ORAL PRESENTATION
Session 1
Autism and Social Functioning
Chair: **Prof. Ravid Doron** *The Open University of Israel, Raanana*

Social cooperation inheritance as a key player to model autism-like symptoms

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Autism spectrum disorder (ASD) diagnosis is based on three behavioural criteria: abnormal social interactions, communication deficits and the presence of restricted repetitive behaviors. Though ASD is increasingly prevalent, with approximately more than 2% occurrence in the general population, there is no designated treatment specifically developed for ASD. Considering the above-mentioned ASD core symptoms, we have established a novel animal model for social interactions and communication. Utilizing our computerized social cooperation (SC) maze, a pair of rats is required to coordinate their shuttling through 3 virtual subzones of the maze, aiming at receiving mutual sucrose reward along 18 days. Additionally, we conducted a selective breeding procedure along 15 generations, in which the selection rule was based on defining the highest or lowest 10% of SC performers. These 15 transgenerational inheritance iterations yielded two distinct subpopulations of 'High' and 'Low' that progressively differed in SC performance. Considering the crucial role of the social factor in ASD, we further the examination of the Low performers' subpopulation as suggested ASD rat model and related to some additional human ASD phenotype. First, we found that female rats performed either better or equal to males, which is in accordance with the decreased ASD prevalence in human females. We also found that the Low SC showed increased sustain attention and decreased ultrasonic vocalization and selective attention. The Low performers significantly showed more repetitive behavior. Finally, similar to human ASD, the Low performers showed elevation of serum BDNF level. Our preliminary results suggest the Low performers as a feasible rat model for ASD. Currently, we are furthering this model and exploring its genetic and proteomic mechanism.

Ugh, what a huge and repulsive spider! The link between emotion regulation and spider size estimation

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Fear can lead to perceptual biases. For example, people who are afraid of spiders perceive spiders as larger than people who are not afraid of spiders. In a series of studies, we have examined the link between this perceptual bias and emotion regulation, the physiological processes that subserve this link, and the role of expertise. Specifically, we conducted three experiments in which individuals were asked to rate the size of spiders, butterflies, and wasps depicted in pictures. Emotion regulation was either assessed via a questionnaire (Experiment 1) or manipulated (Experiment 2). Furthermore, pupillometry recordings were used to assess physiological activity (Experiment 2). Lastly, we conducted the experiment among spider experts (entomologists) to assess the role of expertise in size estimation. Findings show that people with high fear of spiders perceive the spiders' size as larger than butterflies. This effect was not observed among the control group. We also observed a link between spider's size and suppression, a maladaptive emotion regulation strategy. Furthermore, preliminary findings from Experiment 2 indicate a role for physiological arousal in the link between emotion regulation and spiders' size estimation. Lastly, spider-experts did not show a perceptual bias, but an accurate perception of spiders' size. Overall, these findings suggest a link between fear and perceptual biases, which can be either increased or attenuated by different emotion regulation strategies, as well as expertise

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Shank3 mutation impairs oligodendrocyte properties and myelin development in ASD mouse model and human iPSCs-derived oligodendrocytes

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Autism spectrum disorders (ASD) are a group of developmental disorders that are characterized by social and neurocognitive impairments, among other symptoms. Although the underlying mechanisms of ASD remain largely unknown, strong evidence supports a genetic link, particularly with the *SHANK3* gene, a high-risk gene for monogenic ASD. SHANK3 is known to be expressed in excitatory neurons and to have an integral role in neuronal synaptic transmission. Studying the InsG3680 mouse model for ASD with a *Shank3* mutation seen in human ASD patients, we focused on myelination properties and neuron-glia interactions, a less studied aspect in ASD. We revealed a novel role for Shank3 in post-synaptic oligodendrocyte (OL) features, similar to its role in neurons, as shown by impaired molecular and physiological glutamatergic traits. To further investigate the neurobiological mechanisms that occur due to this mutation, we examined myelination properties in the mouse model brain compared to controls. Specifically, we observed structural, physiological, cellular, and molecular myelination-related deficits in several brain regions. In addition, we discovered clinically relevant deficits in induced pluripotent stem cells (iPSCs)- derived OLs associated with the mutation. Collectively, our data provide valuable pathophysiological insights that establish a connection between myelination deficits and ASD-related pathology and have the potential to improve the treatment of ASD.

Extrinsic Emotion Regulation Strategies Among Individuals with Subclinical Depression

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Extrinsic emotion regulation (EER) is the provision of emotion regulation support to another person. An important question is what factors influence peoples' choice of EER strategy. The present study examined the role of depression symptoms in EER strategy use. Fifty-one women who reported high levels of depression symptoms measured by the Major Depression Inventory (MDI) and 48 women who reported low levels of depression symptoms participated in the study. They were asked to read 6 texts that described negative emotional situations ostensibly written by another participant. They were then asked to help the other participants by writing a supportive letter. The participants reported their motivation to help and emotions before and after providing support. Results showed that depressed and non-depressed participants reported more positive and less negative moods post-support. The coding of support letters indicated that depressed participants showed higher use of acceptance compared to non-depressed participants. However, non-depressed participants reported higher use of empathic responding compared to depressed participants. The motivation to help did not differ between the groups. These findings are consistent with previous findings showing that EER benefits support providers. To our knowledge, this study is the first to show which strategies subclinical depressed participants use to help others regulate emotions. Together, these findings imply that EER may be a good way to improve mood and that people with depression differ from nondepressed individuals in the ways they provide support to others. These findings have implications for understanding the role of EER in depression and other psychopathologies.

Not Just a Game: The Effect of Active Versus Passive Virtual Reality Experiences on Anxiety and Sadness

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The use of virtual reality (VR) technology is becoming more common and can be harnessed as a tool to improve various emotional and psychological aspects. The present research explored whether different kinds of VR experience (i.e., Active versus Passive) would differently affect people's mood, anxiety, and sadness. Undergraduate students (n = 133) were randomly assigned to three study conditions: Active Game VR experience, Passive VR experience and control 2D Passive Viewing and filled out a battery of questionnaires before and after manipulation. The results show that following both VR exposures (but not following the control condition), participants' moods improved, and the degree of anxiety was reduced. The degree of sadness was reduced only following the Active Game VR experience. Regarding self-efficacy, it was higher in the Passive VR experience but lower following the Active Game VR experience (and not affected by the control condition). In conclusion, the results indicate that short VR experiences could provide a suitable alternative for the lack of accessible treatments to improve mood and to alleviate levels of anxiety and sadness, although further research is needed to tailor and refine the exact VR experience that would best improve each specific psychological aspect.

Psychedelic social cognition - meta analyses from animal models to humans

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Psychoactive drugs, including psychedelics and empathogens, have been examined regarding their effect on various aspects of social cognition. However, the existing literature presents conflicting results, prompting the need for a comprehensive perspective through meta-analysis. This talk delves into a series of three meta-analyses examining the effects of MDMA-an empathogen, on social cognition in both animal models and human subjects.

Our analyses demonstrate the nuanced impact of MDMA on social interaction and social place preference in animal models, revealing enhancement in certain features while leaving others unaffected. In human studies, MDMA was found to diminish the recognition accuracy of negative emotions without increasing recognition of positive emotions. Expanding our focus to empathy, MDMA demonstrated an increase in emotional empathy while not affecting cognitive empathy.

Broadening the scope to classical psychedelics, we observed analogous effects on empathy as seen with MDMA. The discussion will explore potential mechanisms and interpretations of these findings, offering insights into the intricate relationship between psychoactive drugs and social cognition.

Metabolomic Profiling and Machine Learning in ASD Diagnosis: Toward Precision Treatment

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One in 100 children around the world is diagnosed with ASD. The heterogeneity in autism symptoms, severity, and comorbidities suggest imbalances in underlying biological pathways. Indeed, alterations between children with and without ASD were described in pathways such as digestion, autoimmunity, methylation, trans-sulfation, and more. Urine metabolomics provides a window into biochemical processes in the body and their efficiency in utilizing key components from the diet in interaction with the gut microbiome. Current ASD diagnoses are based on behavioral profiles, potentially neglecting biological variations that could inform precision therapy.

Previous research has identified distinct urine metabolomic profiles in children with ASD versus neurotypical children. In this study, we investigated the metabolic underpinnings of ASD in an Israeli cohort by analyzing first-morning urine samples from 34 children diagnosed with ASD and 19 age-matched neurotypical controls. Through untargeted LC-MS, we profiled over 300 polar metabolites. We then applied a random forest machine learning algorithm to this metabolomic data, achieving an 80% accuracy and an AUC of 0.87 in distinguishing between the ASD and control groups. Interestingly, many metabolites that differentiate between the groups are bacterial metabolites impacting the proper digestion of nutrients necessary for development. Other metabolites highlight specific nutrients required during development for sustainable brain cell survival, functional synapse formation and necessary pruning. Targeting these metabolites may provide a novel direction for therapeutics.

