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P.301 Hippocampal subfield volumetric changes following electroconvulsive therapy in patients with late-life depression

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Background: Volumetric reductions in the hippocampal formation in major depressive disorder (MDD) and increased hippocampal volume following electroconvulsive therapy (ECT) are robust phenomena [1,2]. Whilst hippocampal volumetric increase does not appear to be associated with clinical improvement in depressed patients, two recent studies investigating hippocampal subfields have shown that dentate gyrus increase is positively associated with remission [3] and mood improvement [4]. Investigating hippocampal subfields may therefore provide greater insight into the effect of ECT on the hippocampus.

Objective: Our primary aim was to replicate the latest findings from Takamiya et al. [3] and Nuninga et al. [4] with data from the MODECT study (Mood Disorders in Elderly treated with ECT) i.e to detect volumetric changes in hippocampal subfields following ECT, especially in the dentate gyrus.

Methods: We investigated ECT-induced changes in hippocampal subfields in 77 patients (72 years) with Late-Life Depression (LLD) who were part of the MODECT study. Hippocampal subfield data (CA1, CA2/3 and CA4/DG) were ob-

tained for each hemisphere one week before starting ECT and one week following the last ECT from high resolution 3D T1-weighted MRI scans using the automated MAGeT-Brain (Multiple Automatically Generated Templates) pipeline [5]. Mixed effect linear modelling with subject as random effect was used to determine subfield volumetric changes over time and investigate the relationship of volume change with mood (Montgomery-Asberg Depression Rating Scale) and cognition (Mini-Mental State Examination). To control for the possible effect of study site it was included as a covariate. Results were considered significant if they exceeded a P-value threshold of $p=0.05$ for main effects of subfield, and Bonferroni corrected p -threshold for associations with mood and cognition ($p=0.05/2=0.025$).

Results: Relative to pre-ECT, no changes in any hippocampal subfield (CA1, CA2/3 and CA4/DG) following ECT were detected via multiple linear regression. All regression models failed to reject the null-hypothesis that the 'Time' coefficient was different from zero (all $p > 0.05$). There were no significant associations with volumetric change in any subfield and mood (MADRS) ($> p=.043$, CA1) or cognition (MMSE) ($> p=.047$) after ECT after correction for multiple comparisons.

Conclusion: In our sample, hippocampal subfield structures defined as CA1, CA2/3 and CA4/DG did not change significantly following ECT, nor were any volumetric changes (if present) associated with mood or cognition. We investigated a larger sample using a comparable segmentation approach [3], but did not replicate the increase in dentate gyrus volume and its association with clinical improvement in our population of patients with late-life depression. This could be due to differences in field strength (3T v 7T) [4] or population age [3,4]. However, our results are in line with findings of no increase in other subfields [4]. The relationship between volumetric change in individual hippocampal subfields and increase in whole hippocampal volume following ECT requires further investigation.

References

- [1] Belleau, E.L., Treadway, M.T., Pizzagalli, D.A., 2018. The Impact of Stress and Major Depressive Disorder on Hippocampal and Medial Prefrontal Cortex Morphology. *Biol. Psychiatry* 85 (6), 443-453.

- [2] Oltegal, L., et al., 2018. Volume of the Human Hippocampus and Clinical Response Following Electroconvulsive Therapy. *Biol. Psychiatry* 84 (8), 574-581.
- [3] Takamiya, A., et al., 2019. Acute and long-term effects of electroconvulsive therapy on human dentate gyrus. *Neuropsychopharmacology* 0, 1-7.
- [4] Nuninga, J.O., et al., 2019. Volume increase in the dentate gyrus after electroconvulsive therapy in depressed patients as measured with 7T. *Mol. Psychiatry* 11-14 eprint.
- [5] Pipitone, J., et al., 2014. Multi-atlas segmentation of the whole hippocampus and subfields using multiple automatically generated templates. *Neuroimage* 101, 494-512.

