To bridge these lines of research we sought to map a transcriptome-based polygenic risk score (PRS) onto MRI-assessed dlPFC function and whole-brain structural covariance network properties.
Methods: Using the GTEx database, we developed a PRS based on 243 common cis-eQTL SNPs which bias gene expression in the dlPFC towards a depression-like molecular phenotype. We next examined the effect of this PRS on dlPFC activity during a working memory task (n=183) in the Duke Neurogenetics Study. We further conducted a structural covariance network analysis (n=1063) to probe potentially development-mediated PRS effects on dlPFC network hub status, as well as whole-brain network clustering (transitivity) and integration capacity (mean path length).
Results: Higher PRS was associated with greater left dlPFC activity in the absence of performance differences during a working memory task, but only in participants reporting high childhood trauma (p =0.03). Structural covariance analyses revealed higher PRS was independently associated with decreased left dlPFC "hubness" and increased mean network path length.
Conclusions: Our results suggest a depression-like transcriptome polygenic risk score is associated with inefficient dlPFC activity supporting working memory, particularly in individuals exposed to early life stress. The same molecular phenotype may also disrupt developmentally mediated shared structural plasticity between the dlPFC and other regions, leading to long-term whole-brain network reorganization consistent with reduced integration capacity.
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Keywords: Depression, Working memory, DLPFC, Polygenic Risk Score, Brain networks

255. Greater Gyrification of the Inferior Frontal Gyrus as a Marker of Genetic Risk for Bipolar Disorders

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Background: In our previous genetic high-risk study, we found replicated evidence for a larger right inferior frontal gyrus (rIFG) gray matter volume in both unaffected as well as affected relatives of bipolar probands relative to controls. Structural changes in the rIFG are one of the few replicated biomarkers of familial predisposition to BD. Here we examined gyrification of the IFG in affected and unaffected relatives of BD probands.
Methods: We measured local gyrification index (LGI) using FreeSurfer. LGI is an automated 3-dimensional metric that quantifies the amount of cortex buried within the sulcal folds versus the outer visible cortex. LGI was compared between 38 unaffected, 28 affected relatives of BD probands, and 41 age matched controls.
Results: Multivariate analysis of variance (MANOVA) revealed a significant group difference in the folding (p = 0.02) of the rIFG. The largest between-group gyrification differences were localized to pars opercularis and pars orbitalis of the rIFG, where in all instances we observed the largest gyrification in unaffected participants at genetic risk for BD.
Conclusions: The finding of increased gyrification in those at risk for BP replicates our prior work in a larger sample using a different method of analysis. Measures of gyrification provide a complementary anatomical marker to assist in the understanding of abnormal neurodevelopmental processes in BD.
Supported By: CIHR; NSHRF
Keywords: bipolar disorder, inferior frontal gyrus, neuroimaging, gyrification, genetic risk

256. Hippocampal Tissue Properties, as Evaluated by Flair and Susceptibility Weighted Imaging in a Preliminary Sample of Patients Treated with ECT

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Background: Electroconvulsive therapy is an effective acute treatment of major depressive episodes. Volumetric increases of the hippocampus and other brain areas have been demonstrated after ECT by using MR imaging. Though harmful effects have not been identified, the structural changes have not been characterized by susceptibility weighted imaging (SWI) or Fluid Attenuated Inversion Recovery (FLAIR), MR sequences in common clinical use which are sensitive to tissue parameters found in microbleeds and oedema, respectively.
Methods: Patients in a major depressive episode referred for ECT (n=15) were scanned before and after ended treatment, and a group of healthy controls (n=8) were scanned twice at corresponding time intervals. Structural T1 volumes were segmented using FreeSurfer (V5.3.0). SWI and FLAIR volumes were registered to the T1 volume, and the accuracy confirmed by visual inspection. Mean voxel intensity values in the hippocampus, as segmented by FreeSurfer was then obtained for SWI and FLAIR.
Results: Intensity differences between the two scans were calculated for the hippocampus for each hemisphere. Data was evaluated for normality through Shapiro-Wilk's test, and

longitudinal changes in the hippocampus were compared between groups by independent t-test as well as Cohen's d: FLAIR; right p=0.12 d=−0.44, left p=0.8 d=−0.21 and SWI; right p=0.6 d=−0.16, left p=0.7 d=−0.22.
Conclusions: Volume increase of the hippocampus is known to be associated with ECT. We did not find corresponding changes in hippocampal tissue properties on FLAIR and SWI. Our sample size is limited, and the results should be confirmed in larger samples.
Supported By: Western Norway Regional Health Authority, Haukeland; University Hospital and the University of Bergen, Norway.
Keywords: MRI brain imaging, Electroconvulsive therapy (ECT), Hippocampus