Empathic Disequilibrium is Related to Lower Levels of Hair Oxytocin

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Oxytocin is a social hormone, but its relationship with trait empathy is unclear. This may be because (1) previous measures of oxytocin reflect state levels, whereas empathy is typically measured as a trait, and (2) the cognitive and emotional aspects of empathy were studied independently, neglecting the intra-personal imbalance between them. This is captured by empathic disequilibrium, a stable empathy measure related to autism. We measured oxytocin levels in hair, which reflect long-term exposure in 46 young adults. Oxytocin levels were non-linearly related to empathic disequilibrium in the expected directions (b = -12.29, 95% CI = [-22.04, -2.54], β = -0.46, p = 0.01). The finding suggests that trait oxytocin is a good biomarker of empathic disequilibrium.

ORAL PRESENTATION
Session 2
Depression and Suicidality
Chair: **Dr. Joy Benatov** *The University of Haifa*

Sleep measures as a predictor of suicidal ideation among high-risk adolescents

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Suicide is the second leading cause of death among youth aged 15–24 years. Identifying modifiable risk factors relevant to adolescents is crucial for suicide prevention. Sleep patterns have been linked to suicidality in adults, but lack sufficient study in youth. This ecological momentary assessment (EMA) study aimed to explore the relationship between objectively and subjectively measured sleep characteristics and next-day suicidal ideation in high-risk youth. We included 29 adolescents (12–18 years old) admitted to the inpatient psychiatric ward post-suicide attempt or due to suicidal intent within the previous month. We conducted objective (actigraphy) and subjective (sleep diary) sleep pattern assessments over ten consecutive days. Daily suicidal ideation was evaluated using a questionnaire based on the validated C-SSRS interview. A significant positive association was observed between sleep onset latency (SOL) and expressing a "death wish" the following day (OR = 1.06, 95% CI [1–1.11], p = .04), with each minute of longer SOL increased the risk for a death wish the following day by 6%. In addition, a marginally significant negative association was observed between total sleep time (TST) and expressing a "death wish" the following day (OR = 0.57, 95% CI [0.3–1.11], p = 0.1), with each one-hour decrease in objectively measured TST increasing the odds of a death wish by 43%. Our study highlights the interplay between sleep patterns and suicidal ideation, with SOL and TST playing a significant role that may function as proximal risk factors for suicidality and as a target for intervention while treating suicidal youth.

Active and passive mobile monitoring for suicide risk among high-risk adolescents

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Background: Recent intensive longitudinal assessment studies identified predictors of suicide risk, but the generalizability of the findings to real-world settings is limited. The current study aims to utilize mobile-based active and passive intensive longitudinal assessments to detect elevated risk for suicidal behavior among adolescent patients in a real-world outpatient setting.
Methods: The sample included 90 high-risk adolescent patients aged 11-18 admitted to an outpatient clinic after admission to the emergency department due to suicidal behaviors. Over six months, patients completed weekly assessments for suicidal thoughts, behaviors, and related risk factors. Mobile sensing information for device and data usage was collected to capture activity, sleep, and interpersonal behavior patterns. Machine learning methods were applied to detect anomalies in mobile usage associated with suicidal outcomes.
Results: The response of eligible patients to install the monitoring app was high (72%), and the retention rate was 81% through six months. The average response to weekly surveys was 90% over the follow-up period. Across the reports, 16% included suicidal plans with intent or suicidal behavior. A clinical risk assessment and referral procedures followed these reports. Parents and youth reported a positive experience with the digital monitoring, which was minimally burdensome.
Conclusions: In a real-life outpatient clinic setting, weekly mobile-based assessment and ongoing monitoring of mobile phone usage patterns are feasible and acceptable among high-risk adolescents. Active and passive mobile monitoring may indicate escalations in suicide risk and augment clinical follow-up and suicide risk management throughout a high-risk period post-emergency department discharge.

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Depressive symptoms are associated with differential cognitive and neuroanatomical alterations in young and older adults

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Objective: Depression is a heterogeneous disorder. The purpose of this article is to examine the contribution of age to this heterogeneity by characterizing the associations of depressive symptoms with cognitive performance and brain structure across the lifespan.

Methods: We analyzed demographic variables (age, gender, education), affective measures (Hospital Anxiety and Depression Scale), and cognitive assessments (The Addenbrooke's Cognitive Examination Revised) from the Cambridge Centre for Ageing Neuroscience (Cam-CAN) cohort (N=2591, age 18-99). A subset of this cohort (N=647) underwent structural MRI, which was used for voxel-based brain morphometry.

Results: A linear regression model revealed a significant interaction between age and depression score, indicating that depression-related cognitive dysfunction is more severe in older adults. A comparison of different cognitive domains showed that this effect was consistent across all tested domains but significantly more prominent for fluency. A complementary voxel-based morphometry analysis, based on similar regression models, revealed age by depression interactions in several brain regions, demonstrating preferential age-related reduction in grey matter volume in the left and right hippocampi in older adults. The reciprocal contrast revealed preferential reduction in grey matter in the left superior frontal gyrus, left middle frontal gyrus, and left superior parietal lobule in younger adults.

Conclusions: These findings indicate that the associations of depression with cognitive performance and brain structure are age-dependent, suggesting that the neuropathological mechanisms underlying depression may differ between young and older adults. Recognizing these differences will support the development of better diagnostic tools and therapeutic interventions for depression across the lifespan.

Alterations in serum endocannabinoids levels among individuals with major depression who receive electroconvulsive therapy

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Recently, the role of the endocannabinoid system (ECS) in depression and suicidality has emerged. The purpose of the study was to identify changes in serum endocannabinoid levels of several endocannabinoids and correlate them with depressive symptoms and suicidality in patients with severe major depression undergoing electroconvulsive therapy (ECT). The study included four visits at different stages of the therapy. At each visit depression, anxiety and suicidality symptoms were assessed and blood samples collected. Several endocannabinoid levels increased following six sessions of ECT, as 2-AG ($p < 0.05$) and LEA ($p < 0.01$), and following twelve sessions of ECT, as 2-AG ($p < 0.05$), AEA ($p < 0.05$), LEA ($p < 0.05$) and DH-Gly ($p < 0.05$). Endocannabinoids also correlated with symptoms of depression, anxiety and suicidality at baseline and at the sixth ECT session. Finally, we found one endocannabinoid, L-Gly, that differentiated between remitted and not-remitted patients at the seventh and thirteenth ECT sessions ($p < 0.05$). Our findings suggest that depression is markedly related to imbalance of the endocannabinoid system, and further regulated by ECT. Serum endocannabinoids could be promising biomarkers for detection of depression response and remission.

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Perinatal neuroplasticity of the triple network and its association with mood and anxiety disorders

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Background: Brain-network alterations during the perinatal period, including changes in resting-state functional connectivity (rsFC), are thought to increase vulnerability for perinatal mood and anxiety disorders (PMAD). The Fronto-Parietal Network (FPN), the Default-Mode Network (DMN) and the Salience Network (SN) are three intercorrelated brain networks associated with cognitive and affective functions, also implicated in the neurobiology of mood disorders. However, it is unclear whether these networks are associated with perinatal neuroplasticity and PMAD symptomatology.

Methods: This study prospectively followed 22 women from preconception to postpartum. All participants completed self-report questionnaires measuring anxiety and depression symptoms during five time-points (preconception, 1st, 2nd and 3rd trimesters and postpartum), and underwent functional magnetic resonance imaging (fMRI) scans at preconception and postpartum. The FPN, DMN and SN were defined and differences pre- and post-pregnancy were determined at the whole-brain level. Paired T-test and univariate analysis of variance were conducted to assess within subject connectivity changes, and the association to PMAD symptoms.

Results: Within networks connectivity remained stable from preconception to postpartum. Increased rsFC to the DMN was observed in the left anterior prefrontal cortex. The right ventral posterior cingulate cortex showed a decrease of rsFC to the FPN from preconception to postpartum. While bilateral supplementary motor areas (SMA) showed increased connectivity to the FPN from preconception to postpartum, an opposite connectivity trend was associated in women with anxiety during pregnancy. Additionally, right SMA connectivity at preconception had positive significant relationship with postpartum depression scores ($P<0.05$ for all comparisons).

