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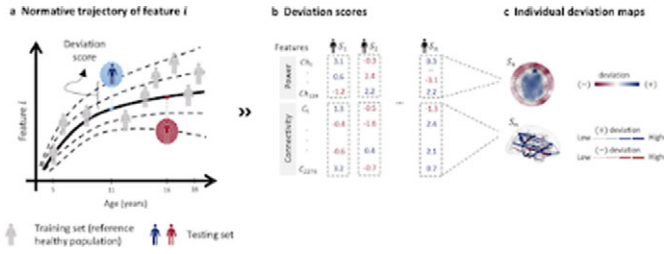
Introduction: Electroencephalography (EEG) has been extensively studied for decades in psychiatric research. However, its integration into clinical practice as a diagnostic or prognostic tool remains unachieved. We hypothesize that a key reason for this is the underlying heterogeneity among patients, which is often overlooked in psychiatric EEG research that relies on a case-control approach.
Objectives: The main objective of this study is to quantify the electrophysiological heterogeneity of psychiatric disorders.
Methods: We combine HD-EEG with normative modeling to quantify this heterogeneity using two well-established and extensively investigated EEG characteristics—spectral power and functional connectivity—across a cohort of 1,674 patients with attention-deficit/hyperactivity disorder, autism spectrum disorder, learning disorder, or anxiety, and 560 matched controls, see figure 1.
Results: Normative models revealed that deviations from population norms among patients were highly heterogeneous and frequency-dependent. The spatial overlap of deviations among patients did not exceed 40% for spectral power and 24% for connectivity. Taking individual deviations into account significantly enhanced comparative analysis and the identification of patient-specific markers, which showed a correlation with clinical assessments.

Image 1:



Conclusions: Our study underscores the necessity of moving EEG research in psychiatry beyond the group-level approach to achieve precision psychiatry.

Disclosure of Interest: None Declared

Psychopharmacology and Pharmacoeconomics

O023

MM120 (lysergide) in a controlled clinical setting: treatment of generalized anxiety disorder without co-occurring psychotherapeutic intervention

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Introduction: Generalized anxiety disorder (GAD) is among the most common psychiatric disorders and has significant impairment on patients' daily life. Effective and well-tolerated pharmacotherapies are needed. The FDA has noted that the inclusion of psychotherapy within trials complicates assessment of psychedelic drug efficacy, although to date many psychedelic trials have included co-occurring psychotherapy.[1] Co-occurring psychotherapy confounds the evaluation of efficacy and may complicate commercial labeling. A phase 2b study of the dose response to single treatment MM120 (lysergide D-tartrate) suggests a safe, rapid, and durable dose-dependent response in participants with moderate-to-severe GAD[2] and design elements are examined herein.
Objectives: To examine the methodological use of Dosing Session Monitors (DSM) within MM120 treatment without co-occurring of psychotherapy.
Methods: This phase 2b (NCT05407064) multicenter, randomized, double-blind, placebo-controlled study enrolled adults aged 18 to 74 years diagnosed with moderate to severe GAD.[2] Two DSMs, meeting FDA recommended qualifications,[1] were assigned to a participant throughout the study duration. Prior to dosing, participants engaged in baseline study education with their DSMs. During dosing, DSMs provided assistance and comfort as needed and monitored the participant for safety. Starting at 8 hours post-dose, a pre-specified checklist to end the session was administered, although all participants were required to stay onsite a minimum of 12 hours. The follow up period for the trial was 12 weeks, and DSMs only followed up with participants at Day 2, Week 1, and Week 2 post-dose. DSM follow up focused on participant safety and did not include focus on producing post-synaptic change.
Results: In total, 198 participants were enrolled in the study. The phase 2b study demonstrated a statistically significant safe, dose-response relationship at the week 4, 8, and 12 primary and secondary endpoints.[1] Utilizing the prespecified checklist, 45% of participants receiving MM120 100µg met criteria for end of session at 8 hours post dose, with 87.5% achieving criteria at 10 hours.
Conclusions: The results demonstrate that a single treatment with MM120 produces a safe and durable clinical response without co-occurring psychotherapy. These findings indicate that MM120 treatment sessions may be safely shortened from a minimum of 12 hours to 8 hours for some participants, and psychotherapy does not appear to be essential for its safety and efficacy.

1. FDA—Center for Drug Evaluation and Research. Psychedelic drugs: considerations for clinical investigations (FDA-2023-D-1987).

2. Karlin, D et al. Rapid and Durable Response to a Single Dose of MM120 (Lysergide) in Generalized Anxiety Disorder: A Dose-Optimization Study. Poster P03-026. Presented at: APA Annual Meeting; May 4-8, 2024; New York City, NY. 2024.

