and miRNA expression considering only the students with IAT> 50 (Spearman r= 0.562; P= 0.031). Data are expressed as the mean of each group ± SEM.
Conclusion: We here report selective modulation of DAT DNA methylation and alterations in miR-491 levels in young adult university students with high IAT score, and in particular in those carrying the 10/10 genotype, suggesting DAT genetic and epigenetic involvement in the vulnerability to develop IA.

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SOCIALISING WITH PAIN – NEUROPHYSIOLOGICAL UNDERPINS IN A NEUROPATHIC PAIN MODEL

J. Fernandes [1], H. Leite-Almeida [2]. [1] *Life and Health Sciences Research Institute, Neurosciences, Braga, Portugal;* [2] *University of Minho, Minho, Braga, Portugal*

Abstract text

Background and aims: Chronic pain entails a great burden of disease, impacting in several aspects of patients' lives, namely interpersonal relationships. In animal models, CP also decreases social motivation and affects social interactions, including the approach of pain-free conspecifics. Oxytocin (OXT) is a neuropeptide known to regulate a wide range of social behaviors and also exerts analgesic effects. We aim therefore to understand the role of OXT in social behavior and explore its neurobiological substrates.
Methods: Spared nerve injury (SNI) was used to model of chronic pain. Behavioral assessment took place 4 weeks post-SNI. Social interaction (SI) was assessed in dyads (SHAM-SHAM, SHAM-SNI, SNI-SNI) and social preference was assessed using a 3-chamber (3CH) paradigm, with SHAM and SNI animals as targets. Sociability was assessed in the 3CH apparatus, with a naïve rat in one side arena, leaving the other empty. Serum OXT levels were quantified after the 3CH test. After the first behavioral assessment, gabapentin was used to treat CP for 4 weeks and behavior was then reassessed. Additionally, in the control groups, behavior was also assessed after a single OXT i.p. injection. To explore the neural substrates of these behaviors, another set of animals was used to record local field potentials (LFP) in the paraventricular nucleus of the hypothalamus (PVN), nucleus accumbens (NAc) and anterior insula (aINS) during SI test. Serum OXT was collected at the baseline and after social behavior.
Results: SNI animals display decreased SI time and biased social preference for pain-free conspecifics in the 3CH. Serum OXT levels of SNI animals tend to be lower than SHAM-operated animals, and only the latter positively correlated with the interaction time in the 3CH, suggesting a CP-related deficit of OXT release upon social contact. Moreover, the behavioral differences together with peripheral OXT measurements suggest the involvement of the OXTergic system. Importantly, both chronic gabapentin treatment and acute OXT injection were able to revert the behavioral phenotype. In the second experiment, SNI animals manifested sociability deficits in the 3CH paradigm and the same trend for biased preference and lower social interaction in the SI test were observed. Moreover, significant between-group differences were found in average power of the alpha band. Interestingly, in homophenotypical (SHAM-SHAM/SNI-SNI) interactions, SNI presented increased power in all regions except for the left NAc whereas in heterophenotypical interactions (SHAM-SNI), SNI animals showed overall decreased power in the same band. Despite no significant between-group differences were found regarding serum OXT levels, these were positively correlated with alpha power in the L-PVN, R-NAc, and R-INS in homophenotypic context, and negatively correlated with R-INS alpha power in the heterophenotypical context.
Conclusions: Altogether, this work shows that CP impacts rats' social behavior and supports a role for OXT in the mediation of CP effects on rodents' sociability and social preference towards pain-free vs CP conspecifics. Moreover, PVN, NAc and aINS' activity during free SI were able to differentiate pain and pain-free animals, with some of those correlating with peripheral OXT levels, further supporting a role for oxytocinergic modulation in this interplay.
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THE CO-LOCALISATION WITH SPECIFIC NEUROTRANSMITTER SYSTEMS DISCRIMINATES SCHIZOPHRENIA PATIENTS FROM HEALTHY CONTROLS