Conclusion: Perinatal-related changes in rsFCwere demonstrated in cognitive and motor regions connected to the DMN and FPN. Among women with PMAD symptoms, changes in SMA rsFC to the FPN were altered, indicating possible vulnerability to PMAD. Characterizing perinatal variations in emotional and cognitive brain networks could advance understanding of the changes that occur during transition to parenthood

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Distinct Homotopic Functional Connectivity Patterns of the Amygdalar Sub-Regions as Biomarkers in Major Depressive Disorder

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Background: Major depressive disorder (MDD) affects multiple functional neural networks. Neuroimaging studies using resting-state functional connectivity (FC) have focused on the amygdala but did not assess changes in connectivity between the left and right amygdala. The current study aimed to examine the inter-hemispheric functional connectivity (homotopic FC, HoFC) between different amygdalar sub-regions in patients with MDD compared to healthy controls, and to examine whether amygdalar sub-regions' HoFC also predicts response to Serotonin Selective Reuptake Inhibitors (SSRIs).
Methods: Sixty-seven patients with MDD and 64 matched healthy controls were recruited. An atlas seed-based approach was used to identify the lateral and medial sub-regions of the amygdala. HoFC of these sub-regions was compared between groups and correlated with severity of depression, and emotional processing performance. Baseline HoFC levels were used to predict response to SSRIs after 2 months of treatment.
Results: Patients with MDD demonstrated decreased inter-hemispheric FC in the medial but not in the lateral amygdala compared with healthy controls. The inter-hemispheric FC of the medial sub-region correlated with symptoms severity and emotional processing performance. Moreover, it modestly predicted treatment response to SSRIs.
Conclusions: Using a unique perspective of the amygdalar distinct areas elucidated differential inter-hemispheric FC patterns in MDD patients compared to healthy controls. Our finding of decreased connectivity between the left and right medial amygdala, which is involved in executing emotional responses and social interest, emphasized the role of interhemispheric communication in depression.

Inflammatory Markers as Predictors of the efficacy of Electroconvulsive Therapy (ECT) in Major Depression Patients

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Background: ECT is an effective treatment indicated for patients with treatment resistant depression. Although most patients display some degree of recovery, 32-52% do not respond or remit at all. Considering the possible side effects and the considerably high cost of treatment, it is important to identify sub-populations who would benefit the most from ECT. In the current study we sought to identify predictive molecular markers in the blood of depressed patients who are responsive to ECT.
Methods: 18 patients, ages 18-70, with the diagnosis of treatment-resistant depression were recruited. Participants underwent psychiatric and psychological assessments, before (baseline) and 12 weeks after ECT initiation. Assessments included the Montgomery-Asberg Depression Rating Scale (MADRAS), Clinical Global Improvement and Severity Scales (CGI-S, CGI-I), Inventory of *Depressive* Symptomatology (IDS), and the State-Trait Anxiety Inventory (STAI). Blood samples for serum and isolation of peripheral blood mononuclear cells (PBMCs) were collected at baseline and the 12 weeks end-of-treatment time points for molecular analysis.
Results: ECT treatment resulted in a significant improvementin measures of depression (MADRAS and IDS) between baseline and end-of-treatment. Compared with baseline levels, the ECT treatment did not result in changes in serum CRP levels (although a slight trend was observed) or in the levels of IL-8, Lag3, and Tnfa mRNA transcripts in PBMCs. However, we found that baseline levels of the immune checkpoint Lag3 mRNA were significantly correlated with the ECT-induced change from baseline to end-of-treatment in the MADRAS scores. Similarly, baseline levels of Tnfa mRNA were also significantly correlated with the change in MADRAS scores in patients with depression post-ECT.
Conclusions: Baseline levels of Tnf-α and Lag3 mRNA in PBMCs may serve as molecular markers to predict responsiveness to ECT treatment in depressed patients in need.

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How do autoimmune diseases and depression cluster in families? A prospective trial

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Background: It has long been claimed that depression might be a manifestation of immune dysregulation involving the CNS.
This study aims to characterize the role of proinflammatory markers by comparing genealogical trees, proteome, and metabolome profiles of depressed patients (DP) , to non-psychiatric individuals (NPI).
So far, 58 DP and 48 NPI were recruited.
Preliminary results: The study's population of 106 participants was categorized into several groups: Control Group: 48 participants (Mean age = 47.8, SD = 15.4; 43.8% females, 56.2% males). Depression Group: 58 participants (Mean age = 54.6, SD = 14.1; 62.1% females, 37.9% males). Subgroups based on Autoimmune Diseases: Further divided into control_autoimmune (5 participants), control_non_autoimmune (43 participants), depression_autoimmune (12 participants), and depression_non_autoimmune (46 participants). A significant negative Spearman correlation was observed between age at depression diagnosis and the number of depressive episodes (rho = -0.43; 95% CI [-0.63, -0.18]; FDR p-value = 0.020). Cytokine Profiling: Analyzed 39 cytokines in pg/ml. No cytokines showed significant differences post-FDR adjustment. Notable trends included IL-33 and IFN_a2.
Metabolite Profiling: The analysis included 209 metabolites. Significant differences were observed in metabolites such as O-Phosphoethanolamine (p = 0.0000284, adjusted p = 0.0059447, log2FoldChange = -1.3212015) in the control_autoimmune vs. depression_autoimmune contrast, and Hexanoic acid (p = 0.0000090, adjusted p = 0.0018755, log2FoldChange = -1.0535119) in the control_non_autoimmune vs. depression_autoimmune contrast.
Conclusion: The absence of significant differences in cytokine levels suggests a complex and potentially subtle immunological interaction in depression. The significant differences in certain metabolites, such as O-Phosphoethanolamine and Hexanoic acid, highlight potential metabolic alterations associated with depression and autoimmune diseases. These findings point towards disrupted metabolic pathways that may play a role in the pathophysiology of these conditions. The study's small sample size is a significant limitation, highlighting the need for continue and add more participants.

ORAL PRESENTATION
Session 3
Stress and Trauma
Chair: **Prof. Eyal Fruchter** *Rambam Health Care Campus*

Reconsidering PTSD Pathophysiology and Treatment in the Light of Recent Events

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As the atrocious October 7th War lingers, and the number of psychological casualties bypasses previous records and challenges services capacities, it is appropriate to go back to basic assumptions regarding the disorder's pathogenesis and biological underpinning. Two sets of evidence are worth considering here: On the one hand data concerning the eventual permanence of amygdala-imprinted emotional memory traces and complimentary animal findings showing time-dependent escape from successful interference with fear memory re-consolidation, and on the other hand the consistent observation of treatment refractory subsets of patients across epidemiological and clinical studies. These two observation, along the frequently observed disassociation between PTSD symptoms severity and survivors' global functional outcome suggest that traumatic stressors' impact affects both a core associative stress-driven learning, which tends to linger and defy unlearning and therapy, and a wide halo of meaning-driven semantically mediated layers of events' recall, interpretation, shattering chaos and grotesqueness, encoded, at the same time, as episodic memories. Whilst therapies of PTSD are critical, one shouldn't ambitiously aim at total recovery of traumatic experiences and associated strong reactions, but rather attempt to modify the degree to which these indelible recollections and alarm responses dominate living, assign negative meaning to novel experiences, define one's expected reality and reinforce survivors' isolation. Such therapies might not always be 'trauma-focused' nor always be delivered by qualified therapists. Assuming an often unrecoverable core psychopathology in PTSD requires moving from curative pretense - when it doesn't work - to thinking 'rehabilitation' , starting at the very early stages of PTSD development

Connectome-based Predictive Modeling of PTSD Development in Recent Trauma Survivors

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Objective: The authors sought to identify early neural networks predictive of the development of posttraumatic stress disorder (PTSD) or recovery from initial traumatic response among recent trauma survivors.

Methods: One-hundred and seventy-one adult civilians (mean age, 34.19 years, SD=11.47; 51% women) admitted to a general hospital emergency department following trauma exposure underwent demographic, clinical, and neuroimaging assessments 1, 6, and 14 months after trauma. The authors applied connectome-based predictive modeling (CPM) to functional connectivity data shortly after trauma, at rest and during tasks, to predict PTSD symptom severity at each time point. The predictive ability of identified networks was then tested in an independent sample of recent trauma survivors (n=357).

Results: CPM significantly predicted PTSD symptoms assessed at both 1-month (rho=0.180, p=0.001) and 14-months post-trauma (rho=0.239, p=0.001), but not at 6 months post-trauma (rho=0.033, p=0.393). Identified networks included connections within and between the middle-frontal, motor, frontoparietal, salience, and subcortical networks. Virtual lesion analyses showed that all networks contributed to the prediction of PTSD severity, though some were more important than others. Concerning specific PTSD symptom clusters, CPM predicted negative changes in mood and cognition (cluster D) and avoidance (cluster C) at 1-month post-trauma. At 14-months post-trauma, CPM predicted specifically intrusion (cluster B) and hyperarousal (cluster B) symptoms. Finally, the same model did not predict PTSD severity in the independent dataset.

Conclusions: These data demonstrate that individual differences in large-scale neural networks shortly after trauma contribute to variability in PTSD symptom trajectories during the first critical year following trauma exposure, which may be targeted in novel interventions.

Childhood trauma cortisol and immune cell glucocorticoid transcript levels are associated with increased risk for suicidality in adolescence

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Rising adolescent suicide rates present a major unmet need. Childhood trauma (CT) has been associated with altered cortisol dynamics and immune cell glucocorticoid reactivity, yet their additive longer term contributions to later suicide outcomes are less clear. The current study compared CT scores, resting salivary free cortisol and mononuclear cell gene expression levels of the nuclear receptor, subfamily 3, member 1 (NR3C1) coding the glucocorticoid receptor, and its co-chaperons FKBP prolyl isomerase 5 (FKBP5) and KIT Ligand (KITLG), between a cohort of adolescents presenting with a suicidal crisis requiring hospital treatment, and matched healthy controls. Childhood trauma scores and glucocorticoid measures were significantly altered among suicidal adolescents, and CT scores correlated with mononuclear cell glucocorticoid transcripts. Both CT scores and glucocorticoid measures explained substantial additive portions of the variance in adolescent suicidality. Long-term perturbations in cortisol dynamics and immune cell glucocorticoid response elements denote chronic dysregulation of immune stress reactivity, and may possess value in prediction and point to modifiable-risk factors in prevention of clinically significant suicidality years after childhood trauma exposure.

