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Association analysis of imbalanced interhemispheric functional coordination and early therapeutic efficacy in major depressive disorder: evidence from resting state fMRI.

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Abstract

Background: The relationship between functional changes in brain and therapeutic efficacy remains an intriguing and complex field of research in depression. Emerging evidence indicates that the alteration of interhemispheric functional coordination plays a critical role in the pathogenesis of major depressive disorder (MDD). However, it remains unclear whether the imbalanced interhemispheric functional connectivity is associated with the treatment response in MDD.

Methods: In the present study, we aimed to explore the potential marker by using voxel-mirrored homotopic connectivity (VMHC) approach, which may be contributing to predict the clinical prognosis in MDD. 82 MDD patients and 50 normal control (NC) subjects participated in this study. We divided the MDD group into unresponder and responder group according to the reduction rate of Hamilton Rating Scale for Depression (HAMD) within 2 weeks.

Results: The study detected significantly decreased VMHC in bilateral precuneus (pCu), inferior temporal gyrus (ITG) and increased VMHC in middle frontal gyrus (MFG) and caudate nucleus when compared remitted depression (RD) group to unremitted depression (URD) group. Meanwhile, when compared with NC group, the URD group presented reduced VMHC in bilateral cerebellum anterior lobe, thalamus and postcentral gyrus. Furthermore, the VMHC in media frontal gyrus, postcentral gyrus and precentral gyrus were significantly decreased in URD compared to NC group, the URD group presented reduced VMHC in bilateral precuneus (pCu), inferior temporal gyrus (ITG) and increased VMHC in middle frontal gyrus (MFG) and caudate nucleus when compared remitted depression (RD) group to unremitted depression (URD) group. Meanwhile, when compared with NC group, the URD group presented reduced VMHC in bilateral precuneus (pCu) but increased in right inferior orbitofrontal gyrus (all P<0.05). The nodal degree in right dorso-lateral prefrontal cortex (DLPFC) was significantly decreased in RD compared with URD (P<0.017, FDR corrected). Receiver operating characteristic (ROC) curve analysis indicated that the area under curve (AUC) of nodal degree in right DLPFC was 0.685 [95% confidence interval (CI): 0.64–0.78, P=0.014], which could serve as a specific predictor to differentiate responded patients from unresponded patients.

Conclusion: The study suggests that the altered interhemispheric functional connectivity might be a novel neural trait involved in the pathophysiology of MDD.

Keywords: Major depressive disorder, Graph theory, Antidepressant, Predictor, Early response.

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Post-transcriptional processes in the main serotonin degrading enzyme MAO-A in the adult human brain investigated in vivo with PET and postmortem data

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Abstract

Introduction: Correlations between mRNA expression and positron emission tomography (PET) protein binding in vivo show high associations for structural proteins but rather weak
associations for proteins involved in cell regulation. Strong correlations were found for the serotonin-1A receptor as well as for monoamine oxidase-A (MAO-A). However, regulatory processes induced via exogenous and endogenous substrates have been described for MAO-A, leading to an altered enzyme activity in smokers or depressive patients. To assess potential influences of post-transcriptional modifications for MAO-A correlations between imaging data and gene expression were performed.

**Methods:** PET total volume of distribution ($V_T$) of 22 healthy non-smokers was calculated for the radiotracer [11C]harmine via arterial input function and kinetic modelling with a 2-tissue compartmental model and graphical analysis using Logan plot. More than 3000 mRNA samples across the whole brain from six healthy donors were downloaded from the Allen Human Brain Atlas to perform region-wise (within automated anatomical labeling regions) and voxel-wise correlations with PET $V_T$ using Spearman’s correlation coefficients ($r_s$).

**Results:** Inter-probe correlations for genomic as well as inter-subject correlations for imaging data were strong, indicating consistency within both modalities. Region-wise correlations of MAO-A $V_T$ and mRNA expression values indicated an interesting association for all brains ($r_s=0.30–0.66$, mean $r_s=0.54$ SD=0.14) as well as for a combined analysis including all samples within one brain template ($r_s=0.66$; Fig.1). Voxel-wise correlations showed weaker effects ($r_s=0.21–0.37$, mean $r_s=0.27$ SD=0.06 and $r_s=0.26$, respectively).

**Conclusions:** Present findings indicate regionally distinct influences of post-transcriptional and translational processes throughout the brain. In contrast to previous results, our analyses show less pronounced associations between gene and protein expression. Generally, a strong association between in vivo protein density and enzyme activity suggests a rather short-term regulation of MAO-A.

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Emotion processing related brain activity assessed with 7 Tesla fMRI predicts early antidepressant response
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