potential, psilocybin (at a dose that significantly induced HTR) induced a strong antidepressant-like effect 48 hours post injection. Our synaptic protein findings suggest that this antidepressant effect may be related to the effect of psilocybin on synaptogenesis. SV2A is a membrane protein of synaptic vesicles and is used as an indirect estimate of synaptic density deficit associated with psychiatric disorders such as depression. GAP-43 is expressed at high levels in neuronal growth during axonal regeneration and after learning. Our results show insights into the mechanism by which psychedelics increase synaptic plasticity and support a novel therapy for treatment-resistant psychiatric disorders.
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MODULATION OF MELANOCORTIN-3-RECEPTOR NEURONS AFFECTS FOOD INTAKE UNDER STRESS EXPOSURE

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Abstract text
Nowadays stress has become a common trigger for inappropriate eating behaviors, yet the mechanism behind is not well established. The central melanocortin system is known to be the key regulator of energy homeostasis, it is mediated through a family of five related G protein–coupled melanocortin receptors, melanocortin 1 receptor through melanocortin 5 receptor, whereas only melanocortin 3 receptor (MC3R) and melanocortin 4 receptor are expressed in the brain. Mice lacking MC3R have been shown to have abnormal responses to fasting, shown by inappropriate refeeding behavior and altered corticosterone levels. However, where these MC3R neurons are acting to mediate effects of nutritional stresses such as fasting is unknown. In addition, recent work shows a role for MC3R in social behaviors as well. Therefore, in this study, we aimed to decipher the role of melanocortin-3-receptor in feeding behavior under various conditions. We also aim to explore the specific projections of MC3R into different brain regions.
We studied the role of MC3R modulation in two different stress paradigms (nutritional and non-nutritional) using the DREADD mouse model. We used MC3R-Cre; ROSA26-LSL-hm3DGq and MC3R-Cre; ROSA26-LSL-hm4DGi mice. Wildtype C57BL/6N mice were also used for control. The mice receive either CNO or Saline on the day of experiment. For the nutritional paradigm, we fasted the mice for 16 hours and tested their refeeding behavior afterwards. Bodyweight change was recorded, nuclear magnetic resonance was conducted to test their body composition change. For the non-nutritional paradigm, we used an adapted social defeat model, where the experimental mouse was defeated by an aggressive CD-1 mouse and cohoused together with a plexiglass-divider for 7 hours afterwards. Food intake, feeding behavior and body weight change was recorded and compared during cohousing for four continual days.
Further, we identified innervation of MC3R neurons to target sites using the MC3R-Cre; ROSA26-LSL-Synaptophysin-TdTomato mouse model. After immunohistochemistry and confocal imaging. We analyzed the images in ImageJ and used Two-Way-ANOVA with Šídák's multiple comparisons for statistics.
Our behavior data showed that MC3R activation rescued the body weight loss of the mice after acute stress exposure, likely due to a higher amount of food intake. MC3R inhibition had the opposite effect, demonstrating a trend towards an increase in body weight loss and a decrease in food intake.
Our immunohistochemistry data identified amygdala as a target of MC3R neurons. Interestingly, we found out a distinct pattern of MC3R projections to the central amygdala and completely absent of projection to the basolateral amygdala (BLA). The amygdala is responsible for fear response, reward mechanisms and promoting anxiety-like behavior. We hypothesize, MC3R regulates neuronal circuits projecting to the AMY to mediate food intake under stress situations. We plan to further study these connections using AAV-mediated tracing techniques, as well as site specific modulations of the MC3R.
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DO BRAIN REGIONS INVOLVED IN THREAT PROCESSING MEDIATE THE ASSOCIATION BETWEEN DEVELOPMENTAL TRAUMA AND PSYCHOSIS

