Reduced hippocampal GABA and Glx levels in patients suffering from TRD using an automated labelling approach for multivoxel MRS

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Introduction

Several studies reported aberrant levels of GABA and Glx in treatment resistant depression (TRD). However, most studies were conducted using single-voxel magnetic resonance spectroscopy (MRS). Single-voxel MRS has the disadvantage that different tissue types may influence the acquired spectrum in the VOI, especially in challenging areas, e.g. the hippocampus. Hence, we investigated neurotransmitter levels in TRD patients using multi-voxel MRS with a novel automated ROI-based labelling approach to specify changes in the hippocampus.

Methods

MR scans of 12 patients suffering from TRD (3♂, mean age: 36) and 12 healthy (HC) subjects (3♂, mean age: 27) were performed on a 3 Tesla MAGNETOM Prisma MR Scanner. MRS data was acquired using a GABA-edited spiral-encoded, 3D-MRSI sequence with MEGA-LASER editing [1] with an acquired matrix size of 10 × 10 × 10 interpolated to 16 × 16 × 16 matrix (VOI = 80 × 90 × 80mm^3 and field of view (FOV) = 160 × 160 × 160mm^3). T1-weighted anatomical reference images were acquired via a MPRAGE sequence (208 slices, 288x288 matrix size, voxel size 1.15x1.15x0.85mm³). Spectral data was processed using LCModel, MINC and MATLAB. CRLB thresholds were set at 40%, while GABA+ and Glx ratios were calculated relatively to tNAA (GABA+/tNAA and Glx/tNAA). Structural images were automatically segmented using FreeSurfer 6.0, extracting subcortical regions [2] for individual masking of the left (HL) and right (HR) hippocampus. GABA+/tNAA and Glx/tNAA maps were interpolated to the resolution of the MPRAGE images (208x208x208) using nearest-neighbour interpolation and overlaid with masks for each ROI. Statistical analysis was performed in SPSS using paired t-tests with Bonferroni correction for multiple testing.

Results

TRD patients showed a significant decrease of GABA+/tNAA (mean±SD: HL (TRD)=0,135±0,025; HL (HC)=0,169±0,031; HR (TRD)=0,132±0,022; HR (HC)=0,173±0,034) and Glx/tNAA ratios (mean±SD: HL (TRD)=0,77±0,08; HL (HC)=0,937±0,127; HR (TRD)=0,776±0,159; HR (HC)=0,921±0,093) in the hippocampus for both the left (GABA+/tNAA: p=0.017, Glx/tNAA: p=0.026) and right (GABA+/tNAA: p=0.038, Glx/tNAA: p=0.040) hemisphere.

Discussion

A variety of single-voxel MRS approaches investigated changes in GABAergic and glutamatergic neurotransmission in depressed patients across different tissue types. Although some studies were performed investigating neurotransmitter changes an area including parts of the hippocampus and surrounding tissue, of depressed patients [3], we are the first to confirm this data using multi-voxel MRS with ROI-based data analysis to specifically cover the hippocampus.

Conclusion

Patients suffering from TRD showed significant reductions of GABA+/tNAA and Glx/tNAA ratios in the hippocampus, a brain region highly involved in the development of depression. However, the hippocampus remains a challenging area for MRS purposes. Automated ROI-based labelling provides a suitable tool especially for challenging regions to measure using MRS. Hence, we provide clinical evidence of reduced neurotransmitter levels, with improved data analysis to confirm prior findings targeting the hippocampus.

References

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