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Sleep Disruption and Physiological Changes following Mass-Trauma: Insights from Survivors of the "Nova" Music Festival Massacre

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Background: Extreme trauma exerts unparalleled and profound impact across nearly every aspect of daily life such as sleeping patterns and arousal level, resulting in significant suffering and disability. Therefore, the importance of understanding the immediate impact of trauma on real life behavior in the aftermath of traumatic events is paramount.
Methods: This study investigates the physiological and sleep-related consequences of severe mass-trauma in a large group of survivors of the “Nova” music festival massacre that occurred during the October 7th terror attack in Israel. Two months following the massacre, over 90 survivors’ physiology was recorded for a one-month period. In this clinically relevant time, survivors’ sleep, heart rate, and activity were continuously monitored unobtrusively while they were keeping their daily routine. The results were compared to those of a control group.
Results: Our findings reveal significant differences between the survivors and the control group. Survivors exhibited a notably higher sleep heart rate, suggesting persistent physiological arousal even during sleep. In addition, survivors displayed a reduction in total sleep time and an increase in sleep instability, reflected by larger day-to-day variance in sleep duration throughout the month, compared to the control group.
Conclusions: These results highlight the enduring impact of traumatic events on sleep quality and physiological responses, indicating disrupted sleep patterns among mass-trauma survivors. Improved understanding of the consequences of such events is essential for developing effective interventions and support strategies for survivors to improve their overall well-being and mental health. Further research is needed to explore the underlying mechanisms and potential therapeutic approaches to address this vital issue.

Dog training alleviates PTSD symptomatology by emotional and attentional regulation

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Post-Traumatic Stress Disorder (PTSD) symptoms include re-experiencing, avoidance, hyperarousal, and cognitive deficits, reflecting both emotional and cognitive dysregulation. In recent years, non-pharmacological approaches, and specifically animal-assisted therapy have been shown to be beneficial for a variety of disorders such as Attention-Deficit/ Hyperactivity Disorder, Autism Spectrum Disorder, and PTSD. However, little is mentioned in the literature about the reciprocal effects of the animal-human interaction.

To evaluate the effects of a one-year dog training program on PTSD symptomatology in youngsters with PTSD and on dogs' behavior.

Fifty-three adolescents, previously exposed to interpersonal trauma, were clinically diagnosed with PTSD and assigned to a dog-training program group (*n = 30*) and a control group (*n = 23*) that engaged in other training programs (e.g. cooking, hairstyling, etc.). Both groups were evaluated at baseline and following 12 months by The Clinician-Administered PTSD Scale for DSM-5 in Children and Adolescents (CAPS-CA-5) and Beck-Depression Inventory (BDI). Additionally, we physiologically measured both emotional and attention dysregulation.

Post-12-months training, a significant alleviation of PTSD symptomatology accompanied by lower depression severity was observed in the dog-training group, compared with an insignificant recovery in the control group. Furthermore, improved emotional and attentional regulation was observed in the dog-training group. Measuring the dogs' behavior revealed increased anxiety and decreased selective attention performance, which was inversely correlated with the beneficial effects observed in the dog-training program group.

Our findings emphasize the role of emotional and attentional regulations on the dog–handler interface, as evidence-based support for the beneficial effects of the dog-training program, as either a non-pharmacological intervention or as complementary to anti-depressants treatment of PTSD. Though pharmacological treatments increase the patients' well-being by treating certain PTSD symptoms, our suggested dog-training program seems to influence the PTSD diagnostic status and thus may be implemented in civilians and veterans with PTSD.

Neural patterns differentiate traumatic from sad autobiographical memories in PTSD

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For people with post-traumatic stress disorder (PTSD), recalling traumatic memories often displays as intrusions that differ profoundly from processing of 'regular' negative memories. These mnemonic features fueled theories speculating a unique cognitive state linked with traumatic memories. Yet to date, little empirical evidence supports this view. Here, we examined neural activity of PTSD patients who were listening to narratives depicting their own memories. An intersubject representational similarity analysis of cross-subject semantic content and neural patterns revealed a differentiation in hippocampal representation by narrative type: Semantically similar sad autobiographical memories elicited similar neural representations across participants. By contrast, within the same individuals, semantically similar trauma memories were not represented similarly. Furthermore, we were able to decode memory type from hippocampal multivoxel patterns. Finally, individual symptom severity modulated semantic representation of the traumatic narratives in the posterior cingulate cortex. Taken together, these findings suggest that traumatic memories are an alternate cognitive entity that deviates from memory per se.

Hyperbaric oxygen as an early intervention therapy to prevent PTSD-like behavior in acute stress rat model

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PTSD is a severe, debilitating disorder that is difficult to treat, with a prevalence of 8% in the general population and over 15% in combatants. PTSD can develop from a single, brief, intense traumatic event (e.g., sexual assault, car accident, terrorist attack) or more prolonged trauma such as combat exposure. The high prevalence of trauma exposure highlights the importance of early intervention to prevent PTSD development. However, clinicians remain limited in their ability to intervene effectively in the aftermath of trauma, and the available treatments are limited and highly unsatisfactory. Therefore, there is a strong need to develop a new therapeutic strategy for early intervention applied within hours of trauma exposure to prevent trauma survivors from developing PTSD. Research suggests that hyperbaric oxygen therapy (HBOT) improves PTSD symptoms. Therefore, we hypothesize that HBOT can serve as an early intervention treatment to prevent the development of PTSD symptoms. Here, we examined the effect of HBOT, as early intervention therapy, on reducing or preventing PTSD-like symptoms in adult rats and elucidated the molecular mechanism of this therapy approach. To this end, prolonged stress was applied, followed by hyperbaric oxygen treatment (2.8 ATA, 100% oxygen for 90 minutes, two sessions/day for four days). Results showed that the HBOT reduced anxiety-like behaviors and increased exploratory behavior and sociability 7 and 30 days after the treatment. In comparison, the untreated stress group exhibited anxiogenic behavior and social impairment. At the molecular level, elevation in the protein levels of IBA1 and BDNF was observed in the amygdala and hippocampus of stressed animals, which normalized after HBOT. Moreover, cFos gene expression was lower in the stressed group, suggesting lower activity in the amygdala. These results imply that HBOT can be a non-invasive and promising early intervention or secondary treatment for preventing PTSD development.

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Stress-Induced Change in Heart-Rate During Sleep as an Indicator of PTSD Risk among Combat Soldiers

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Background: Combat soldiers are typically exposed to high-stress environments, elevating their risk for Post-traumatic Stress Disorder (PTSD). Disturbances in sleep behavior and physiology have emerged as both risk factors and consequences of PTSD development. Nevertheless, majority of studies were cross-sectional and did not include sleep assessment in natural settings, hence the contribution of sleep behavior and physiology to PTSD risk has yet to be defined.
Methods: In this longitudinal study, measurements were taken during basic training week (T1), intensive stressed training week (T2), and following operational service week (T3). Participating combat soldiers were all from the same combative unit and at the same stage of training to ensure uniformity in their schedules. At each measurement week participants completed the Depression Anxiety and Stress Scale (DASS) and PTSD Checklist for DSM-5 (PCL-5). Heart-rate (HR) during sleep and sleep behavior (duration, efficacy) were monitored continuously in T1 and T2 using wearable sensors.
Results: Repeated measures ANOVA showed a progressive increase in PCL-5 scores from T1 to T3, suggesting an escalation in PTSD symptom severity over the course of military service. Hierarchical linear regression analyses indicated a significant relationship between the increase in DASS stress scores from T1 to T2 and PCL scores at T3 (p = 0.011). Incorporating the change in sleep HR from T1 to T2 markedly enhanced the model's predictive accuracy (R^2 = 0.636), with increased sleep HR emerging as a significant predictor of PTSD symptoms at T3 above and beyond the contribution of DASS stress (p = 0.017). Sleep behavior (duration, efficacy) did not add to the accuracy of the model.
Discussion: Our findings underscore the critical role of sleep physiology, recorded continuously in natural settings, in augmenting PTSD prediction models beyond traditional self-report psychological assessments.

