participated in two sessions, receiving 2 mA cathodal tDCS to the left dorsolateral prefrontal cortex (dlPFC) or sham tDCS in a crossover design. Participants completed the alcohol approach Implicit Association Test (IAT), drinking identity IAT, flower-insect IAT and Stroop task concurrent with tDCS.

Results: Preregistered ANOVAs revealed significant implicit alcohol-avoidance ($F(1, 28) = 15.16$, $p = .001$, $\eta p^2 = .35$) and non-drinking identity biases ($F(1, 29) = 8.11$, $p = .008$, $\eta p^2 = .22$). Cathodal tDCS did not modulate IAT results. Explicit ratings showed a preference for non-alcoholic drinks and non-drinking identity, correlating moderately with IAT scores ($r = 0.35$ and $r = 0.41$). Exploratory analyses indicated that cathodal tDCS might inhibit the increase in nicotine craving during sessions ($\chi^2 = 3.91$, $p = .048$).

Conclusions: This study confirms previous findings of negative alcohol-related cognitions in abstinent individuals with AUD and highlights the role of environmental influences on implicit cognition. Additionally, it demonstrates that cathodal tDCS to the left dorsolateral prefrontal cortex does not alter implicit associations in AUD.

Keywords: Transcranial Direct Current Stimulation (tDCS), implicit association, Alcohol Use Disorder (AUD), Neuromodulation

618. Phase 1 Open-Label Pilot Trial of Deep Repetitive Transcranial Stimulation of the Lateral Prefrontal Cortex and Insula for Adults With Moderate-To-Severe Cannabis Use Disorder

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Background: Cannabis use disorder (CUD) has a lifetime prevalence in Canada of 6.8%, yet no treatments are currently approved. Deep repetitive transcranial magnetic stimulation (rTMS) provides a novel treatment option. In particular, Brainsway's H4 rTMS coil, which stimulates the bilateral insula and prefrontal cortex, may be effective given its recent clearance as an aid for short-term smoking cessation. Consequently, this Phase 1 clinical trial aims to establish the feasibility, tolerability, and efficacy of treating CUD using the d-rTMS H4 Coil.

Methods: Six participants were recruited from the greater Hamilton area as part of the ongoing treatment trial (Mage = 31.67, 66.7% Female). Eligible participants were aged 25-65 years, inhaled cannabis 4+ days/week, and possessed 4+ DSM-5 symptoms for CUD and a readiness to change > 5. Participants were excluded due to comorbid substance use, unstable medical conditions, contraindications to rTMS (e.g., history of seizure), and recurrent headaches. Participants attend18 rTMS treatments after a brief provocation, including cannabis images and paraphernalia. Participants also completed weekly motivational interviewing sessions.

Results: Results show significantly (p=.017) reduced cannabis consumption by the end of treatment, with daily use decreasing by an average of 1.8 grams. Further, significant reductions were observed in cannabis demand metrics (p=.003-.009) and cannabis craving (p=.017) over the course of treatment.

Conclusions: While data collection is still ongoing, the current results suggest that the H4 Coil is an effective novel treatment for reducing cannabis consumption, demand, and craving, and support the development of a future Phase II trial.

Funding Source: Peter Boris Centre for Addictions Research

Keywords: Repetitive Transcranial Magnetic Stimulation, Cannabis use disorder, Neuromodulation, Phase I trial

619. Prenatal Maternal Inflammation and Psychological Symptom Domains in Offspring During Late Midlife: The Influence of Timing of Exposure and Fetal Sex

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Background: Prenatal maternal inflammation (PNMI) is associated with offspring psychopathology throughout development in childhood and adolescence. We sought to determine whether there is specificity in offspring psychological symptom domains in late midlife following PNMI and explore differential effects of timing of exposure and fetal sex assigned at birth.

Methods: Dataset included 139 mother-offspring dyads from the Child Health and Development Studies cohort with inflammatory biomarkers [interleukin (IL)-6, IL-8, IL-1 receptor antagonist (IL-1RA), soluble tumor necrosis factor receptor-II (sTNF-RII)] from maternal first (T1) and second (T2) trimester sera. The Center for Epidemiologic Studies Depression Scale (CES-D), State-Trait Anxiety Inventory (STAI-Trait), Community Assessment of Psychic Experiences-Positive scale (CAPE-15), and Structured Clinical Interview for the DSM-5 (SCID-5) were administered to adult offspring (mean age=59). Analyses consisted of multiple linear regressions stratified by trimester and sex, controlling for maternal education and maternal depression.

Results: T1 PNMI predicted greater depressive (IL-6: b=3.70, $p < 0.05$) and anxiety symptoms (IL-6: b=2.00, $p < 0.05$) and increased risk of a substance use disorder [IL-6: OR=5.34 (1.40, 27.76), $p < 0.05$; IL-1RA: OR=3.63 (1.16, 13.77), $p < 0.05$] in male offspring, and greater psychotic-like experiences (IL-6: b=2.10, $p < 0.05$) in female offspring. T2 PNMI predicted greater depressive (IL-6: b=7.68, $p < 0.001$, IL-8: b=2.39, $p < 0.05$) and anxiety symptoms (IL-6: b=3.09, $p < 0.001$, IL-1RA: b=2.39, $p < 0.05$) in female offspring only.

