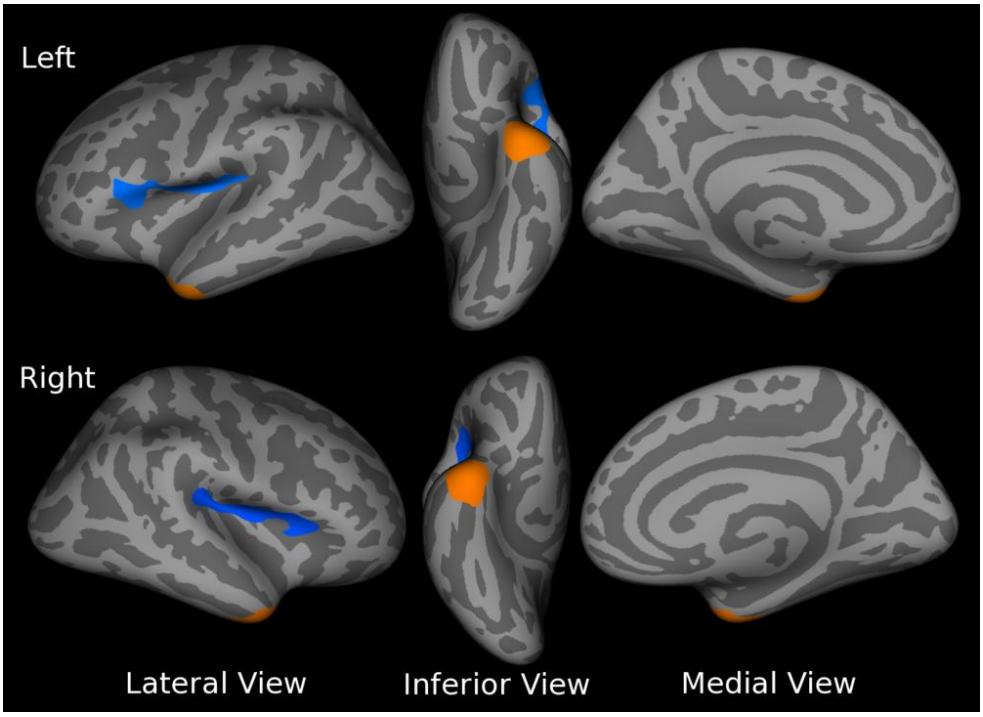
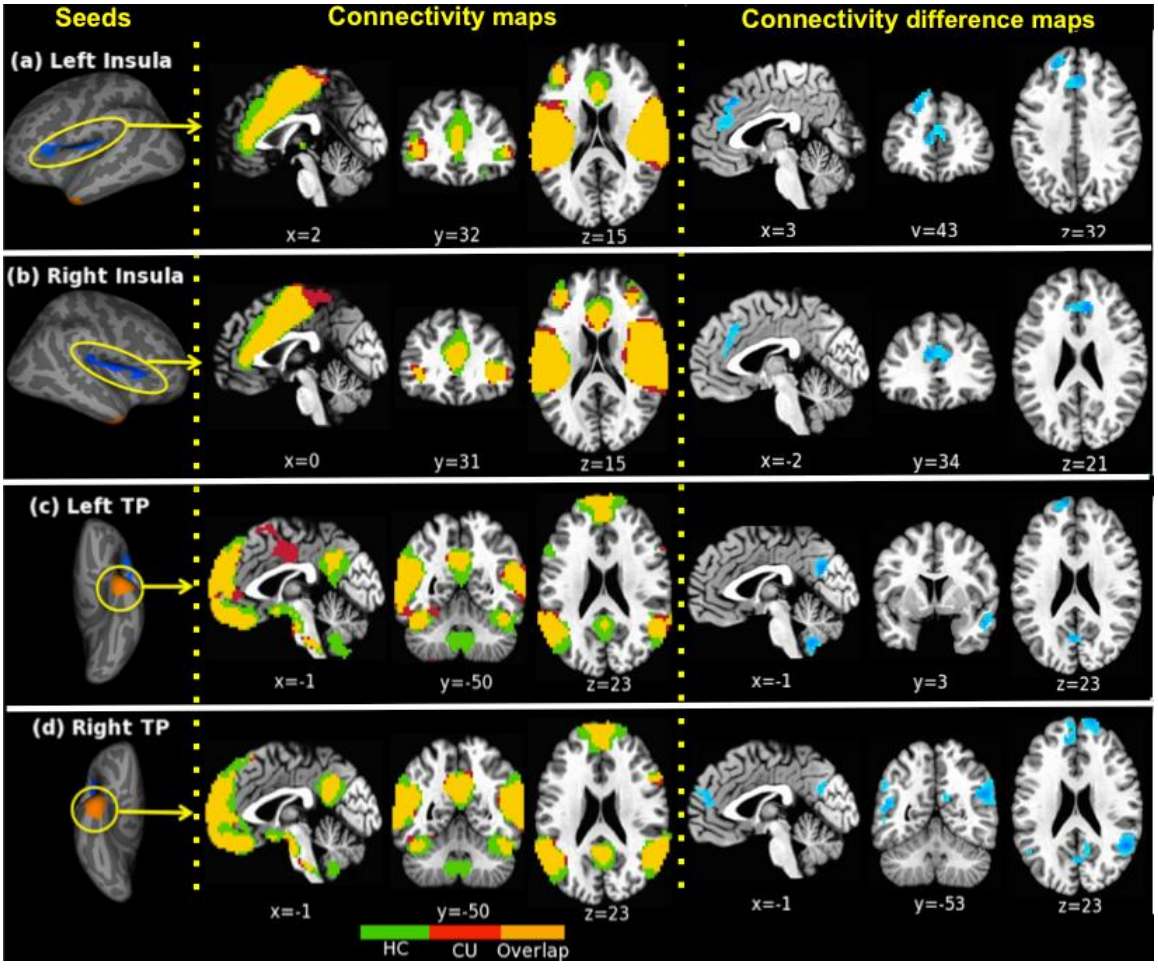
INTRODUCTION: In rats, cocaine alters dendritic morphology (1), a determinant of cortical thickness (CT). In humans, addiction vulnerability traits such as anxiety and impulsivity relate to CT (2, 3). In human cocaine users, CT differences have been noted (e.g.,(4)) but little has been done to elucidate network functioning related to these differences. Numerous studies have also noted resting state functional connectivity (rsFC) differences in cocaine users (5, 6); however, how these may relate to structural differences is unknown. We identify cortical thickness differences in cocaine users, then probe relationships to rsFC and use characteristics in order to clarify structure:function relationships and better understand the underlying disease process.

