

$p=0.923$) were significantly reduced in MDD. SPM with region-of-interest (ROI) analysis revealed that the gray-matter of right hippocampus (PFWE-corrected=0.001) was significantly reduced. Results from the analysis of hippocampal subfields showed the reduction of areas included total Cornu Ammonis (CA) 2/3, subiculum, CA4/DG (Dentate Gyrus), presubiculum, hippocampus, CA1, and fimbria. No any other areas showed significantly changed. Importantly, the reduction of CA2/3 ($r=-0.367$, $p=0.023$), and CA4/DG ($r=-0.403$, $p=0.012$) areas were significantly correlated with the clinical severity of depressive symptoms.

Conclusion: Our data indicate that the hippocampal volumes were reduced in patients with first-episode, drug-naïve MDD. The reduced hippocampal CA2/3 and CA4/DG, which were well correlated with the clinical severity of depressive symptoms, reflect the important role of these areas in the pathophysiology of MDD.

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Association between BclI C/G (rs41423247), Hippocampal Shape, and White Matter Integrity of the Parahippocampal Cingulum in Major Depressive Disorder

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Abstract

We investigated the interactive effects of BclI C/G (rs41423247) allelic variants and the diagnosis of major depressive disorder (MDD) on hippocampal shape and integrity of the left parahippocampal subdivision of the cingulum. Fifty-two patients with MDD and 52 healthy controls (HCs) underwent T1-weighted structural magnetic resonance imaging and BclI C/G (rs41423247) genotyping. We analyzed hippocampal shape using the FIRST module of FSL and analyzed white matter (WM) integrity using diffusion tensor imaging (DTI) and tract-based spatial statistics (TBSS). Significant alterations in left hippocampal shape and decreased fractional anisotropy (FA) values of the left parahippocampal cingulum were observed in MDD patients, compared to HCs. In addition, MDD patients of the BclI minor (G-) allele carrier group showed significant alterations in left hippocampal shape (FDR-corrected, $p < .05$) and decreased FA values of the left parahippocampal cingulum compared to BclI minor (G-) allele carrier HCs. No significant differences between diagnostic subgroups of the C/C homozygotes were observed. Our study provides evidence for alterations in hippocampal shape and decreased integrity of the WM region associated with the hippocampus in MDD, and for the influence of BclI C/G (rs41423247) on hippocampal shape and integrity of the parahippocampal subdivision of the cingulum in depression.

PS183

Effect of electroconvulsive therapy on monoamine oxidase A binding - a preliminary report

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Abstract

Electroconvulsive therapy (ECT) is an effective treatment option in major depression. Despite its approved effectiveness

the underlying neurobiological mechanisms remain unclear. Neuroimaging findings particularly stress an involvement of the serotonergic neurotransmitter system in its mode of action [1]; however, so far investigations have been focussed solely on serotonin transporter and receptors [2]. The aim of this ongoing study is to assess the effects of ECT on monoamine oxidase A (MAO-A). Preliminary data of two patients are shown here.

Two subjects (1 female, aged 48 years, 1 male, aged 25 years) with severe unipolar depression (HAM-D₁₇ score ≥ 24) participated in this study. ECT was carried out unilaterally (right-sided) according to international standard operating procedures; meanwhile antidepressant medication remained unchanged. Patients underwent 2 positron emission tomography (PET) scans using the radioligand [¹¹C]harmin, one before and one after 8 ECT sessions. PET images were co-registered to structural magnetic resonance imaging scans and normalized using SPM12. PET scans were analysed using arterial input functions and the modelling tools in PMOD 3.509. Quantification of MAO-A distribution volume (V_T) maps was carried out voxel-wise with the Logan plot.

Relative change of MAO-A V_T before and after ECT was assessed for 47 brain regions (AAL atlas [3]). The vast majority of the regions showed a decrease of MAO-A V_T (42 and 46 regions, respectively) following ECT, with maximum decreases of 12.9% in the gyrus rectus. Decreases could be noticed also in regions with approved involvement in depression, such as the amygdala, the hippocampus and the cingulate cortex.

These preliminary findings point towards a reduction of MAO-A V_T following treatment with ECT. This is in agreement with studies showing elevated MAO-A V_T in major depression [4], indicating that ECT might lead to a normalization of MAO-A levels.

Reference

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PS184

Biophysical Alterations of the Brain in First-Episode, Drug-Naïve Patients with Major Depressive Disorder: A Magnetization Transfer Imaging Study

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Abstract

Objectives: Previous structural imaging studies have found evidence of brain morphometric changes in patients with major depressive disorder (MDD), which rarely excluded compounding effects of medications and long duration of illnesses. In this study, we aimed to explore the neurobiological mechanism of the macroscopic findings of structural alterations in first-episode, drug-naïve MDD patients.