ORAL PRESENTATION
Session 4
Psychiatric Illnesses
Chair: **Prof. Avi Weizman** Tel Aviv University

Aperiodic and periodic components of oscillatory brain activity in relation to cognition and symptoms in pediatric ADHD

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Children with ADHD show deficits in executive functions (EFs) and in processing speed (PS), as well as aberrant neural oscillations. Here, we examined differences in periodic and aperiodic components of resting-state (RS)-EEG between children with (N=33) and without (N=33) ADHD, and their association with behavioral metrics. We found that Children with ADHD had worse EFs and PS compared to the control group. Traditional RS-EEG spectral analyses revealed increased power in fronto-central theta and beta oscillations for the ADHD group, but no differences in the theta/beta ratio. Using parameterization method, we found higher aperiodic exponent for the ADHD group compared to controls. While theta power correlated with clinical symptoms for the ADHD group only, the aperiodic exponent was negatively correlated with PS across the entire sample. Finally, the aperiodic exponent was significantly correlated with periodic parameters calculated by both methods. These results elucidate the associations between aberrant RS periodic and aperiodic activity, behavioral measures, and symptoms in pediatric ADHD. The results highlight the different and complementary contribution of periodic and aperiodic components of the neural spectrum as metrics for evaluation of cognitive function in ADHD. Future studies should further clarify the roles of periodic and aperiodic components in cognitive functions.

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Computationally Dissociable Abnormalities in Semantic Representation and Semantic Retrieval in Psychosis and Formal Thought Disorder

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Background: Abnormalities in language and semantic cognition are suggested as biomarkers for psychosis. Such abnormalities are evident in Formal Thought Disorder (FTD), diagnosed based on speech atypicality. However, the precise components of semantic cognition that go awry in psychosis, and particularly those distinguishing patients who have FTD, have yet to be specified. We combine computational modeling with neural decoding of semantic representation to disaggregate core abnormalities in semantic structure from abnormal retrieval and executive dysfunction, and detail how they interact in psychosis and FTD.
Methods: Patients with schizophrenia, varying in FTD, and healthy controls (N=62) completed a word association task during MEG. We characterized abnormalities in semantic structure by modeling the estimated strength of participants` associations and by mapping semantically meaningful spaces to participants` neural representations of cues. Derived structures were used, together with responses and response times, to model semantic retrieval dynamics as a product of attractor-based accumulation of internal evidence.
Results: Patients tended to produce more atypical associations (OR CI=[1.11,1.36]). However, only patients without FTD acknowledged the weakening of their own associations (CI=[-0.14,-0.01], and correspondingly showed computational evidence for alterations in semantic retrieval and control. Patients` neural representation of cues diverged from cues` semantic representation (Cohen`s d=[-1.49,-0.40]), and this reflected abnormal associative structure in patients with FTD (CI=[0.04,0.26]).
Conclusions: Mechanisms of FTD can be partially dissociated from those explaining general semantic cognition abnormalities in psychosis. The formation of an abnormal semantic structure in FTD may reflect a compensatory response to a fundamental loss of precision in structure and retrieval, akin to theoretical accounts of other psychotic symptoms.

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Effect of sub-chronic blockade of the ErbB pathway in adolescence on behavioral changes related to anxiety and depression in adult mice

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Depression and anxiety disorders rank among the top ten most critical public health issues and have surged to epidemic levels in recent years. Despite having distinct symptoms, they frequently coexist and mutually impact each other. Presently, selective serotonin reuptake inhibitors (SSRIs) stand as the primary pharmacological treatment for depression and various anxiety disorders. However, due to efficacy reaching only 50% and a range of side effects, there is a real need for exploring new and alternative effective treatments.

ErbB4 signaling pathway plays a crucial role in various cellular processes during brain development, while abnormal ErbB4 signaling was found to be correlated with anxiety and depressive behaviors. We have recently reported that a potent and selective inhibitor of the ErbB receptor family given to adolescent mice alleviated anxiety-like behavior in the offspring of dams exposed to immune activation. These findings indicate that inhibition of the ErbB signaling pathway may be a potential solution to the need for alternative effective treatment of depression and anxiety.

In this work, we investigate whether pharmacological blocking of the ErbB signaling pathway in adolescence in a stress model mouse can prevent or protect against the development of anxiety and depression-like behavior later in life and elucidate the molecular mechanism underlying these effects. For that, adolescent CD-1 mice were exposed to traumatic stress and received a sub-chronic treatment of a potent and selective ErbB receptor family inhibitor – JNJ 28871063. At the end of the treatment, a battery of behavioral tests and a molecular analysis were conducted.

We have demonstrated that adult mice exposed to dramatic stressors during adolescence, a critical period of brain development, displayed anxiety-like behavior while blocking the ErbB pathway demonstrated normalization of this behavior. These effects may be associated with changes in the expression of NRG1, GAD67, and brain-derived neurotrophic factor (BDNF).

Causal interplay between pain and distress in Fibromyalgia: An ecological momentary assessment (EMA) study in real-life settings

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Background: Fibromyalgia (FM) is a chronic, poorly understood, stress-related condition. FM patients tend to exhibit fluctuations in their pain severity and other symptoms over short periods of time, with periods of sharp symptom exacerbation or worsening, colloquially referred to as “flares”. Psychological distress was found to play a prominent role in flares emergence, and in fact, pain and stress seem to reciprocally impact each other in FM, yiedling a vicious cycle for the patients.
Methods: An ecological momentary assessment (EMA) study was conducted in order to investigate in real-life settings the nature of pain fluctuation in FM and the potential causality of psychological distress. Sixty-five FM patients aged 18–60 years completed a laboratory session including self-report measures, cognitive and physiological assessment, and subsequently used a smartphone application for EMA data collection three times each day (morning, noon, evening) for 14 days. Each survey instructed participants to report on their current pain and distress levels.
Results: Mixed model analysis revealed that overall, current pain and distress levels predicted pain at the next data collection time point. In contrast, current pain and distress levels did not predict distress at the next time point. Interestingly, current pain and distress levels predicted pain at the next time point with respect to mornings predicting noon and noon predicting evenings, but not evenings predicting next morning pain.
Conclusions: Taken together, these results provide the first ever causal evidence in real-life settings for distress intensifying pain and not vice versa in FM. Results further suggest that pain and distress are predictive of what is likely to occur during the course of each day in terms of pain severity, but that during night these relationships change, potentially due to the involvement of additional sleep related factors.

The Vascular-Bipolar Link: A Nationwide Population-Based Case-Control Study

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Importance Increased risk of cardiovascular diseases (CVD) was found among patients diagnosed with bipolar disorder (BPD), and may be considered as an inherent feature of BPD.
Objective To assess the risk to develop CVD, CVD risk factors (CVRF), and related mortality among BPD patients compared to the general population and other severe mental illnesses (SMI).
Design, Setting, and Participants A population-based nested case-control study was conducted utilizing Clalit health services nationwide database. Included in the study all individuals that were 15-40 years old at January 1, 2000. Follow-up period ended at December 31, 2022 or with termination of membership or death. BPD patients were matched to controls without SMI (ratio 1:5) and to patients diagnosed with schizophrenia or schizoaffective disorders (SCZ)(ratio 1:1).
Exposure BPD and SCZ cases were identified according to electronic health records diagnoses.
Main Outcome and Measures The primary outcome was a diagnosis of CVD or death. The secondary outcomes are CVRFs. Potential confounders or mediators were also retrieved from the database.
Results A total of 5,055 patients with BPD, 5,055 patients with SCZ and 25,273 controls were included in the analysis. In all groups, females accounted for 53.4% and the mean age at the start of follow-up was 29.23 (SD=7.1). CVD rate was higher among BPD patients (n=961, 19%) compared to SCZ (n=743, 14.7%) and controls (n=3,181, 12.6%), (p>0.001). CVD mean age at diagnosis was younger among SCZ patients (43.47, SD=9.49) and BPD (44.65, SD=8.90) compared to controls (45.26, SD=9.10), (p>0.001). Death rate was significantly higher for SCZ patients (n=387, 7.7%) and BPD (n=168, 3.3%) compared to controls (n=382, 1.5%), (p>0.001).
Conclusions The presentedpreliminary results suggest higher rates of CVD and death among patients with BPD and SCZ compared to control group. Our next in-depth analysis will explore specific mediators for the associations found.

Developing a Machine-Learning-Based Diagnostic Tool for Fibromyalgia Using Resting-State fNIRS: Insights into Stress Response Mechanisms

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FM (Fibromyalgia) is a complex chronic pain syndrome affecting approximately 7.5% of women. The underlying mechanisms of this syndrome remain unclear, but there is evidence of altered stress responses and an increased prevalence of PTSD (Post-Traumatic Stress Disorder), depression, and anxiety among FM patients. The diagnosis of FM is challenging due to its subjective nature, necessitating the development of objective tools to enhance accuracy. In this study, we aim to create a machine-learning-based tool for FM diagnosis, utilizing hemodynamic responses measured by resting-state fNIRS (functional Near-Infrared Spectroscopy).

We conducted a study with a cohort of 30 female patients diagnosed with FM and 30 healthy controls who underwent resting fNIRS recordings. The recordings consisted of two 7-minute sessions using an fNIRS device, encompassing both baseline and post-stress exposure, induced by the TSST procedure (Trier Social Stress Test). Our montage covered frontal and sensory cortices, utilizing 46 channels and 8 short channels to capture non-cortical hemodynamic activity. This comprehensive approach allowed us to consider non-cortical influences on cortical hemodynamic responses, thereby enhancing the precision of our analysis of resting-state brain activity.