Disclosure of Interest: S. Karas Employee of: Mind Medicine, Inc., R. Barrow Employee of: Mind Medicine, Inc., C. Conant Employee of: Mind Medicine, Inc., J. Freedman Employee of: Mind Medicine, Inc., P. Jacobsen Employee of: Mind Medicine, Inc., J. Jemison Employee of: Mind Medicine, Inc., D. Karlin Employee of: Mind Medicine, Inc., T. Solomon Employee of: Mind Medicine, Inc.

Neuroimaging

O025

Affective Go/NoGo fMRI study of adults living with ADHD reveals differential BOLD activation in ACC, insula, and secondary visual cortex

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Introduction: Attention-Deficit/Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder that begins in childhood and persists into adulthood in 35-50% of cases, resulting in a prevalence of 2-4% in the adult population. The core symptoms are inattention, hyperactivity, and impulsivity, while emotional dysregulation is considered an associated symptom. Several lines of evidence support structural and functional brain imaging alterations in ADHD. Decreased volume of the accumbens and amygdala persist from childhood into adulthood, and several resting-state and task-related functional alterations have also been reported.
Objectives: To investigate differential brain activation patterns in adults diagnosed with ADHD as compared to healthy controls (HC) during an affective Go/NoGo task, to understand the neural background of selective inhibition in emotionally demanding situations.
Methods: Data of 61 subjects were analyzed: 34 adult ADHD patients meeting DSM-IV diagnostic criteria (17 women, 17 men, mean age 37.3 years) and 19 HCs (10 women, 9 men, mean age 30.2 years). HCs were screened using the 90-item Symptom Checklist to exclude current psychiatric comorbidity. Symptom severity was assessed using the Conners' Adult ADHD Rating Scale (CAARS). During the MRI scan in a Philips Achieva 3.0T scanner, we used a block design delivering positive, negative and neutral stimuli from the IAPS System applying a Go/NoGo paradigm. The fMRI analysis focused on contrasts between task and rest, emotional and neutral, and Go and NoGo conditions (activation or deactivation). Contrast between activation and deactivation in the ADHD and HC groups were tested.
Results: Based on the pooled data from both groups, we found significant contrasts between the task and rest conditions, including an activation of primary and secondary visual cortex, frontal areas, corresponding to the Visual Network (VN), the Dorsal- and Ventral- Attention Networks (DAN, VAN), and the Central Executive Network; and a deactivation of the anterior cingulate, precuneus and parietal areas, corresponding to the Default Mode Network (DMN). During emotional vs neutral conditions, we detected activation of the secondary visual cortex, while contrasts between NoGo vs Go conditions manifested as activation of ACC and insular regions. ADHD subjects showed increased BOLD activation in the DAN and VAN areas. In all conditions, DMN areas showed higher deactivation in the ADHD group.
Conclusions: Here, we report differences in VN, DAN and VAN brain regions and the DMN in adult ADHD patients suggestive of distinctive pattern of activation and deactivation during an emotional Go/NoGo task. The results have clinical implications for understanding ADHD patients under in emotionally demanding situations.
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Old Age Psychiatry

O026

Temporal Trajectories of Depressive Symptoms, Apathy, ADL and Cognitive Decline in Older People; a Dynamic Time Warping network analysis

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Introduction: The prevalence of depressive symptoms and cognitive decline increases with age. Understanding the temporal dynamics of these symptoms could provide valuable insights into the early stages of cognitive decline, allowing for more timely and effective treatment and management.
Objectives: Our objective was to explore how depressive symptoms, apathy, limitations in daily life activities, and cognitive impairment evolve and interact over time in older individuals. Specifically, we aimed to determine whether changes in these symptoms could help identify subsequent cognitive decline. We used Dynamic Time Warping analysis to model and characterize the progression of these symptoms, examining their relationships both at individual and group levels.
Methods: Participants from the Prevention of Dementia by Intensive Vascular Care (preDIVA) trial cohort with baseline and ≥3 follow-up measurements were included, with a median of 6.7 years of follow-up. Dynamic Time Warping analysis was used to model temporal dynamics of individual constituents of the Mini Mental State Exam (MMSE), activities of daily living (ADL) using the Amsterdam Linear Disability Scale (ALDS) and depressive symptoms using the 15-item Geriatric Depression Scale (GDS-15).
Results: The 1537 participants had an average age of 74 years at baseline, 56.5% were female, and 19.9% had finished a higher education. The directed analyses revealed a nuanced temporal pattern, wherein certain depressive symptoms preceded cognitive decline indicators, and vice versa. The GDS-15 symptoms with the