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P.302 Healthy women who use oral contraceptives show lower brain serotonin 4 receptor binding relative to nonusers

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Background: The lifetime incidence of depression reaches 21% in women, which is about twice the incidence in men. Strong epidemiological evidence supports that women are at higher risk for depression during hormonal transitions, i.e. peripartum and perimenopause. This may extend to exogenous hormone exposure; a large register-based Danish study of more than one million women showed that initiating oral contraceptives (OCs) is associated with subsequent use of antidepressants targeting serotonin (5-HT) neurotransmission [1]. The mechanisms behind this remain elusive, however, OCs may affect 5-HT brain architecture, i.e. reproductive hormones can affect the level of 5-HT synthesis, reuptake, degradation and 5-HT receptor expression. No studies have addressed whether use of OCs affects serotonergic architecture in terms of 5-HT₄ receptor (5-HT₄R) binding, which is sensitive to 5-HT manipulation and provides an indirect biomarker for in vivo brain 5-HT levels [2].

Objectives: We investigate if brain 5-HT₄R binding differs between OC users and nonusers among healthy women. In a secondary analysis we explore if 5-HT₄R binding differs between users of OCs containing gestodene vs. levonorgestrel. **Methods:** [11C]-SB207145, ligand for the 5-HT₄R, positron emission tomography (PET) imaging data were available from the Center for Integrated Molecular Brain Imaging (Cimbi) database [3] for 54 healthy women, of which 17 used OCs (mean age of users = 25.8 vs. nonusers = 26.4, $p=0.71$). Five brain regions, considered important for depression pathophysiology, were co-registered to a magnetic resonance imaging (MRI) image and 5-HT₄R non-displaceable binding potential (BPND) was determined by using the simplified reference tissue model with cerebellum as a reference region. The type of OC was known for 13 of the 17

users, all were combined oral contraceptives (COCs), mainly containing gestodene or levonorgestrel in combination with ethinylestradiol. For this reason the secondary analysis was restricted to these two types of COCs. The association between use of OC and regional BPND was evaluated using multiple linear regression models adjusting for age, scanner type (GE-Advance vs. HRRT Siemens PET scanner), injected [11C]-SB207145 mass per bodyweight and familial risk for depression.

Results: We found a negative association between BPND and use of OCs in all explored regions with the following percentage difference to nonusers; pallidostriatum: -7.6% (CI [-13.9;-0.85], $p=0.03$), caudate nuclei: -8.9% (CI [-15.5;-1.7], $p=0.02$), hippocampus: -11.6% (CI [-19.7;-2.7], $p=0.01$), anterior cingulate: -9.9% (CI [-17.2;-2.0], $p=0.02$), frontal cortex: -8.6% (CI [-16.3;-0.2], $p=0.05$). Women using COCs containing gestodene showed higher BPND in frontal cortex compared to COCs containing levonorgestrel; 16.9%, (CI [6.1;28.7], $p=0.009$). P-values are uncorrected.

Conclusions: Women using OCs have lower cerebral 5-HT₄R binding compared to nonusers. We propose that this reflects an effect of OC hormone exposure on 5-HT₄R expression rather than a change in serotonergic tone. This offers a plausible link between OC exposure and subsequent risk of developing depression, particularly in hormone sensitive individuals. Future intervention studies must elucidate if withdrawal from OCs rescues 5-HT₄R brain architecture and help identify women who are sensitive to OCs.

References

- [1] Skovlund, C.W., Mørch, L.S., Kessing, L.V., Lidegaard, O., 2016. Association of Hormonal Contraception With Depression. *JAMA Psychiatry* 73 (11), 1154-1162.
- [2] Haahr, M.E., Fisher, P.M., Jensen, C.G., Frokjaer, V.G., Mahon, B.M., Madsen, K., Baare, W.F., Lehel, S., Norremolle, A., Rabiner, E.A., Knudsen, G.M., 2014. Central 5-HT₄ receptor binding as biomarker of serotonergic tone in humans: a [11C]SB207145 PET study. *Mol Psychiatry* 19 (4), 427-432.
- [3] Knudsen, G.M., Jensen, P.S., Erritzoe, D., Baaré, W.F., Ettrup, A., Fisher, P.M., Gillings, N., Hansen, H.D., Hansen, L.K., Hasselbalch, S.G., Henningsson, S., Herth, M.M., Holst, K.K., Iversen, P., Kessing, L.V., Macoveanu, J., Madsen, K.S., Mortensen, E.L., Nielsen, F.A., Paulson, O.B., Siebner, H.R., Stenbæk, D.S., Svarer, C., Jernigan, T.L., Strother, S.C., Frokjaer, V.G., 2016. The Center for Integrated Molecular Brain Imaging (Cimbi) database. *Neuroimage* 124, 1213-1219.

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P.303 Multidisciplinary approach to mental illness: do inflammation and telomere length form a loop?

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