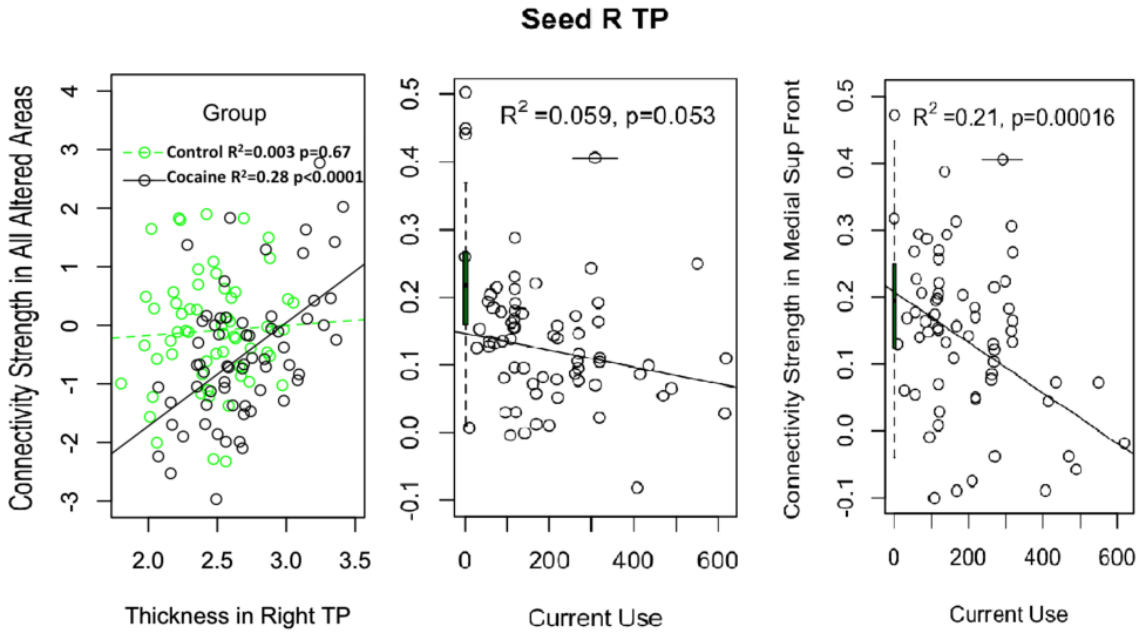
METHODS: 64 chronic cocaine users (CU) and 67 healthy controls (HC) matched on age, gender, IQ and education underwent an MPRAGE structural scan and a 6 minute resting state fMRI scan. Cortical thickness was estimated using Freesurfer and compared between groups using a general linear model, controlling for nicotine dependence, which differed between the groups. Regions of cortical thickness difference were used as seed regions for rsFC analyses. Time courses from each voxel in the seed region were averaged to create a reference time course for each region which was then correlated with the time course of every other voxel in the brain for each participant. rsFC maps were generated separately for CU and HC and compared using a general linear model controlling for nicotine dependence. The relationship between seed region cortical thickness and rsFC in the regions where connectivity differed between CU and HC was examined with a regression analysis. Regression analyses were also performed between cortical thickness/rsFC differences and cocaine use characteristics (years of use and intensity of current use).

