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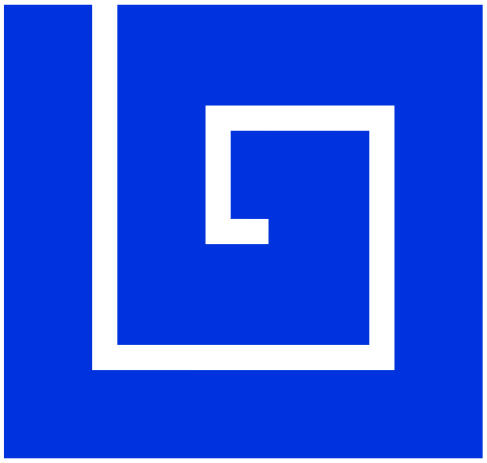

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The 7th Finnish Symposium on
Biological Psychiatry

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ABSTRACT BOOKLET

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ABSTRACTS OF SHORT TALKS

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HELAAKOSKI V. [1], *KAPRIO J.* [1], *OLLILA HM.* [1,2,3,4], *LATVALA A.* [5]

SLEEP PROBLEMS AND ALCOHOL USE: A LONGITUDINAL TWIN STUDY ACROSS 36 YEARS

Alcohol is associated with several health issues, including sleep problems. Despite the fact that acute effects of alcohol intake on sleep have been widely investigated, the longitudinal associations between alcohol use and sleep problems remain relatively underexplored. The objective of our research was to shed light on cross-sectional and longitudinal associations between alcohol consumption and sleep problems over time, and to elucidate the role of genetics in such associations. Using self-report questionnaire data from the Older Finnish Twin Cohort (N=4,259), we examined how short sleep duration and poor sleep quality are associated with heavy alcohol consumption and binge drinking during a period of 36 years. Cross-sectional regression analyses revealed significant associations between sleep and alcohol traits at all time points, suggesting that increased alcohol intake is associated with poor sleep quality and shorter sleep duration over the years. Longitudinal cross-lagged analyses indicated that both heavy drinking and binge drinking predict lowered sleep quality, but not vice versa. The results from within-pair analyses were too weak for any conclusions to be drawn about genetic influences. In conclusion, our findings support previous literature in that heavy alcohol use is associated with short sleep duration and poor sleep quality. Additionally, our research suggests that drinking predicts poor sleep quality later in life.

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EFFECTS OF ACUTE LYSERGIC ACID DIETHYLAMIDE ON INTERMITTENT ETHANOL AND SUCROSE DRINKING AND INTRACRANIAL SELF-STIMULATION IN C57BL/6 MICE

Rationale: Psychedelics, like lysergic acid diethylamide (LSD), are again being studied as potential therapies for many neuropsychiatric disorders, including addictions. At the same time, the effects of psychedelics on acutely rewarding behaviours have been scarcely studied. Objectives: The current study aimed to clarify if LSD could decrease intermittent ethanol drinking in mice, and whether the observed acute effects on ethanol consumption would be generalisable to a natural reinforcer, sucrose, and if the effects stemmed from some aversive or reward-attenuating effects caused by LSD. Methods: The effects of acute LSD were examined using 2-bottle choice intermittent ethanol (20%) and sucrose drinking (10%), discrete-trial current-intensity threshold method of intracranial self-stimulation, and short-term feeding behaviour experiment in C57BL/6 male mice. Results: The results showed that 0.1 mg/kg dose (i.p.), but not 0.05 mg/kg, of LSD reduced intermittent ethanol drinking acutely with no observed prolonged effects. Similar effects were not seen on intermittent sucrose drinking. The tested LSD doses had no effect on the intracranial self-stimulation current-intensity thresholds, nor did LSD affect the threshold-lowering, or rewarding, effects of simultaneous amphetamine treatment. Further, LSD did have small, acute diminishing effects on food and water intake. Conclusions: Based on these results, LSD can decrease binge-like ethanol drinking in mice, but only acutely. This effect is not likely to stem from reward-attenuating effects but could be due to reduced consummatory behaviour.

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GIGLIOTTA A., CAFARO F., LAINE M., TRONTTI K., AND HOVATTA I.

GENETIC BACKGROUND MODULATES THE EFFECT OF CHRONIC PSYCHOSOCIAL STRESS ON MICROGLIAL FUNCTION

Anxiety disorders constitute the most prevalent psychiatric disorders and cause significant disability. Our group recently identified myelin plasticity as a major brain stress response using a mouse model of chronic social defeat stress (CSDS). The observed differences in myelin thickness were influenced by the genetic background of the mice and varied between animals that developed social avoidance after CSDS (susceptible) and mice that did not (resilient). Our RNA-sequencing data from the medial prefrontal cortex after CSDS indicate that genes associated with microglia activation and phagocytosis are overrepresented within the differentially expressed genes in B6 susceptible vs control mice. Microglia have been shown to affect oligodendrocyte progenitor cell (OPC) proliferation and differentiation. To investigate whether CSDS affects the microglia-OPC crosstalk, we compared the number of activated microglia (CD68+/IBA1+ cells) and the number of microglia in contact with OPCs (PDGFRa+ /IBA1+ cells) between C57BL/6NCrl (B6; mostly stress resilient) and DBA/2NCrl (D2; mostly stress susceptible) mice after CSDS. We observed less microglia engulfing OPCs and a longer distance between OPCs and the closest microglia cell in D2 susceptible animals vs controls, suggesting decreased microglia-OPC communication. While this crosstalk was not affected in B6 defeated animals, we found that the area of CD68+ staining of lysosomes was larger in B6 susceptible animals compared to controls, suggesting an alteration of microglial phagocytosis. Taken together, our results suggest that chronic psychosocial stress affects microglial function in a strain-specific manner. Our data underscore the importance of considering the genetic background when studying stress-induced activation of microglia.