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Abstract text
Background: There is growing evidence that developmental trauma - psychologically traumatic events during childhood and/or adolescence – is causally associated with increased risk of psychosis in adulthood [1]. However, an understanding of the precise mechanisms underlying this is lacking. Consistent with biopsychosocial and computational theories of psychosis [2,3], multiple lines of evidence converge on the role of altered threat processing in the pathway linking developmental trauma and psychosis [4,5]. Here, in a well-characterised birth cohort, we investigate prospectively, the effect of developmental trauma on volumes of brain structures involved in threat processing, and examine their roles in the association between developmental trauma and psychotic experiences in adulthood.
Methods: We used data from the Avon Longitudinal Study of Parents and Children (ALSPAC) study, a large population-based cohort in the United Kingdom. Data from 418 participants were derived from parent- or self-reported assessments. Trauma variables represent trauma exposure (between 0-17 years), the number of types, and timing of trauma: childhood (0-10.9 years) or adolescence (11-17 years). Psychotic experiences were assessed using the psychosis-like symptoms semi-structured interview at 12 and 18 years. Magnetic resonance imaging was used to measure volumes of the whole brain, amygdala, vmPFC, and striatum at age 18. We used logistic and linear regression, and mediation analyses to examine associations. In addition, we explored whether these associations could be explained by genetic confounding or reverse causation, by repeating analyses (1) whilst adjusting for schizophrenia polygenic risk scores (PRS), and (2) in a subgroup of individuals who did not report psychotic experiences at age 12 (n=304).
Results: Exposure to developmental trauma was associated with an increased odds of psychotic experiences at age 18 (OR=1.80; 95% CI=1.17-2.81, p<.001), with evidence supporting dose-response effects for exposure to multiple trauma types (B=.18, p<.001, R2=.05), and at both age periods (B=.15, p<.001, R2=.03). Developmental trauma was associated with reduced left amygdalar volumes in adulthood (B=-.01, p<.01, R2=.02), with evidence supporting a dose-response association, whereby exposure to three or more types of trauma (B=-.004, p<.05, R2=.01), and exposure to trauma during both childhood and adolescence (B=-.003, p<.05, R2=.01), had a greater effect compared with exposure during childhood or adolescence only. Developmental trauma was not associated with alterations in vmPFC and striatal volumes. Reduced left amygdalar volumes mediated 16% (95% CI=2%-80%, p=.03) of the association between developmental trauma and psychotic experiences (mediation effect: 0.04, 95% CI=0.01-0.08, p=.015). These findings substantively remained the same in sensitivity analyses aimed to minimise the effects of reverse causation and genetic confounding.
Conclusions: In this study, we found evidence of a dose-response association between developmental trauma and reduced left amygdalar volumes in adulthood, and of a mediating role of left amygdalar volumes in the trauma-psychosis association. These findings were not explained by reverse causation or genetic confounding. These findings provide observational evidence for the hypothesis that a causal association between developmental trauma and altered threat

processing underlies vulnerability to psychosis. Importantly, our identification of a neurobiological mediator of the trauma-psychosis relationship informs strategies for secondary and tertiary prevention of psychosis associated with developmental trauma.

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EXPLORING DEFINITIONS OF IMMUNOMETABOLIC DEPRESSION

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Abstract text

Objective: Depression is a major driver of disability and related health-care costs. Current treatment options for depression are effective but not for everyone, creating a currently unmet need for personalised treatment. As the role of (neuro) inflammation in depression is emerging, augmentation of antidepressant treatments with anti-inflammatory drugs such as celecoxib has shown encouraging preliminary results. Such treatments may in particular be beneficial to persons with Immuno-Metabolic Depression (IMD), characterized by the clustering of inflammatory and metabolic dysregulations and atypical, energy-related symptoms (hyperphagia, weight gain, hypersomnia, fatigue and leaden paralysis)1, for which we are currently also evaluating in an RCT the extent to which the anti-inflammatory drug celecoxib add-on is effective (INFLAMED; clintrails.gov nummer). However, how different features of IMD overlap or how the concept of IMD can best be described has not been systematically investigated.
the aim of this study is to study overlap of IMD features and to identify whether (change in) inflammatory markers (hsCRP, IL-6, TNFa) and metabolic markers (cholesterol, triglycerides, glucose, leptin) are predictive of depression severity and chronicity.