257. Effects of Electroconvulsive Therapy on Amygdala Function in Major Depression — A Longitudinal fMRI Study

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Background: Electroconvulsive therapy (ECT) is one of the most effective treatments for severe depression. However, little is known regarding brain functional processes mediating ECT effects.
Methods: In a non-randomized prospective study, fMRI data during the automatic processing of subliminally presented emotional faces were obtained twice, about six weeks apart in patients with major depressive disorder (MDD) before and after treatment with ECT (ECT, n=24). Additionally, a control sample of MDD-patients treated solely with pharmacotherapy (MED, n=23), and a healthy control sample (HC, n=22) were obtained.
Results: Before therapy, both patient groups equally showed elevated amygdala reactivity to sad faces compared to HC. After treatment, a decrease in amygdala activity to negative stimuli was discerned in both patient samples indicating a normalization of amygdala function, suggesting mechanisms potentially unspecific for ECT. Moreover, a decrease in amygdala activity to sad faces was associated with symptomatic improvements in the ECT sample (rspearman=−.48, P=.044), and by tendency also for the MED sample (rspearman=−.38, P=.098). However, we did not find any significant association between pre-treatment amygdala function to emotional stimuli and individual symptom improvement, neither for the ECT sample, nor for the MED sample.
Conclusions: In sum, the present study provides first results regarding functional changes in emotion processing due to ECT treatment using a longitudinal design, thus validating and extending our knowledge gained from previous treatment studies. Limitation: ECT patients received concurrent medication treatment.
Supported By: RE111604 to RR
Keywords: Electroconvulsive therapy (ECT), Affective Disorders, Treatment Response, Longitudinal Brain Imaging, Amygdala

258. The Effect of Clinical Course on Longitudinal Changes in Hippocampal Volume: A 2-Year Follow-Up Study in Patients with Major Depressive Disorder

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Background: Structural brain alterations in major depressive disorder are well studied in cross-sectional designs, but little is known about the causality between onset and course of depression, as well as neurobiological changes over time. To explore the direction of causality, longitudinal studies with a long time window are needed, but only few have been undertaken so far. In the present study we explored the effect of the clinical course during a two year interval on changes in hippocampal volume.
Methods: In a longitudinal design we examined 55 patients with DSM-IV major depressive disorder at baseline and after two years using high-resolution magnetic resonance imaging (MRT). Gray matter (GM) volumes have been analyzed by Computational Anatomy Toolbox (CAT12) for SPM12. A 2(time)x2(group) ANOVA was conducted using the hippocampus as ROI. Depending on the clinical course during the follow-up interval, we divided patients into two groups: patients suffering from further depressive episodes and patients with no episodes during baseline and follow-up.
Results: There was a significant interaction effect between time and group in the right hippocampus (x,y,z=14, -8, -18; T(104)=3.77; p<0.0001; k=161 voxels) resulting from an increase in GM volume in the group with no episodes during follow-up and a trend of decrease of GM volume in the group with further episodes.
Conclusions: The results suggest that depressive episodes have a neurotoxic effect on hippocampal volume (neurotoxicity hypothesis). Symptom-free periods seem to be neuroprotective or neuroregenerative, potentially mediated by a medication effect.
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Keywords: Longitudinal Brain Imaging, Major Depressive Disorder (MDD)

259. NIRS Observation of Changes in Brain Activity following Low Field Magnetic Stimulation

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Background: Low Field Magnetic Stimulation (LFMS) is a novel electromagnetic treatment for depression. LFMS acts immediately on depressed states but does not alter mood in those without depression. To understand and develop the treatment, studies of physiologic change in response to LFMS are needed.
Methods: Nine healthy controls were recruited to participate in this randomized, sham controlled, single blinded study. Subjects received either active or sham LFMS on two