L. Hahn [1,2], F.J. Raabe [1,3], D. Keeser [1,4], M.J. Rossner [1,5], C. Vetter [1], A. Hasan [6], I. Papzova [6], J. Kambeitz [7], R.K.R. Salokangas [8], J. Hietala [8], A. Bertolino [9,10], P. Brambilla [11,12], R. Upthegrove [13,14,15], S.J. Wood [13,16], R. Lencer [17], S. Borgwardt [18,19], A. Meyer-Lindenberg [20], E. Meisenzahl [21], F. Fabbro [22,23], E. Schwarz [20], C. Pantelis [24], M. Nöthen [25], M. Mann [26], R. Paul [1], A. Ruef [1], N. Koutsouleris [1,2,27]. [1] *Ludwig-Maximilian University, Department of Psychiatry and Psychotherapy, München, Germany;* [2] *Max-Planck Institute of Psychiatry, Munich, Germany;* [3] *Max-Planck Institute of Psychiatry, International Max Planck Research School for Translational Psychiatry IMPRS-TP, Munich, Germany;* [4] *Ludwig-Maximilians University, Clinical Radiology, Munich, Germany;* [5] *Systasy Bioscience GmbH, Munich, Germany;* [6] *University of Augsburg, Department of Psychiatry- Psychotherapy and Psychosomatics- Medical Faculty, Augsburg, Germany;* [7] *University of Cologne, Department of Psychiatry and Psychotherapy- Faculty of Medicine and University Hospital of Cologne, Cologne, Germany;* [8] *University of Turku, Department of Psychiatry, Turku, Finland;* [9] *University of Bari Aldo Moro, Group Department of Basic Medical Sciences of Psychiatric Neuroscience- Neuroscience and Sense Organs, Bari, Italy;* [10] *Azienda Ospedaliero-Universitaria Policlinico di Bari, Azienda Ospedaliero-Universitaria Policlinico di Bar, Bari, Italy;* [11] *Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Department of Neurosciences and Mental Health, Milan, Italy;* [12] *University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy;* [13] *University of Birmingham, School of Psychology, Birmingham, United Kingdom;* [14] *University of Birmingham, Institute of Clinical Sciences- College of Medical and Dental Science, Birmingham, United Kingdom;* [15] *Forward Thinking Birmingham and Birmingham and Solihull Mental Health Foundation Trust, Birmingham, United Kingdom;* [16] *University of Melbourne, Centre for Youth Mental Health, Melbourne, Australia;* [17] *University of Münster, Department of Psychiatry and Psychotherapy, Münster, Germany;* [18] *University of Basel, Department of Psychiatry, Basel, Switzerland;* [19] *University of Lübeck, Department of Psychiatry- Psychosomatics and Psychotherapy, Lübeck, Germany;* [20] *Central Institute of Mental Health, Department of Psychiatry and Psychotherapy- Medical Faculty Mannheim, Mannheim, Germany;* [21] *Heinrich-Heine University, Department of Psychiatry and Psychotherapy- Medical Faculty, Düsseldorf, Germany;* [22] *University of Udine, Cognitive Neuroscience Laboratory-DILL, Udine, Italy;* [23] *IRCCS "E. Medea" Udine, Udine, Italy;* [24] *The University of Melbourne and Melbourne Health, Melbourne Neuropsychiatry Centre-Department of Psychiatry, Melbourne, Australia;* [25] *University of Bonn, Institute of Human Genetics- Medical Faculty & University Hospital Bon, Bonn, Germany;* [26] *Max Planck Institute of Biochemistry, Department of Proteomics and Signal Transduction, Martinsried, Germany;* [27] *King's College London, Institute of Psychiatry- Psychology and Neurosciences, London, United Kingdom*

Abstract text

Background: Aside to common psychotic symptoms such as hallucinations, delusions and disorganized thinking, schizophrenia (SCZ) is characterized by structural alterations such as volume reductions in the temporal, frontal, and parietal lobes 1. Only little is known about the underlying mechanisms leading to the anatomical constraints of the pathophysiology. Here, we evaluated if these alterations are linked to the distribution of specific neurotransmitter systems. Furthermore, we assessed the predictive value of these associations by building a supervised machine learning classifier for the differentiation of SCZ patients and healthy controls (HC).
Methods: Maps of grey matter volume (GMV) were derived from T1-weighted structural magnetic resonance imaging for 67 SCZ patients (mean age = 35.6 ± 12.0, 15 females) and 56 HC (mean age = 33.1 ± 11.8, 31 females). The data were collected within the scope of the MIMICSS (Multimodal imaging in chronic

Schizophrenia Study; part of the PsyCourse study) 2 study. To test for group differences in GMV, pairwise group t-contrasts were performed in SPM12 using a one-way ANOVA with group (SCZ patient or HC) as independent variable and age, sex and TIV as covariates (family wise error corrected voxel threshold: $p < .05$). Furthermore, we examined if these structural alterations co-localize with the known non-pathological distribution of 25 specific neurotransmitter systems using the JuSpace toolbox [3]. Finally, we used the co-localization features to build a support vector classifier discriminating between groups. The model was trained in a nested cross validation structure with five folds and ten permutations at each level.

Results: Compared to HC, SCZ patients displayed significantly reduced grey matter volume in the left and right amygdala. Moreover, these alterations significantly co-localized with the distribution of serotonin and dopamine receptors (5-HT1a: mean r = -.14, $p < .001$; 5-HT2a: mean r = -.07, p = .01; D1: mean r = .08, $p < .001$), serotonin, dopamine, and acetylcholine transporters (DAT: mean r = .10, $p < .001$; SERT: mean r = .07, p = .002; VAChT: mean r = .14, $p < .001$), and FDOPA (mean r = -.09, $p < .001$). Whereas negative correlation coefficients point to GMV reductions in areas with high density of those neurotransmitters in health, positive correlation coefficients suggest increased GMV in areas with high neurotransmitter density. Finally, using the Fisher's z transformed correlation coefficients of GMV with 25 neurotransmitter systems as features the classifier discriminated SCZ from HC with a balanced accuracy of 70.6 %.

Conclusion: GMV volume reductions in SCZ follow the distribution of specific neurotransmitter systems, supporting the notion of the preferential vulnerability of specific neurotransmitter systems. Moreover, SCZ was clearly distinguishable from HC based on the association of structural alterations with 25 neurotransmitter systems. These findings suggest that the association with specific neurotransmitter systems might serve as a diagnostic biomarker.

