

Methods: Our sample consisted of 17 healthy individuals (mean age 39,8±8 years, 9 females) and 40 schizophrenic patients (mean age 39,4±9 years, females 19).

Images were acquired by using a 1.5-T imager (Magnetom Essenza; Siemens, Germany) with implication of fast three-dimensional whole-brain MPF mapping protocol [3]. Statistical analyses were performed in the program Statistica 10.0. To take into account partial volume effects, four tissue classes were prescribed within the single-channel segmentation procedure. These classes correspond to pure weight matter (WM), pure gray matter (GM), mixed voxels that contained partial volumes from WM and GM (PVWGM), and mixed voxels that contained a partial volume from cerebrospinal fluid - boundary layer (BL).

Patients were grouping according to duration of the disease: group №1 - 2-7 years duration of disease, group №2 - 7-14 years, group №3 - more than 15 years disease duration. **Results:** Patients with Schizophrenia had significantly reduced volume of cortical GM.

There was detected significant reduction in the volume of cortical gray matter in patients with leading negative symptoms (mean GM mm3 368816,9; T-Test $p=0.039576$) compared to the control (mean GM mm3 398588,4).

Significant decrease in volume indices in the corticoid GM was found in patients with schizophrenia with different duration of the disease (mean GM mm3; median Test $p=0.0192$): group 1 - 402660.156 mm3, group 2 - 400726.563, group 3 - 358348.633.

A positive correlation ($r=0.36$) was observed between reduces GM volumes and MPF GM which may indicate a reduction in myelinated brain structures. Whereas decrees in MPF BL negatively correlated ($r=-0.37$) with volume changes in BL which can be an indirect evidence of the formation of edema of the meninges on the background of the inflammatory process.

Conclusion: These changes can be explained by activation of inflammatory processes (inflammation of microglia, general activation of the immune system), which are widely represented in the pathogenesis of mental disorders. This point of view is supported by our previous results about the increased level of antibodies to MBP in patients with schizophrenia and the presence of MBP-hydrolyzing antibodies.

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References

- [1] Dietsche, B., Kircher, T., Falkenberg, I., 2017. Structural brain changes in schizophrenia at different stages of the illness: a selective review of longitudinal magnetic resonance imaging studies. *Aust N Z J Psychiatry* 51 (5), 500-508.
- [2] Underhill, H.R., Rostomily, R.C., Mikheev, A.M., Yuan, C., Yarnykh, V.L., 2011. Fast bound pool fraction imaging of the in vivo rat brain: association with myelin content and validation in the C6 glioma model. *Neuroimage* 54 (3), 2052-2065.

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P.368 Dynamics of ketamine-related resting state functional connectivity changes in healthy controls

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Introduction: It is well known that ketamine alters resting state functional connectivity (rsFC) assessed with magnetic resonance imaging (MRI). However, the methodology used to assess ketamine-related rsFC changes varies, and subsequently, so do the results attained. The time-scheme of ketamine administration and rsFC assessment, as well as the rsFC analysis method used are among these potentially influential factors. Many, particularly seed-based approaches, are associated with selection bias, which may however be mitigated through utilization of brain-wide analyses. In addition, many studies treat rsFC in a static manner and do not address the dynamic nature of rsFC.

Aims: The aim of this study was to investigate the dynamics of brain-wide rsFC under and after ketamine infusion using two complementary brain-wide rsFC computation methods.

Methods: 27 healthy controls were included in this study, data from which has been previously published [1]. Two 60 min resting state scans were performed in each subject. MR was performed on a 3 Tesla MR scanner (Siemens Trio, Erlangen, Germany) using a single-shot gradient-recalled EPI sequence (TR/TE: 1.8/0.038 sec, matrix: 128 × 128 voxel, field of view: 190 × 190 mm). Subjects were randomized to one of two arms in a double-blind crossover design. Both arms consisted of one i.v. esketamine infusion and one i.v. placebo (0.9% NaCl) infusion, both administered during a resting state scan, over the course of 20 minutes, and using a MR-compatible infusion-pump. However, the sequence of esketamine/placebo administration was randomized. Esketamine/placebo administration started after 10 minutes of baseline, of which the second five minutes consisted of an i.v. 0.9% NaCl infusion given so that subjects would not recognize the start of study drug infusion. Esketamine dosage consisted of 0.11 mg/kg bolus (1 min), followed by 0.12 mg/kg constant infusion (19 min). Esketamine plasma levels from a pilot study ($n=5$) described in [1] were utilized. For estimation of dynamic rsFC the sliding-window correlation method based on Zalesky et al. [2] and multiplication of temporal derivatives (MTD, Shine et al.) [3] with steps of 1 TR were used. Both methods were performed on the atlases described in Craddock et al. [4] and Power et al. [5] in order to reduce the chance of parcellation-specific results. The association between dynamic rsFC and ketamine plasma level time course was computed via ordinary least-squares regression. The resulting matrices of regression coefficients were entered into a permutation test (10,000 permutations), correcting for multiple comparisons at $\alpha=0.05$.

Results: A negative association between dynamic rsFC in right to left lingual region and ketamine plasma levels was determined using both methods and both atlases (all $p < 0.05$).

Conclusions: Previous studies demonstrate a reduction in lingual rsFC after ketamine infusion. In our study, the negative association of dynamic rsFC, assessed brain-wide, between the right and left lingual regions and ketamine plasma levels was highly reproducible in four separate analyses (2 methods, 2 atlases each). Assessment of brain-wide dynamic rsFC aims to circumvent methodological deficits associated with seed-based and static rsFC approaches.