Conclusions: These findings indicate timing- and sex-specific relationships between PNMI and offspring psychological symptom domains observed in late midlife, where T1 PNMI exposure mostly influences male offspring and T2 PNMI influences female offspring.

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Keywords: Maternal Inflammation, Prenatal exposure, Psychological Symptoms, Offspring Outcomes, Substance Use Disorder (SUD)

620. Comparing Quality of Life Trajectories Across Substance Use Disorders: Treatment Implications

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Background: While research highlights the importance of assessing quality of life (QOL) during substance use disorder (SUD) treatment (Tomlinson et al., 2022), few studies compare outcomes across different SUDs. Understanding such differences could inform more tailored interventions (NIDA, 2018).
Methods: QOL scores (Quality of Life Enjoyment and Satisfaction Questionnaire, Endicott, 1993) were evaluated among patients from 5 SUD clinics every 3-6 months for up to 13 timepoints from 1990-2024. Groups included alcohol, cannabis, opioid, sedative, stimulant, and other use disorders.
Results: At baseline, pairwise comparisons indicated that the alcohol group had higher baseline QOL than sedative ($p < 0.01$) and opioid ($p = 0.02$) groups. A mixed-effects model was fit with timepoint (fixed effect) and individual (random effect) to assess change over time. All groups experienced improvements in QOL over time, with individuals in the sedative group showing the steepest improvement (slope = 0.1227), significantly higher than other groups ($p < 0.0001$). Those with sedative use disorders improved most on domains of mood, ability to function, economic stability, overall sense of well-being, and sexual drive, while the "other" group declined in physical health, social functioning, leisure, and overall sense of well-being.
Conclusions: Understanding how QOL evolves in different SUD groups, along with their specific strengths and challenges, offers valuable insights for designing substance-specific interventions as well as inclusive treatment approaches. Future analyses could incorporate demographic covariates to explore moderating effects. A limitation of this analysis is the heterogeneity of the "other" group that included poly-substance use disorder, which complicates meaningful conclusions for this group.
Keywords: Substance Use Disorders, treatment outcomes, Longitudinal modeling, Quality Of Life, Trajectories

621. Plasmatic Biomarkers of Brain Suffering During Alcohol Withdrawal in Patients With AUD

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Background: Neurofilament Light Chain (NfL), a protein originating from the brain, can be assessed in the cerebrospinal fluid or in the plasma in case of axonal injury. NfL is proposed as a predictive biomarker in neurodegenerative disorders, and more recently, has been studied in substance use disorders. NfL have been shown to be elevated in patients with AUD, but our objective is to describe its time course over the event of alcohol withdrawal.
Methods: Patients with severe AUD scheduled for an inpatient alcohol detoxification were assessed at three times: Day 1, Day 3-4, D13-15 after entry. NfL plasmatic dosage was measured with a highly sensitive ELISA test (Quanterix* Simoa). The outcome in terms of medical complications of alcohol withdrawal (Wernicke's encephalopathy clinical signs) and the dosage of prescribed benzodiazepines to control for withdrawal symptoms were recorded.
Results: The number of recruited subjects was 24, 18 with a complete set of 3 assessments. The age-adjusted plasmatic rate of NfL increased from D1 to D3-4 ($p=0.045$), and then seems to decrease D1- D13-15 ($p=0.097$). Repeated measure ANOVA identified a significant time x diazepam dose interaction for NfL plasmatic rate. No association was observed between NfL plasmatic rates and the presence of ataxia or other sign of Wernicke's encephalopathy, but only 7 subjects were concerned.
Conclusions: This work strongly suggests that even with the recommended medical care, brain suffering occurs during alcohol withdrawal. The development of validated, accessible, plasmatic biomarkers is warranted in order to test preventive strategies.
Funding Source: INSERM (Institute National de la Recherche), France, FHU NOR-SUD
Keywords: Alcohol Dependence, Alcohol Withdrawal, Neural candidate biomarkers

622. The Role of the Endocannabinoid System in Social Stress Reactivity Among Non-Medical Prescription Opioid Users

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Background: The ongoing opioid crisis in North America is gradually spreading globally, emphasizing the need for a better understanding of the neurobiological mechanism underpinning opioid use disorder (OUD). Animal studies have highlighted opioids' modulatory role in stress response mechanisms, but human evidence is inconsistent. Moreover, animal and human studies indicate that the endocannabinoid system (ECS) plays a crucial role in stress response processes. We recently showed dysfunctional stress reactivity of the hypothalamic-pituitary adrenergic (HPA) axis in individuals with non-medical prescription opioid use (NMPOU) after the psychosocial stressor of social exclusion induced by the Cyberball task.
Methods: Here, we tested peripheral endocannabinoids response to the Cyberball task in the same sample of NMPOU ($N=21$) and matched healthy opioid-naïve controls ($N=29$). We examined plasma levels of the endocannabinoids anandamide and 2-arachidonoylglycerol (2-AG), as well as ECS-related