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LOW-GRADE INFLAMMATION IN DEPRESSION IS ASSOCIATED WITH INCREASED MISCLASSIFICATION OF NEGATIVE FACIAL EMOTIONS

M. Aichholzer [1], C. Schiweck [1], E. Brandt [1], M. Schneider [1], T. Hamzehloiya [1], A. Reif [1], S. Edwin Thanarajah [1]. [1] *University Hospital Frankfurt- Goethe University, Department for Psychiatry- Psychosomatic Medicine and Psychotherapy, Frankfurt am Main, Germany*

Abstract text

Background: Biased processing of emotional stimuli is one of the core cognitive features of depression [1]. The facial emotion recognition task (FERT) is a well-established method for measuring impaired emotional processing, that is associated with symptom severity of depression and is sensitive to alterations generated by medication or acute stress exposure [2]. There is growing evidence, that low-grade inflammation including the subtle elevation of peripheral inflammatory parameters plays a relevant role in major depressive disorder (MDD) [3]. However, its impact on emotional processing and stress response is unclear. In this study, we aim to analyse if peripheral inflammation is related to impaired emotional processing in patients with MDD after acute stress exposure.

Methods: MDD patients (n=17) and healthy controls (HC, n=24), matched by age and body mass index were recruited at the University Hospital Frankfurt. The Mini International Neuropsychiatric Interview was conducted to confirm the diagnosis of MDD in patients and to exclude a psychiatric diagnosis in healthy controls. All participants completed the questionnaires and interviews for perceived stress (Perceived Stress Scale), symptom severity of depression (Montgomery-Åsberg Depression Rating Scale), and anhedonia (Snaith-Hamilton-Pleasure-Scale). Blood for interleukin-6 and C-reactive protein (CRP) measurements was sampled after an overnight fast. Afterward, participants underwent the FERT twice: before and after a mental arithmetic stress task with psychosocial elements. MDD is associated with a negative bias that leads to a greater tendency to misclassify positive or neutral faces as faces expressing negative emotions 1. Therefore, we evaluated the misclassification of negative facial expressions and the reaction time for detecting negative facial expressions under baseline and stress conditions. We performed linear mixed effect models to investigate the interaction between group and condition, as well as the effect of inflammatory parameters on the misclassification rate and reaction time. The significance level was $p<0.05$. Statistical analysis was performed in R (version 4.2.1).

Results: For the misclassification of faces, we did not find an effect of stress, but we found an interaction between the group and the inflammatory parameter CRP (timepoint x CRP, $F(1,37)=6.8$, $p=0.01$). Across baseline and stress conditions, higher CRP levels were associated with a higher misclassification rate in MDD patients. For the reaction time, we only found a main effect of stress condition ($F(1,37)=63.62$, $p<0.001$). After acute stress, both groups performed faster in the FERT.

Conclusion: This study shows that low-grade inflammation in MDD is associated with higher misclassification rates independent of acute stress exposure. In contrast, reaction time was rather dependent on stress conditions and was not predicted by the inflammatory parameter. These findings suggest that misclassification rates in the FERT might be a tool to detect MDD patients with enhanced peripheral inflammation. The results must be interpreted in the context of the currently still low sample. Despite this low sample size significant results can already be presented while recruitment is still ongoing.

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THE EFFECTS OF DEEP BRAIN STIMULATION ON COGNITION IN TREATMENT-RESISTANT DEPRESSION

N. Runia [1], G. Mol [1], T. Hillenius [1], Z. Hassanzadeh [2], D. Denys [1], I. Bergfeld [1]. [1] *Amsterdam UMC location University of Amsterdam, Department of Psychiatry, Amsterdam, Netherlands;* [2] *University of Amsterdam, Department of Psychiatry, Amsterdam, Netherlands*

Abstract text

Background – Approximately a third of patients with major depressive disorder (MDD) do not achieve remission after several adequate therapeutic interventions and are referred to as suffering from treatment-resistant depression (TRD). TRD is a debilitating condition associated with higher medical costs, increased illness burden, and reduced quality of life compared to non-treatment-resistant MDD. Deep Brain Stimulation (DBS) is a promising intervention for TRD. Research in Parkinson's disease has shown that DBS may lead to cognitive impairments. It is unknown whether DBS leads to cognitive impairments in patients with TRD as well.

Aim – To assess if DBS leads to cognitive impairments in TRD, we investigated the effects of DBS on cognitive functioning in TRD with a meta-analysis.

Methods – A systematic search in PubMed/MEDLINE was performed using terms related to DBS combined with terms related to cognitive functioning. Articles were eligible if standardized neuropsychological tests were used to assess cognitive functioning in patients with TRD (≥18 years of age) who were treated with DBS. Each study had to include a preoperative assessment and a follow-up assessment between 6 to 18 months. Separate meta-analyses were performed for different cognitive domains (verbal memory, visual memory, executive functioning, verbal fluency, working memory, attention/psychomotor speed,