Methods: The participants were 27 first-episode, drug-naïve MDD patients and 28 healthy controls matched for age and gender. The study was approved by local ethical committee and written consent was obtained from parents of all the subjects. We utilized magnetization transfer imaging (MTI)¹, a quantitative measure of the macromolecular structural integrity of brain

tissue, to identify biophysical alterations, which are represented by a magnetization transfer ratio (MTR). Whole brain voxel-based analysis was used to compare MTR across groups controlling for age and gender, thresholded at $p < 0.05$ (corrected) for a minimum cluster size of 132 voxels. Moreover, we conducted correlation analyses between the average regional values in affected regions with age, 17-item Hamilton Rating Scale for Depression (HRSD) and illness duration.

Results: The patients exhibited significantly reduced MTR in left superior parietal lobule (SPL) and left middle occipital gyrus (MOG) compared to healthy controls ($p < 0.05$, corrected for multiple comparisons). These abnormalities were not correlated with age, HRSD or illness duration.

Conclusions: The first-episode, drug-naïve MDD patients displayed biophysical alterations in the SPL and MOG which were involved in the attentional² and cognitive dysfunction³. These findings in first-episode, drug-naïve MDD patients may reflect illness-related macromolecular changes close to illness onset, and thus potentially provide important new insight into the early neurobiology of depression.

References

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PS185

Opposite 1-H MRS Cho changes in amygdala and DLPFC in responders after SSRI as monotherapy in MDD

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Abstract

Objective: To identify pattern of proton magnetic resonance spectroscopy (1-H MRS) choline (Cho) and other metabolite changes in left amygdala and in left dorsolateral prefrontal cortex (DLPFC) after SSRI treatment as a single psychoactive medication in major depressive disorder (MDD).

Methods: In 17 responders and 11 non-responders Cho, N-acetyl aspartate (NAA), creatine (Cr), myo -inositol (MI), lactate and glutamine and glutamate (Glx) peaks and their ratios were analysed by 1-H MRS on 3T scanner in left amygdala and in left DLPFC prior and after 2 months of SSRI treatment as monotherapy.

Summary of results: In responders, Cho/Cr in DLPFC significantly increased post-treatment (by 16.0%), whereas in amygdala it significantly decreased (by 6.1%). In non-responders there was no change in Cho/Cr in DLPFC, while Cho/Cr in amygdala moderately rose (by 2.5%). No significant changes in MI were observed in any group. Post-treatment improvement rate positively correlates with Cho/Cr increase in DLPFC ($r=0.62$) and inversely with Cho/Cr decrease in amygdala ($r=-0.45$). Cho/Cr changes between two analysed regions are highly correlated themselves ($r=0.82$). Metabolite changes were not dose dependent.

Conclusion: Our findings corroborate the evidence that Cho changes in 1H-MRS reflect metabolic effects of treatment. Results indicate the increased membranes turnover rate in responders in DLPFC (presumably due to phosphorylcholine-to-glycerophosphorylcholine mediated synthesis-to-breakdown overbalance) and decreased in amygdala, a finding congruent to amygdala-to-DLPFC functional connectivity shift observed in neuroimaging studies. High correlation in Cho/Cr changes between the two regions may likely be attributed to their involvement in the same functional circuitry. More profound and eventually class-specific 1-H MRS detectable effects appear to emerge as study medication was used as monotherapy, thus avoiding modulating effects of other psychoactive medications.

PS186

Light exposure and seasonal variation of the serotonin degrading enzyme monoamine oxidase A in the healthy human brain revealed by PET

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Abstract

Objectives: Monoamine oxidase (MAO) A is the key enzyme responsible for the oxidative degradation of several biogenic amines including serotonin in the human brain [1]. A previous positron emission tomography (PET) study revealed elevated MAO-A levels in patients with depressive symptoms, potentially leading to lower serotonergic neurotransmission in these subjects [2]. Seasonal changes in mood, like blues during the dark time of the year, are common within healthy controls living in areas of high latitude [3, 4]. We aimed to demonstrate a light dependent seasonal difference in MAO-A distribution volume (V_T) in a healthy study population.

Methods: 16 healthy subjects (mean age: 37; 14 female) underwent 2 PET scans, one in summer and one in winter, using the radioligand [¹¹C]harmine. PET images were co-registered to structural magnetic resonance imaging scans and normalized using SPM12. Quantification of MAO-A V_T was carried out in PMOD 3.509 using Logan plots for 13 regions of interest [5]. Statistical analysis was performed in SPM12 using Pearson's correlation between regional MAO-A V_T and the cumulated amount of individual exposure to global radiation (total light intensity) during the days (1–30) before the PET scans.

Results: We found significant negative correlations between cumulated global radiation and MAO-A V_T in the amygdala, anterior cingulate cortex and caudate nucleus ($r=-0.561$, $r=-0.550$ and $r=-0.569$; $p<0.05$, highest correlation coefficient for the period of 5 to 14 days) in winter PET scans only.

Conclusions: These findings suggest an increase in MAO-A during winter associated with light deprivation in regions implicated in previous imaging studies on depression. Although the subjects in our study population showed no signs of depressive symptoms these results shed light on the often experienced "seasonality" in healthy people. The lack of a relation between MAO-A and light exposure during the summer months might be explained by a ceiling effect.