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References

- [1] Höflich, A., Hahn, A., Küblböck, M., Kranz, G.S., Vanicek, T., Windischberger, C., Saria, A., Kasper, S., Winkler, D., Lanzenberger, R., 2015. Ketamine-induced modulation of the thalamo-cortical network in healthy volunteers as a model for schizophrenia. *Int J Neuropsychopharmacol* 18 (9).
- [2] Zalesky, A., Fornito, A., Cocchi, L., Gollo, L.L., Breakspear, M., 2014. Time-resolved resting-state brain networks. *Proc Natl Acad Sci U S A* 111 (28), 10341-10346.
- [3] Shine, J.M., Koyejo, O., Bell, P.T., Gorgolewski, K.J., Gilat, M., Poldrack, R.A., 2015. Estimation of dynamic functional connectivity using multiplication of temporal derivatives. *Neuroimage* 122, 399-407.
- [4] Craddock, R.C., James, G.A., Holtzheimer, P.E., Hu, X.P., Mayberg, H.A., 2013. Whole brain fMRI atlas generated via spatially constrained spectral clustering. *Hum Brain Mapp* 33 (8), 1914-1928.
- [5] Power, J.D., Cohen, A.L., Nelson, S.M., Wig, G.S., Barnes, K.A., Church, J.A., Vogel, A.C., Laumann, T.O., Miezin, F.M., Schlaggar, B.L., Petersen, S.E., 2011. Functional network organization of the human brain. *Neuron* 72 (4), 665-678.

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P.369 Effects of sexual orientation in homo- and heterosexual men and women on brain structures.

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Background: Sex differences in brain morphology have been extensively investigated up to today. Differences between men and women have been observed in gray and white matter volumes and density of phylogenetically old structures including the insula, hippocampus, thalamus, putamen, amygdala, and cerebellum [1]. Sexual preference (i.e. one's preference for hetero- or homoerotic partners) has been related to subcortical structures of the brain by functional magnetic resonance imaging (fMRI) studies, such as the thalamus and hypothalamus, the parahippocampus and septal area [2,3]. However, the structural correlates of sexual orientation (hetero- versus homosexuality) have rarely been investigated. Moreover, studies investigating the effects of biological sex on brain morphology usually

included heterosexual participants only. Considering these shortcomings, the present study aimed to disentangle the associations of sexual orientation and biological sex with brain morphology using voxel-based morphometry (VBM) in a sample of heterosexual and homosexual men and women.

Methods: The total sample comprised 74 participants, 37 men (21 homosexual [HoM], 16 heterosexual [HeM]) and 37 women (19 homosexual [HoW], 18 heterosexual [HeW]). Participants were recruited via university bulletin boards and LGBT organizations in Aachen and Cologne and surrounding areas as well as by word-of-mouth recommendation. Sexual orientation was assessed via self-report. To measure traits sex-role identity (masculinity and femininity), the Bem Sex Role Inventory (BSRI) scale was used [4]. VBM data were preprocessed using the Computational Anatomy Toolbox (CAT12) implemented in the current version of SPM12 running under MATLAB 2012b. Whole-brain analyses were performed using full factorial designs to compare grey matter volumes (GMV) between the four groups (HoM, HeM, HoW, HeW), with age, total intracranial volume (TIV), education and handedness included as regressors of no interest. To control for multiple comparisons, a family-wise error (FWE) correction at $p < 0.05$ was applied at the voxel level. Additionally, to test for possible relationships between GMV and gender role self-concepts, correlations were run between the resulting GM clusters and BSRI masculinity and femininity scores.

Results: Irrespective of biological sex, hetero- versus homosexual participants exhibited more GMV in the thalamus and precentral gyrus. Sex-specific analysis revealed that hetero- compared to homosexual women had increased GMV specifically in the precentral gyrus, while hetero- versus homosexual men exhibited more GMV in the thalamus. Moreover, significant differences for BSRI masculinity scores were observed between males and females and between heterosexual and homosexual males.

Conclusion: In summary, these findings suggest that sexual orientation in humans is associated with structural differences in the thalamus and precentral gyrus, and that the effects of sexual orientation differ between men and women. The results provide new insights into the neurobiology of biological sex and sexual orientation. Importantly, our findings demonstrate that sexual orientation has unique effects on brain morphology and should thus be taken into account in future studies investigating sex differences in the brain.

References

- [1] Ruigrok, A.N., Salimi-Khorshidi, G., Lai, M.C., Baron-Cohen, S., Lombardo, M.V., Tait, R.J., Suckling, J., 2014. A meta-analysis of sex differences in human brain structure. *Neuroscience & Biobehavioral Reviews* 39, 34-50.
- [2] Poepl, T.B., Langguth, B., Rupprecht, R., Laird, A.R., Eickhoff, S.B., 2016. A neural circuit encoding sexual preference in humans. *Neuroscience & Biobehavioral Reviews* 68, 530-536.
- [3] Abé, C., Johansson, E., Allén, E., Savic, I., 2014. Sexual orientation related differences in cortical thickness in male individuals. *PloS one* 9 (12), e114721.
- [4] Bem, S.L., 1974. The measurement of psychological androgyny. *Journal of consulting and clinical psychology* 42 (2), 155.