We preprocessed the fNIRS data and extracted features using connectivity and graph theory measures, including both node-specific and global measures. Machine learning techniques were deployed and compared to create a diagnostic signature for FM in both resting state and during stress conditions. Interpretability analysis was employed to assess the contribution of specific features to the diagnostic model.

Our study sheds light on the mechanisms underlying FM, particularly its response to stress. This research has the potential to provide valuable insights that may guide the development of targeted treatments for FM patients, addressing a critical gap in diagnosis and facilitating personalized therapeutic interventions.

Mapping Emotion Dysregulation in ADHD: Ecological Momentary Assessments and Cluster Analysis Unveil Dynamic Profiles of Emotional Variability

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Emotion dysregulation deficits, and particularly emotional instability, are well-established symptoms in adults with ADHD. In this talk we will present a recent study, in which we employed continuous monitoring of emotional states (EMA) in a sample of adults diagnosed with ADHD (n = 57) and healthy controls (n = 54). EMA enables to conduct a dynamic analysis of intra-individual emotional changes, aiming for a nuanced understanding of unique emotion dysregulation patterns in ADHD. Individuals with ADHD exhibited heightened intra-individual variability and lability in their emotional state reports, indicating increased emotional instability. Notably, emotional intensity did not differ between groups. Emotional variability was specifically associated with reported emotion regulation difficulties in the ADHD group. Cluster analysis revealed that individuals with ADHD predominantly occupy a cluster characterized by heightened emotional variability and emotion regulation difficulties. These findings underscore that adults with ADHD face greater challenges in emotion regulation and experience heightened emotional instability in daily life, which contribute to the predictive value of these characteristics for an ADHD diagnosis.

Orthorexia and Orthorexia Nervosa: Prevalence, Risk Factors, Diagnosis, Treatment, and Recent Findings

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Orthorexia nervosa is an emerging and controversial eating disorder characterized by an obsessive preoccupation with healthy eating and an extreme fixation on food purity. Despite growing public interest in orthorexia, its classification as a distinct eating disorder remains a subject of ongoing debate in the mental health community. This lecture will concisely review the current literature on orthorexia nervosa, exploring the prevalence rates, risk factors, diagnosis, and treatment options. An overview of orthorexia, its historical context, and the challenges and considerations in diagnosing orthorexia and orthorexia nervosa will be presented. The distinction between “orthorexia” and “orthorexia nervosa” is a debated issue in eating disorder research due to a lack of clear diagnostic criteria, making it challenging to accurately differentiate between an obsession with healthy eating and a more severe form with potential distress and impairment. The existing treatment approaches for orthorexia nervosa will be presented as well. Recent data collected from young adults and its relation to intuitive eating, sense of control, and embodiment will be shown further to highlight the complex and multifaceted nature of orthorexia nervosa. This topic should contribute to the ongoing discourse surrounding orthorexia and provide valuable insights for clinicians, researchers, and stakeholders in the mental health and eating disorders fields.

POSTER PRESENTATIONS

The effects of dopamine on social cooperation performance

Shlomit Aga Mizrachi[1,2], Inon Maoz[1], Lilach Simchi[1], Liron Azulay[1,2,3], Avi Avital[3]
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Social cooperation is defined as a behavior acted in pairs or groups to achieve mutual or individual reinforcement. Social cooperation performers necessitate motor ability, attention to the cooperating counterpart and emotional state. All these underlying processes of social cooperation involve the dopaminergic system.
Using the social cooperation maze established in our lab, we created two lines of High and Low social cooperation subpopulations, following selective breeding along 20 generations.
The aim of the current study is to examine the involvement of the dopaminergic system in the ability of the High and the Low social cooperation performers.
The involvement of the dopaminergic system in social cooperation was examined through a pharmacological manipulation using the agonist Methylphenidate (MPH) and the antagonist Haloperidol (Hal) in the High and Low social cooperation performers.
We found that following 18 days of training in the social cooperation maze the Naive group showed an intermediate performance between the High and the Low subpopulations. While MPH treatment didn't affect the Naïve and the high, it exerted improvement in the low performers. Hal treatment impaired social cooperation in all 3 groups. In the rotarod test, while MPH treatment didn't affect the motor learning in all 3 groups, treatment with Hal impaired motor learning in both high and low performers. In the object recognition test High performers showed the best selective attention ability. While MPH treatment didn't affect selective attention in the High and the Naïve groups, Hal decreased this ability. In contrast, MPH treatment impaired selective attention in the Low performers while Hal had no effect. This study provides evidence for the specific involvement of the dopaminergic system in social cooperation performance level and specifying the advantages and the side effects of dopamine modulation on social cooperation components.

Developing objective chronic pain assessment based on linguistic characteristics of patients' narratives

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Background: Chronic pain, with prevalence about 30% in Israel and worldwide, presents a major challenge due to its subjective nature. While self-reporting remains the main tool, its limitations call for more objective measures. Recent research shines a light on using patients' own words: analyzing the language in their narratives through Natural Language Processing (NLP) has shown promise in predicting pain levels. However, such models mostly are based on synthetic lab-based data. In this study, we targeted narrative-based pain content, collected in daily life of chronic pain patients to predict their pain levels.

Methods: Twenty-eight chronic pain patients were invited to participate in the study using digital web platform. They rated their pain levels and recorded themselves talking about their pain by answering specific open-ended questions regarding pain characteristics, triggers and factors causing pain. The collected data was used to build a computational model for predicting pain levels based on linguistic features extracted from the speech of chronic pain patients using machine learning and Zero-Shot Text Classification (ZSTC) approaches.

Results: The model, focused on factors causing pain, demonstrated strong performance with an out-of-sample AUC of 0.73 (Sensitivity = 78.9%, Specificity =66.6) for current pain prediction. The model, based on perception of pain interference predicted average pain with AUC of 0.70 (Sensitivity = 66.6%, Specificity =73.6 %).

Conclusions: Narrative-based models can predict current & average pain, empowering clinicians with objective insights and paving the way for personalized treatments tailored to individual stories, triggers, and coping mechanisms helping gap between patient experience and clinician understanding.

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Maternal immune activation induced strain-specific hippocampal DNA methylation changes in dominant and submissive mice

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[1]Molecular Biology Ariel University, Ariel, [2]Molecular Biology, Ariel University, Ariel, [3]Adelson School of Medicine, Ariel University, Ariel, Israel

Background: Past studies have revealed the lasting effects of stress susceptibility and deficient maternal care on hippocampal DNA methylation landscape in adult offspring. Yet, the extent and specific nature of alterations in the DNA methylation landscape during early postnatal developmental stages and following maternal immune activation remain less studied.

Methods: We used two mouse strains characterized by social dominance (Dom) and submissiveness (Sub), exhibiting inherent traits of elevated and diminished stress sensitivity and maternal care behaviors. Additionally, Poly IC was administered to a subgroup of the dams at gestational day 14 to induce maternal immune activation in order to explore whether stress susceptibility is a contributing factor for the heightened effects of Poly IC on DNA methylation and behavior. To conduct genome-wide DNA methylation analysis, we used reduced-representation bisulfite sequencing (RRBS-Seq) on hippocampal DNA extracted from 7-day-old Sub and Dom pups.

Results: We observed significant changes in DNA methylation levels in both the intergroup comparisons of sub and dom, as well as in sub and dom subjects exposed to Poly IC. This analysis revealed a noteworthy enrichment of differentially methylated CpGs, particularly within gene promoters responsible for regulating behavior and neuronal development. These findings were associated with significant behavioral changes, mostly in exploration and MK801-induced hyperlocomotion.

Conclusion: We discerned distinct alterations in the DNA methylation landscape between submissive (Sub) and dominant (Dom) mouse models. Additionally, when exposed to Poly IC, both Sub and Dom groups exhibited unique methylation patterns, further highlighting the nuanced epigenetic differences between Sub and Dom phenotypes, particularly under the influence of maternal immune activation. These molecular findings were associated with behavioral effects later in life.

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Early developmental milestones as predictors of tics and comorbid psychopathology, an EMTICS study

Tamar Steinberg[1], Dana Feldman--Sadeh[2], Alan Apter[2], Yael Bronstein[2], Noa Elfer[2], Miri Carmel[3], Elena Michaelovsky[3], Avi Weizman[3], Matan Nahon[4], Danny Horesh[4], Astrid Morer[5], Blanca Garcia Delgar[6], Pieter J. Hoekstra[7], Andrea Dietrich[7], **Noa Benaroya-Milshtein[2]**

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Background: Chronic Tic disorders (CTD) including Tourette Syndrome (TS) are highly associated with psychiatric and neurodevelopmental comorbidities. Neurodevelopmental disorders like autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD) and specific learning disorders have been correlated with delays in early developmental milestones. However, only few studies have investigated the relationship between early developmental milestones, tics' severity, and psychopathology comorbidity.

