Effect of electroconvulsive therapy on 5-HT_{1A} receptor binding in major depressive disorder

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INTRODUCTION:

Electroconvulsive therapy (ECT) is a highly effective treatment option when employed against treatment-refractory depression. In recent years, ECT has been increasingly used, due to itsameliorated practicability and safety level. To date, despite its apposed effectiveness, the neurobiological mechanisms underlying ECT remain unclear, the findings related to this topic being quite inconsistent. However, a number of preclinical studies point toward a significant involvement of the serotonergic system, particularly the main inhibitory 5-HT_{1A} receptor, in the mode of action of ECT [1, 2]. Since alterations of the 5-HT_{1A} receptor are consistently reported in major depressive disorder [3], this study aims to investigate the effects of ECT on the 5-HT_{1A} receptor in the human brain in vivo using positron emission tomography (PET).

METHODS:

10 subjects (8 female, 2 male, mean age ± SD= 49.8 ± 7.9 years) with severe unipolar depression, determined by a structural clinical interview and the 17-item Hamilton Rating Scale for Depression (HAMD_{17}, score ≥ 23), participated in this longitudinal PET study. ECT was carried out unilaterally according to international standard operating procedures, whereby 5 subjects received additional bilateral ECT, due to initial insufficient symptom relief (9.4 ± 2.4 ECT sessions). Drugs with a high affinity to 5-HT_{1A} receptor were excluded and the current medication remained in steady-state 10 days prior inclusion and during treatment.

Patients underwent 2 PET scans using the highly specific radioligand [carbonyl-^11C]WAY-100635, one before and one after completed ECT session. PET scans were normalized to MNI-space (SPM8). Quantification of 5-HT_{1A} receptor binding potential (BP_{ND}) was carried out in PMOD 3.3 using the multilinear reference tissue model 2 with the cerebellar grey (excluding vermis) as reference.

RESULTS:

The paired-samples t-test showed a significant decrease (t= 7.77, p< 0.001; mean= 18.01 ± 7.37) after ECT compared to baseline scores.

Voxel-wise repeated-measures ANOVA revealed a global decrease of the 5-HT_{1A} receptor binding potential (5-HT_{1A} BP_{ND}) after ECT (p< 0.05, FDR-corrected) using sex and anticonvulsant therapy as covariates. The over-all change of 5-HT_{1A} BP_{ND} corresponded to one interconnected cluster of 632mm³ with peak areas in the anterior cingulate cortex (ACC: t* = -9.18, x/y/z = -8/36/-2mm MNI space), the orbitalfrontal cortex (OFC: t* = -7.83, x/y/z = -6/48/-24mm) and the subgenual part of the cingulate cortex (sgACC: t* = -6.88, x/y/z = 0/22/-14mm).

As anticipated, no changes were found in the occipital cortex.

CONCLUSIONS:

To begin with, our results display once again the efficacy of ECT in depression, given the significant reduction of HAMD-D scores after ECT, testifying for a successful treatment response.

Furthermore, we determined a significant global decrease of 5-HT_{1A} BP_{ND} in depressed patients after ECT, which undermines the hypothesis, implying 5-HT_{1A} receptor changes might be involved in the effectiveness of ECT. We did not replicate the findings of Saigo et al. [4], equally using PET with [carbonyl-^11C]WAY-100635 and suggesting unchanged 5-HT_{1A} BP_{ND} in major depression after ECT. These discrepancies may be due to differences in the method applied and the clinical characteristics of the study participants. However, our results play in concert with previous findings, emphasizing the role of the ACC, sgACC and OFC in controlling emotional and cognitive processes and showing altered function and activity as well as grey matter reductions in these regions in depressed patients [5]. To our knowledge, this is the first study, substantiating the role of serotonergic neurotransmission in the mode of action of ECT in vivo. Our results suggest, that antidepressant treatment using ECT acts - similarly to SSRIS - through a reduction of 5-HT_{1A} receptor binding.

References:

[4] Saigo T., Takasaka A., Suhara T., Araiwa R., Okuma M., Ishiihara K., Ito H., Okubo J. 2010 Electroconvulsive therapy on 5-HT_{1A} receptor binding in patients with depression: a PET study with [carbonyl-^11C]WAY-100635 and suggesting unchanged 5-HT_{1A} BP_{ND} in major depression after ECT. These discrepancies may be due to differences in the method applied and the clinical characteristics of the study participants. However, our results play in concert with previous findings, emphasizing the role of the ACC, sgACC and OFC in controlling emotional and cognitive processes and showing altered function and activity as well as grey matter reductions in these regions in depressed patients [5]. To our knowledge, this is the first study, substantiating the role of serotonergic neurotransmission in the mode of action of ECT in vivo. Our results suggest, that antidepressant treatment using ECT acts - similarly to SSRIS - through a reduction of 5-HT_{1A} receptor binding.

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