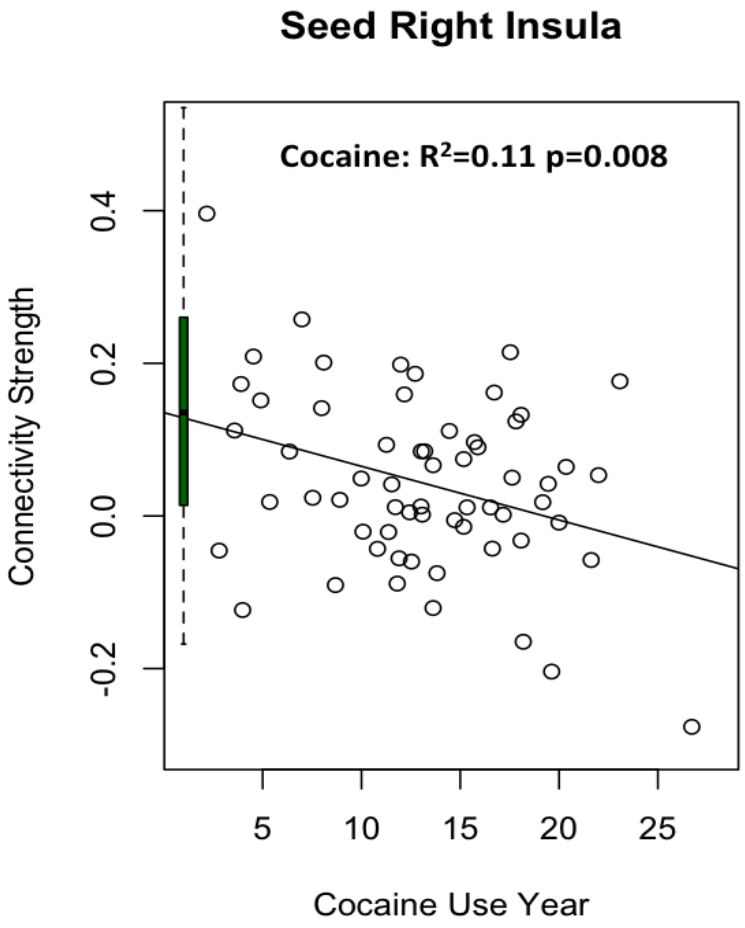
RESULTS: CU group had reduced cortical thickness in bilateral insulae and increased cortical thickness in bilateral temporal poles (TP) (Fig 1). Using these four regions as seeds for rsFC, CU had reduced rsFC from both insulae to dACC and from left insula to left SFG/MFG. CU had reduced rsFC from both TP to MTG/STG, PCC/precuneus and SFG. In addition, right TP had reduced rsFC to mPFC and supramarginal gyrus and left TP had reduced rsFC to cerebellum (Fig 2). rsFC in regions showing group differences from the right TP was correlated with right TP cortical thickness only in CU, and this rsFC correlated negatively with intensity of current cocaine use (trend), especially from right TP to medial SFG (Fig 3). Finally, rsFC in the regions differing from the right insula seed (primarily the dACC) correlated negatively with years of cocaine use (Fig 4).



·Cortical thickness differences: blue=reduced in CU; orange=increased in CU







CONCLUSIONS: We demonstrate both reductions (insula) and increases (TP) in cortical thickness and associated differences in rsFC in networks involving these regions of structural

difference. In particular, insula thickness reductions related to reduced rsFC in a network known as the salience network, which is involved in identifying and orienting attention to physiologically relevant stimuli, both internal and external. Further, this rsFC was most impaired in those with the longest duration of cocaine use, making it likely to be a consequence of use. TP, thought to be involved in social emotional functioning, showed increased thickness in CU but reductions in rsFC to numerous nodes of the default mode network, also important for emotional functioning including empathy. Intriguingly, right TP thickness correlated positively with rsFC only in CU, however the rsFC in CU was negatively correlated with current use. Social emotional difficulties are a risk factor for addiction. While addicts often report improved social functioning while high, objective measures of social and emotional functioning in addiction indicate impairment. These complex relationships may be reflected in the changes found in TP thickness and rsFC. Supported by NIDA Intramural Research Program

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