Method: 383 participants aged 3-16 years (76.8%, n=294 boys) with CTD from the baseline assessment of *European Multicenter Tics in Children Study* (EMTICS), were evaluated for early developmental milestones (sitting, walking, first words, complete a sentence, bladder and bowel control), as well as tic symptom severity, tic-related functional impairment, obsessive-compulsive disorder (OCD), oppositional defiant disorder (ODD), ADHD and ASD, utilizing gold-standard self- and clinician reporting instruments. Analysis included correlations matrix and logistic regressions.

Results: Correlations between the acquisition of developmental milestones and tic's severity or impairment were insignificant to weak. However, logistic regression analyses revealed that early developmental milestones, specifically later acquisition of first words significantly predicted neurodevelopmental disorders: ADHD, ODD, ASD and mental/learning disabilities (Reporting Odds Ratio (ROR): .95-1.06, .36-1.13, 1.13 and 1.08-1.18, respectively), while later walking acquisition predicted OCD (ROR: 1.13-1.16).

Discussion: In line with previous evidence, delay in language development predicted neurodevelopmental disorders, including ASD, mental and learning disabilities, ODD and ADHD. Our findings underscore the difference in phenotypic characteristics of children with only tics and those with both tics and comorbidities to enhance future diagnoses and treatments.

New technology to use artificial intelligence (AI) for continuous PTSD severity assessment from natural video recording

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Early detection and assessment of Post-Traumatic Stress Disorder (PTSD) are crucial for timely treatment. However, the current diagnostic approach relies on subjective evaluation conducted by clinicians, which often suffer from limited accessibility, subjectivity, and fail to capture the natural behavior of individuals in their natural environment.

To overcome these limitations, we propose leveraging AI-based tools, specifically Large Language Model (LLM) models, which can recognize patterns within the text as part of Artificial Intelligence (AI). In this talk, we demonstrate how LLM models can be utilized to continuously evaluate the severity of PTSD in patients within their home settings and track their PTSD biomarkers.

Our methodology involves building a database of subjects with varying levels of PTSD who have participated in online interviews with clinicians. We extract textual data from these interviews and employ trained LLM models to predict total PTSD severity, DSM-based major symptoms, and questionary scores. By comparing these predictions with results from traditional scoring tests using advanced statistical methods, we can determine the accuracy of the different prediction approaches.

Preliminary findings indicate a high level of compatibility between the LLM-based PTSD evaluation and the scores obtained from traditional questionnaires. These results serve as a foundation for the development of an AI tool to support clinical decision-making. By utilizing data from follow-up interviews, our algorithm can provide continuous information on PTSD severity, track the progression of symptoms over time, and assist in designing treatment plans that optimize efficiency and follow-up protocols.

This research represents an important step towards the integration of AI tools as clinical decision support systems. By augmenting traditional questionnaire assessments, our approach has the potential to enhance the accuracy of PTSD evaluations, improve treatment outcomes, and facilitate more effective follow-up care.

Comparative pharmacological characterization of the head twitch response induced by 5-MeO-DMT and N, N-DMT and their effects on synaptic plasticity

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Background: Like other serotonergic psychedelics, 5-MeO-DMT and *n, n*-DMT are thought to act via the 5-HT2A receptor to which they bind with high affinity. In rodents, both induce a characteristic head twitch response (HTR). We sought to determine dose related HTR response for 5-MeO-DMT, DMT and modulators, as well as the effect of both compounds on synaptic plasticity.
Methods: Male C57BL/6J mice (11 weeks, ~30g) were administered 5-MeO-DMT (i.p., 1.25-80 mg/kg), preceded by the 5-HT2A antagonist M107900, 5-HT1A agonist 8OH-DPAT, 5-HT1A antagonist NAD-299, 5-HT2C antagonist RS-102221, 5-HT7 agonist AS-19 and 5-HT7 antagonist SB-269970. HTR was measured for 20 minutes, mice were sacrificed 12 days post-injection and western blot was performed on the frontal cortex, amygdala, hippocampus, and striatum for the synaptic proteins PSD-95, GAP43, synaptophysin, and SV2A. A similar protocol is being implemented for DMT.
Results: 5-MeO-DMT induced a dose-dependent increase in HTR over 20 minutes. The 5-HT2A antagonist/5-HT1A agonist significantly attenuated whereas 5-HT1A antagonist significantly increased 5-MeO-DMT-induced HTR. 5-MeO-DMT (10 mg/kg) significantly increased GAP43 and PSD95 levels in both the frontal cortex and striatum, PSD95 and synaptophysin in the hippocampus, and SV2A in the amygdala 12 days post injection. Co-administration of 5-MeO-DMT (10 mg/kg) and 5-HT1A antagonist caused a reduction of all the synaptic proteins in the hippocampus and an increase of synaptophysin/decrease of SV2A in the striatum compared to 5-MeO-DMT alone. Results for DMT are pending.
Conclusions: We have shown a clear dose response relationship for 5-MeO-DMT, which was modulated by a 5-HT2A antagonist and 5-HT1A agonist/antagonist. The increase in synaptic proteins we observed reflects enhanced synaptic plasticity. We have also observed that while the 5-HT1A antagonist increased 5-MeO-DMT-induced HTR it decreased synaptic proteins induced by 5-MeO-DMT in the hippocampus, hinting that the synaptogenic effect of 5-MeO-DMT may not be directly related to short term psychedelic effects.

The potential impact of Δ9-Tetrahydrocannabinol on Alzheimer's disease cognitive deficits in 5xFAD female mice model over a 15-weeks period

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Background: Alzheimer's Disease (AD) is a progressive neurodegenerative disease, characterized by impaired episodic memory function. Medical treatment of AD today is limited and a need to search for additional medicinal mechanisms is necessary. Δ9-Tetrahydrocannabinol (THC), which in conventional doses damages memory and cognitive functions, has been revealed to induce a neuroprotective effect and improve age and AD-related cognitive decline in mice when administrated in ultra-low doses (ULD-THC, 0.002 mg/kg). Our Previous experiments showed that a single administration of ULD-THC alleviated AD-related cognitive deficits in female 5XFAD mice model 3 weeks after treatment. The current study aimed to determine the behavioural and biological effect of a single ULD-THC treatment beyond 3 weeks.
Method: 6-month-old 5xFAD female mice and their wildtype littermates received a single injection of ULD- THC or saline. 3, 8, and 13 weeks after treatment cognitive assessment was performed. After the last behavioural assessment, mice were sacrificed and the expression of AD biological hallmarks, neuroinflammatory markers, and neurotrophic factors was measured in the Hippocampus.
Results: In accordance with our previous studies, a single treatment of ULD-THC significantly improved AD mice's spatial and long-term memory three weeks post-treatment. Nine weeks post-treatment, AD-treated mice were not significantly different from wildtype mice, while non-treated AD mice showed significantly worse cognitive ability compared to wildtypes, suggesting a long-term effect of the single ULD-THC injection. Notably, 15 weeks post-treatment, biological examinations revealed slight (although less pronounced) differences between treated and non-treated AD mice in aspects of neuroinflammatory biomarkers and neurotrophic factors, suggesting that the treatment's long-term effect may derive from changes in neuronal mechanism. In conclusion, the long-term effects of ULD-THC on cognitive function as well as neuroinflammatory and neurotrophic markers, suggests intriguing possibilities for AD intervention strategies using ULD-THC.

Neuroinflammatory and estrogen receptor markers associated with anti-depressive effects of cannabidiol in male and female rats

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Background: Accumulating evidence suggests a crosstalk between depressive symptoms and neuroinflammatory processes. An anti-inflammatory agent, the cannabis derivative cannabidiol (CBD) shows promise as a potential treatment for depression, but the extent of its antidepressant properties and its mechanisms of action are yet to be fully understood.
Methods: In this study, we assessed the effects of chronic CBD treatment (10 mg/kg/day, i.p.) on male and female rats exposed to the unpredictable chronic mild stress (UCMS) model of depression. We then examined the expression of genes coding to cannabinoid receptors (cnr1 and cnr2), neuroinflammatory markers (TNF-α and nfkb1) and estrogen receptors (ERα and Erβ) in the ventromedial PFC (vmPFC) and hippocampal CA1 and ventral subiculum (VS) brain areas.
Results: In males, CBD restored UCMS-induced increased immobility time in the forced swimming test (FST), upregulation of the TNF-α gene in the CA1 and downregulation of the CB1, ERα and ERβ genes in the VS. In females, CBD restored UCMS-induced decreased immobility in the FST, and led to downregulation of the NF-κB1 gene in the vmPFC in all groups, regardless of UCMS. In both sexes, UCMS rats travelled longer distances in the open field test compared to No UCMS rats, and showed downregulation of the CB1 gene in the vmPFC and upregulation of the NF-κB1 gene in the VS, with no effect of CBD.
Conclusions: Our findings suggest sex dependent effects of UCMS on despair-like behavior, which may be mediated by differences in neuroinflammatory markers and estrogen receptors.

