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Abstract

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PI Title:	ASSISTANT PROFESSOR
Project Title:	DEVELOPMENTAL NEUROMORPHOMETRY IN YOUNG DEPRESSED TWINS

Abstract: DESCRIPTION: Early onset major depressive disorder (MDD) is highly heritable and associated with structural changes in prefrontal-limbic-striatal circuit structures. In young adult females with early onset MDD, the investigators have demonstrated structural differences in the subgenual prefrontal cortex(SGPFC) and amygdala. Specifically we and others have demonstrated reduced volume in the left SGPFC and the right amygdala. Their pilot studies provide evidence that the contributions of genetic and environmental influences differ between the two regions. In recent studies of monozygotic twins discordant for MDD, the investigators have demonstrated that 1) left SGPFC volume reduction in MDD is consistently present in the twin with MDD in comparison to their unaffected co-twin and 2) right amygdala volume reduction and loss of usual amygdala asymmetry is demonstrated in both twins. Thus, they currently have evidence for at least two types of findings: structural changes which are present in ill twins (reduced left SGPFC) and changes which are present in at risk twins (amygdala). They hypothesize that these structural differences may be neurodevelopmental in origin and secondary to environmental or genetic factors, respectively. An alternative hypothesis is that these changes may be secondary to the illness process and represent a neurodegenerative or "scar " phenomenon. Relevant to the neurodevelopmental hypothesis, they have recently demonstrated significant age related increases in SGPFC volume in normal 8 to 21 year old girls in a cross-sectional design. The investigators propose a study examining an sample of epidemiologically ascertained young twins using high resolution MRI in order to examine four interrelated goals: 1) to quantify differences in prefrontal-limbic circuit neuromorphometry in young females with MDD; 2) to characterize neurodevelopmental or neurodegenerative patterns of change in these circuits using a prospective longitudinal design; 3) to estimate through twin genetic modeling the contribution of additive genetic or environmental influences to observed structural differences; and 4) to increase the power of neuromorphometric characterization through the use of automated cortex extraction methods and high-dimensional fluid warping in order to precisely delineate shape changes between subject populations and across developmental time periods. The twin subjects derive from a large established epidemiologically ascertained sample of female twins born in Missouri. The investigation of a twin population

will allow for the direct estimation of genetic and environmental contributions to structural changes and developmental changes noted longitudinally. The combination of cutting edge genetic modeling and automated image analysis with newer sophisticated shape analysis offers a unique constellation of resources which will allow for a powerful exploration of the above hypotheses.

Thesaurus Terms:
adolescence (12-18), amygdala, developmental neurobiology, disease /disorder onset, dizygotic twin, limbic system, major depression, middle childhood (6-11), monozygotic twin, morphometry, prefrontal lobe /cortex
disease /disorder proneness /risk, family genetics, female, gene environment interaction, longitudinal human study, mental health epidemiology, structural biology
brain imaging /visualization /scanning, clinical research, genetic model, human genetic material tag, human subject, interview, magnetic resonance imaging

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