Methods: Two waves of data (from baseline to 2-year follow-up) of the Netherlands Study of Depression and Anxiety (NESDA) were used 2. Our sample consisted of patients with a current MDD diagnosis within 6 months of baseline (N=675). Depression was profiled using the self-rated Inventory of Depressive Symptomatology (IDS-SR). Univariate and multivariate linear regressions were performed to study how biological measures predicted atypical, energy-related depression symptoms (AES) at baseline and over 2-year follow-up, while controlling for covariates. Logistic regression was used to analyse which measures were linked with chronic depression.

Results: Of all cases, 21% presented with at least two out of three selected IMD features (relevant AES symptoms, elevated CRP, obesity) while only 6% presented with all three features. Change in biomarkers did not predict change in atypical, energy related symptoms over two year follow-up, with the exception of total and LDL cholesterol ($p = 0.024$ and $p = 0.014$, respectively). However, change in cholesterol, glucose and IL-6 was associated with change in CRP, but not with atypical, energy related symptoms. Additionally, the analysis showed that across all depressed patients, measures of triglycerides:HDL ratio (OR 1.255 (95% CI 1.011, 1.567), inflammation (IL-6; OR 1.101 (95% CI 1.019, 1.226), and atypical, energy related symptom severity (OR 1.121 (95% CI 1.058, 1.189) predicted chronicity of depression over two year follow-up.

Conclusion: Our preliminary results showed an association between IL-6, triglycerides:HDL ratio, and atypical, energy-related symptoms in predicting chronicity of depression. This confirms that immuno-metabolic dysregulation has an impact on depression outcomes. To best describe or define the IMD concept, more biomarkers should likely be considered besides AES, CRP and obesity. Future analyses will include multiple waves of NESDA data to further investigate this.

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GENETICS AND EPIGENETIC OF DOPAMINE TRANSPORTER GENE IN INTERNET ADDICTION

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Abstract text

Introduction: The use of internet has brought dramatic changes in interpersonal communications and relationship, these are not necessarily positive if there is no balance between the time online and the time offline, leading to abuse symptoms and causing potentially mental health problems. Internet addiction (IA) has been classified as impulse-control disorder or a behaviour addiction 1 and several criteria for its diagnosis and assessment have been suggested with the Internet addiction test (IAT) resulting as the most used 2. It is of clear relevance to analyze genetic and environmental differences between individuals to understand individual predisposition to potentially develop IA 3. Among the different neuromodulatory systems a key role in IA is played by the dopaminergic system 4.

Aim: The aim of this study is to evaluate the genetic and epigenetic of dopamine transporter (DAT) gene in young University student reporting high and low IAT scores.

Methods: 127 voluntary participants (Male = 39; Female = 88; Mean age: 21.6 ± 3.33) recruited from undergraduate University students with no psychiatric or drug addiction history participated in the study after providing written informed consent. Each student completed a self-reported test to collect socio-demographic data and the IAT test to assess the risk of IA. Genomic DNA from self-collected saliva samples was prepared using the salting-out method and DNA methylation status of 6 CpG sites in 5'UTR of DAT gene was assessed using pyrosequencing assays. Moreover, we analysed the 3′-untranslated region (3′-UTR) DAT1/SLC6A3 polymorphism, a 40 bp VNTR (variable number tandem repeat). Furthermore, from salivary exosomes we measured the expression of miR-491-5p, targeting this specific VNTR.

Results: We observed a selective increase in DNA methylation % of DAT gene at CpG sites 5 and 7 in young adults with high IAT score (IAT>50: CpG5: 13.78 ±1.1; CpG7: 11.88 ±1.0) compared to those with low score (IAT<29: CpG5: 9.96 ±0.48; CpG7: 8.70 ±0.83) ($P<0.05$). No association between IA scores and the VNTR was observed, however higher levels in DNA methylation at CpG site 5 and 7 in those students with high IAT carrying the 10/10 VNTR (CpG5: 15.64 ±1.2; CpG7: 13.50 ±0.77) ($P<0.05$). Furthermore, we observed in miR-491 an increase gene expression in students with high IAT scores (IAT>50: 2.93 ± 0.45) compared to the control group (IAT<29: 1.03 ±0.22) ($P<0.05$) and the Spearman's correlation analysis revealed a positive correlation between the IAT scores