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INDIVIDUAL NEUROFEEDBACK LEARNING PROFILES OF ADHD PATIENTS

Attention deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder, which causes severe difficulty in education and life of children and adults. Current treatments for ADHD, behaviour therapy and medication, present serious limitations in terms of long-term maintenance of symptom remission and side effects. Neurofeedback training (NF) is a promising non-invasive method with minimal side-effects and sustained outcome. Yet, Finland's ADHD Current Care Guidelines do not support the use of NF. Mechanisms of NF remain unclear. We found that NF is a form of skill acquisition (Veilahti et al., 2021), so NF should be learned, not merely conditioned. However, there is no single best training strategy for every learner. We study a large data set from a double-blind, sham-controlled randomised clinical trial of theta/beta ratio (TBR) NF for ADHD (Neurofeedback Collaborative Group, 2020). To find which patients benefit from NF, we first ask which patients learn the skill of controlling their own EEG. We model the learning process in TBR data with various methods: learning curve, performance consistency analyses; mixed linear models; continuous-time structural equation models (Driver et al., 2017). Ratio of patients classified as learners in the training vs sham groups (based on individual learning curve slopes) increased with more training. Moreover, within-session TBR variability was more stable in the training group. Subjects with a higher expected value of within-session TBR variability had wider variance of the same. The expected value-variance dependance followed a power law. The power coefficient was lower for the training group, which manifested better sensitivity to own brain state (while TBR served as brain state indicator). Understanding particular NF learning parameters of ADHD patients, especially temporal, will lead to optimised protocols to train NF skill learning, and reliable prediction of treatment inefficiency for non-learners.

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LAMMI V., NAKANISHI T., JONES SE., RICHARDS B., OLLILA H.

INTERNATIONAL HOST GENETICS COLLABORATION TO TACKLE LONG COVID

While the world is still fighting the spread and casualties of the acute disease caused by SARS-CoV-2 virus, there is also a need for mitigating the long-term effects of this pandemic. WHO has estimated that 10-20% of Coronavirus Disease 2019 (COVID-19) patients suffer from lingering symptoms, termed Long COVID (/Post-acute sequelae of COVID-19, PASC / Post COVID-19 conditions). Various symptoms have been reported in virtually all organs, with debilitating fatigue, exercise intolerance, cognitive dysfunction, anxiety, depression, and loss of smell or taste among the most prevalent.

We have established an open world-wide collaboration for elucidating genetic risk factors predisposing to Long COVID. Currently, the Long COVID Host Genetics Initiative includes 46 studies across 23 countries with genotype data combined to questionnaire information of symptoms and/or electronic health record (EHR) data of diagnoses.

Using questionnaire data, we have defined Long COVID as any symptoms that cannot be explained by alternative diagnoses, or impact on everyday functioning, 3 months after the onset of COVID. With EHR data, we have used specific diagnosis codes for Post COVID-19 conditions or Coronavirus as the cause of other diseases (ICD-10: U09, B97.2).

In the first data freeze, we have 10 studies from 8 countries, with 1,475 Long COVID cases and 800,200 controls, of which 96,692 have had COVID but not Long COVID. We perform genome-wide association analyses comparing Long COVID 1) to population controls and 2) to individuals who have recovered from COVID within 3 months.

GWAS of individual cohorts have suggested potential variants associated with Long COVID but without genome-wide statistical significance. We are currently running meta-analyses to increase statistical power by combining data from these studies.

Genetic variants may help shed light to the pathophysiological mechanisms of Long COVID and suggest potential targets for treatment development.

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FUNCTIONAL CHANGES IN THE SALIENCE NETWORK CORRELATE WITH DELUSION INTENSITY IN FIRST-EPISODE PSYCHOSIS PATIENTS

Reality distortion symptoms are characteristic of psychotic disorders, however, the brain correlates of delusions remain poorly known. To increase sensitivity, and validity for naturalistic brain functioning, we collected individual fMRI signal-time series, time-locked to movie stimulus, after remission of psychosis. These voxelwise signal time series were used to model corresponding fMRI signal time series during the first episode psychosis, characterized by delusions. From the Helsinki Early Psychosis Study (HEPS), we selected those patients who presented without delusions at the one-year follow-up. The magnitude of FEP-related functional brain alteration negatively correlated with the baseline delusion severity in bilateral insula. In addition, we observed a similar negative correlation in the anterior cingulate. Functional connectivity between both insulas with the precuneus was decreased in the baseline patient group when compared with control subjects and with the same patients at remission. The results support earlier evidence on involvement of the cortical hub regions in delusions, especially of the salience network (SN). Further studies should assess role of SN in (dys)regulation of meso-striatal dopaminergic pathways.

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