ECT-INDUCED STRUCTURAL CHANGES IN THE HUMAN BRAIN; A CASE SERIES

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Introduction

Electroconvulsive therapy, ECT, is by many clinicians regarded as the most effective acute treatment of major depression. Yet, we lack a good understanding of what ECT does to the brain and how it alleviates depression. Neurogenesis occurs in the hippocampus[1], and one hypothesis is that ECT mediates neuroplasticity also in the human brain, as has previously been shown in animal studies[2]. ECT-induced structural changes have been shown by manual delineation of the hippocampi[3] at 3T and by using FreeSurfer[4] or complex voxel-wise modeling at 1.5T[5].

Objective

We wanted to test if by applying distortion correction and rigorous image co-registration it would be possible to visualize structural changes at the level of the individual patient.

Material & Methods

Six patients (one man; age 48.3 ± 11.7 years) receiving their first series of right unilateral brief-pulse ECT for major depression were included. ECT was applied three times a week (mean number of sessions; 11.8 ± 4.7). Structural T1 isotropic (1 mm) volumes were acquired at a 3T GE Signa MR system 1-2 hours before (MR1) and after their first ECT (MR2) and at 7-14 days after ended treatment series (MR3). After correcting the images for distortions caused by gradient non-linearity, analysis was done with FreeSurfer (all patients and time points run independently; normalization to intracranial volume). In addition, for each individual the follow-up images were registered to MR1 and regional change quantified using Quarc[6].

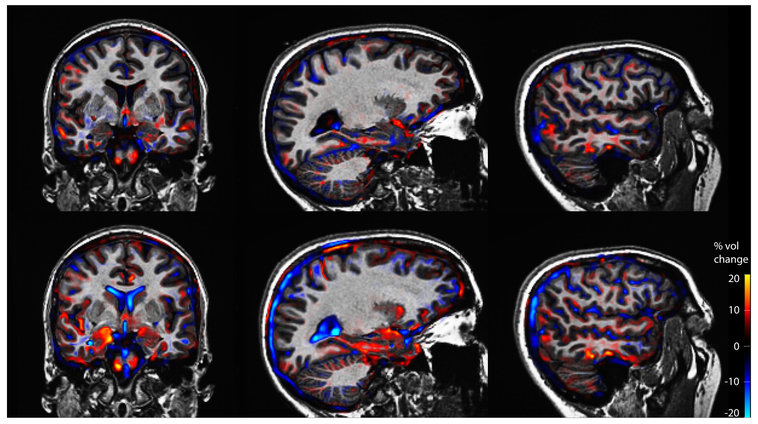

Fig. 1. Volumetric change map (Quarc, single subject). Before treatment *versus* after first ECT (MR1 to MR2; upper row), or after end of treatment series (MR1 to MR3; lower row). Color code indicates areas of increase (red) and decrease (blue). Notice increased hippocampal volume and reduced CSF spaces after ended treatment.

Results

All patients improved; mean MADRS (Montgomery and Aaberg depression rating scale) score was 33.7 ± 4.2 before and 16.3 ± 9.2 after treatment, but three of the patients were classified as non-responders (reduction in MADRS score < 50%). Quantification by FreeSurfer showed increased hippocampal volume by 7% (± 4) after ended treatment series ($p < 0.01$) while it was unchanged by the first ECT (change ~1%, $p > 0.5$). In addition, the striatum (putamen + caudate nucleus) and the total subcortical gray matter volume showed a significant increase (Table 1). Visual inspection of accurately rigid-body co-registered slices from intra-individual T1 volumes, confirmed volumetric changes at the level of individual patients. The volumetric change map from Quarc analysis (Fig 1.) shows the spatial pattern of volume increase (red) or decrease (blue) from MR1 to MR2 and from MR1 to MR3 for a representative subject.

ROI	MR2/MR1	MR3/MR1	*p*
Hippocampus	1 ± 3	7 ± 4*	< 0.01
Amygdala	1 ± 9	9 ± 12	
Putamen	1 ± 5	5 ± 5	
Caudate nucleus	2 ± 2	1 ± 3	
Striatum (**P**+**C**)	1 ± 3	4 ± 4*	= 0.05
Subcortical gray	0 ± 2	4 ± 2*	< 0.02

Table 1. Mean change in volume (% ± SD; FreeSurfer; n=6). Regions of interest (ROI) are left and right side combined.

Discussion

Structural changes were not apparent after a single ECT session, suggesting that the volumetric change is a cumulative treatment effect and not an immediate phenomenon caused by a single seizure. Structural changes were confined to gray matter, which is consistent with a neurotrophic mechanism, although not limited to the hippocampus – also the striatum and the subcortical gray matter volume increased. Results from FreeSurfer were confirmed by independent analysis with Quarc. Furthermore, by use of accurate methods for rigid-body intra-individual co-registration, structural changes could be observed by visual inspection at the level of individual patients.

Conclusion

We confirm prior studies of ECT induced volumetric changes at group level analysis. In addition, we show that after accurate distortion correction and co-registration, these changes may be identified at the level of the individual patient by visual inspection. Changes were confined to gray matter, and largest in, but not limited to, the hippocampus.

References

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