ACNP 2011

Print

Abstract Number: 21 Submitted By: Tomas Hajek
Last Modified: August 3 2011

Structural plasticity of the right inferior frontal gyrus in the course of bipolar disorders - interplay between compensatory changes, illness burden and lithium treatment

Tomas Hajek[1, 2], Jeffrey Cullis[1], Ryan Blagdon[1], Anne Duffy[1], Lukas Propper[1], Miloslav Kopecek[2], Tomas Novak[2], Cyril Hoschl[2], Martin Alda[1, 2]. *[1]Department of Psychiatry, Dalhousie University, Halifax, Nova Scotia, Canada; [2]Prague Psychiatric Centre, Charles University, Prague, , Czech Republic*

BACKGROUND: Bipolar disorders (BD) have a strong genetic underpinning and a typical onset in adolescence/early adulthood. Studies of unaffected as well as affected offspring of bipolar parents transitioning through the at-risk age (genetic high-risk design) are thus useful for separating biological vulnerability markers for BD from the effects of illness burden/medication exposure.
METHODS: We performed a replication-design neuroimaging study. High-risk (HR) participants (aged 15-30 years) were recruited from families affected with BD in Halifax for the initial and in Prague for the replication study. They included 50 unaffected (30 in Halifax, 20 in Prague), 36 affected (21 in Halifax, 15 in Prague) subjects at genetic risk of BD, matched on age and sex with 49 controls (31 in Halifax, 18 in Prague) without personal or family history of psychiatric disorders. We also recruited bipolar subjects selected for substantial burden of illness (>10 years of illness, >5 episodes) and either at least 2 years of regularly monitored lithium exposure (Li group, N=17) or <3 months lifetime lithium exposure over 2 years ago (non-Li group, N=12). These BD patients were matched to 11 healthy controls. Structural imaging data from 1.5T magnets were analyzed using optimized voxel based morphometry in SPM8. Using a replication design, we first performed exploratory contrasts in the Halifax HR group to generate hypotheses, followed by replication tests in the Prague HR cohort as well as in the subjects selected for substantial burden of illness.
RESULTS: Among the clusters of differences between the groups in the Halifax sample, increases in the right inferior frontal gyrus (rIFG), Brodmann area 47, which were present in both the affected and unaffected HR subjects relative to controls were replicated in both the affected and unaffected HR subjects relative to controls in the Prague cohort (replication corrected $p<0.001$). The clusters of increased rIFG relative to controls directly overlapped between the unaffected and affected subjects in each center. The rIFG volume negatively correlated with duration of illness. Furthermore rIFG was significantly smaller among subjects selected for substantial burden of illness and limited exposure to Li (non_Li group), but not among those with comparable illness burden and substantial exposure to Li treatment (Li group).
DISCUSSION: The replicated finding of increased right inferior frontal gyrus gray matter volume in both affected and unaffected relatives of bipolar probands combined with a decrease in the same region in subjects selected for substantial illness burden, may indicate

a compensatory upregulation of neurotrophic mechanisms, which is gradually overcome by the cumulative illness burden. The latter effect may be prevented by lithium treatment. The observation, that structural brain changes indicating neurobiological vulnerability for BD could be a result of an interplay between two opposing processes, has implications for early diagnosis, prevention and interpretation of neuroimaging findings in BD.