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Effectiveness of psilocybin and psychedelic mushroom extract in alleviating the OCD like behavioral phenotype of SAPAP3 knockout mice

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Background: In recent years there has been an increase in violence at mental health centers in Israel where seclusion and restraint were mostly applied. Recently, effort has been applied to reduce the use of these means, with the main alternative being medication 'as required' and de-escalation techniques, one of which is a sensory room.
Purpose: Exploring the effectiveness of a sensory room in reducing seclusion, restraint, and aggressive behavior in an acute psychiatric unit.
Method: This experimental longitudinal study included two phases: 1. without intervention (control group) 2. with intervention that also included qualitative research (study group). Each phase lasted 133 days. Participants comprised a convenience sample of eighty men hospitalized in an acute ward, aged 18-50, who signed a hospitalization consent. Throughout the two phases, data on restrictions and incidents of aggressive behavior performed in the ward were collected. In addition, second phase (research group) participants were interviewed regarding their experiences in the sensory room.
Results: A statistical decrease demonstrating medium effect in using 'as required' medication (Beta = -.30, p = .010), and a statistical decrease demonstrating high effect in the events of aggression (Beta = -.50, p < .001), were found. No statistically significant decrease and low effect were found in the use of seclusion and restraint (Beta = -.08, p = .527).
Conclusions: This study, the first of its kind, indicates the effectiveness of using a sensory room in reducing aggression and the use of 'as required' medication among men in an acute psychiatric ward. It is suggested that integrating a sensory room in a psychiatric ward may positively impact the ward climate.

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Effects of pre-reproductive maternal exposure to social or physiological stress on offspring behavior: a rat model

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Introduction: Stress has behavioral and physiological consequences across generations, but few studies have examined the consequences of female stress, particularly in adolescence, on offspring. Furthermore, the consequences of different stressors on offspring phenotypes have not been assessed. The first aim of this study was to examine whether exposure to social or physiological stress in adolescent female rats would affect their social-emotional behavior and the expression of molecules associated with HPA axis function, sociability and cognition in blood and brain. Next, we studied the impact of different stress types on maternal behavior. Finally, we investigated social-emotional behavior in stress-naïve offspring across three generations.

Method: Adolescent female rats were exposed to social isolation (**SI**) or Food and Water Deprivation (**FWD**) stress for 7 days. Two weeks later, they were tested for (i) behavioral abnormalities, (ii) changes in CORT, Oxytocin and BDNF in blood/serum and (iii) mRNA expression of CRHR1, OXT-R, and BDNF in PVN and NAc. A subset of behaviorally naïve females was mated with stress-naïve males. F0 dams were examined for changes in maternal care. First-second and third generation (F1, F2 and F3) were tested for behavioral alterations.

Results: Both SI and FWD F0 SI exposed rats spent more time in the closed arms of the EPM, but SI alone led to immobility in the FST and elevated blood CORT levels immediately after stress. Furthermore, while social behavior remained intact in F0, increased Oxytocin and OXTR levels were found among SI-exposed rats in blood and PVN, respectively. Sexually dimorphic deficits in social recognition were found in F1 and F2, primarily in SI offspring.

Conclusions: Although SI didn't affect social behavior or maternal care, it did impact oxytonergic markers and offspring social recognition in F1 and F2 offspring. These findings indicate that some stress-specific information is selectively passed on to subsequent generations.

The impact of medical clowns on emotional and attentional regulation in children undergoing upper gastrointestinal endoscopic procedures

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Medical clowns are part of multidisciplinary medical teams, principally in pediatric wards. They are known to reduce levels of anxiety, such as during the induction of anesthesia in children.
These effects have previously been measured with subjective questionnaires; however more objective tools are needed. Therefore, this randomized controlled trial aimed to examine emotional and attentional regulation of children undergoing upper gastrointestinal endoscopy, through physiological tools in addition to traditional self-reports.
We included 99 children aged 1 to 18 years who were scheduled for upper gastrointestinal endoscopies. The children of the experimental group (n=52) and their parents were accompanied by a medical clown from the arrival to the hospital to the induction of anesthesia, and after recovery. In the control group, the children (n=47) were accompanied by their parents only. We examined anxiety levels and attentional regulation of the children and their parents, the pre- and postoperatively for the children and perioperative for the parents, using the electrodermal activity (EDA), Auditory Sustained Attention Test (ASAT), vital signs and self-reports.
It was found that in the medical clown group compared with controls, children specifically over the age of eight had significantly lower physiological measures of stress and better emotional regulation during and after the procedure.
Our findings support the use of medical clowns as an effective intervention to reduce perioperative stress levels and improve postoperative emotional regulation in a pediatric population. The physiological tools provide novel insights regarding the potentially relevant age groups for such interventions.

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Graph analysis uncovers an opposing impact of methylphenidate on connectivity patterns within default mode network sub-divisions

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Background: The Default Mode Network (DMN) is a central neural network, with recent evidence indicating that it is composed of functionally distinct sub-networks. Methylphenidate (MPH) administration has been shown before to modulate impulsive behavior, though it is not yet clear whether these effects relate to MPH-induced changes in DMN connectivity. To address this gap, we assessed the impact of MPH administration on functional connectivity patterns within distinct DMN sub-networks and tested their putative relations to variability in state and trait impulsivity.
Methods: Fifty-five right-handed healthy adults underwent two resting-state functional MRI (rs-fMRI) scans, after acute administration of either MPH (20mg) or placebo, via a randomized double-blind placebo-controlled design. Graph modularity analysis was implemented to fractionate the DMN into distinct sub-networks based on the impact of MPH on DMN connectivity patterns with all other neural networks.
Results: MPH administration led to an overall decreased DMN connectivity, particularly with the auditory, cinguloopercular, and somatomotor networks, and increased connectivity with the parietomedial network. Graph analysis revealed that the DMN could be fractionated into two distinct sub-networks, with one exhibiting MPH-induced increased connectivity and the other decreased connectivity. Decreased connectivity of DMN sub-division with the cinguloopercular network following MPH administration was particularly evident among individuals with elevated trait impulsivity.
Conclusions: Current findings highlight the intricate effects of MPH administration on DMN rs-fMRI connectivity, uncovering its opposing impact on distinct DMN sub-divisions. MPH-induced dynamics in DMN connectivity patterns with other neural networks may account for some of the effects of MPH administration on impulsive behavior.

The potential of micro-dosing MDMA in a translational model for PTSD: A brief post-reminder treatment study

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Introduction: MDMA (3,4-methylenedioxymethamphetamine), combined with psychotherapy, has shown efficacy for the treatment of PTSD patients. Recent research indicates that a single dose of MDMA could reduce anxiety-related behavior and attenuate PTSD-related responses. However, acute doses have been linked to neurotoxicity and adverse-effects. This controlled prospective study aimed to assess the bio-behavioral underpinnings of micro-dosing MDMA in a translational-model of PTSD, in order to mitigate potential adverse-effects.
Objective: To evaluate the effects of the continuous administration of MDMA micro-doses(200µg/kg) on behavioral and molecular parameters in the Predator-Scent-Stress (PSS) model of PTSD. We aimed to investigate whether micro-dosing MDMA, administered adjectively during trauma-cue exposure, reduced PSS-induced anxiety-like responses and shifts PTSD phenotype prevalence rates.
Hypothesis: We hypothesized that micro-dosing MDMA supplementation post-trauma reminder would result in:
Methods: Adult male Sprague-Dawley Rats were assigned to five groups: Vehicle or MDMA treated rats with or without paired-traumatic-cue and a MDMA treated group with unpaired-traumatic-cue. Behavioral assessments were conducted: elevated-plus-maze, acoustic-startle-response and Open-Field tests. Subsequently, rats were sacrificed, and their brains processed for immuno-histochemistry.
Preliminary Results: Initial findings suggest that MDMA micro-dosing paired with trauma-cue exposure reduced freezing responses, indicating a potential effect on memory-related processes. Immuno-histochemistry results indicate a possible up-regulation of BDNF and serotonin in treated groups. The results were indistinguishable MDMA and Saline in the EPM or ASR tests.
Discussion: The results show that in the short-term, micro-dosing of MDMA administered subcutaneously over 30 days attenuated anxiety-like behaviors related to trauma. This study demonstrates that micro-dosing of MDMA might be valuable in alleviating anxiety symptoms without producing adverse-effects. Taken together, this study demonstrates that micro-dosing of MDMA might be valuable in the alleviation of trauma-related anxiety symptoms.

Oxytocin's role in shaping the relation between executive control and emotion

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Cognitive functioning is influenced by emotional stimuli, and negative stimuli might hamper cognitive performance. Prior research indicates that recruitment of executive control can mitigate this emotional interference, improving emotional regulation. This study examines the impact of oxytocin, a hormone involved in socioemotional processing and motivation, on the interplay between emotions and executive control. Using a double-blind placebo control design, 108 male students (age 25.2 ± 3.1 years) received intranasal oxytocin or a placebo, and completed self-report questionnaires, an emotional flanker task and an emotional rating task.

We hypothesized that under oxytocin administration, negative stimuli will be more salient and less anxiety-provoking leading to higher emotional rating, and to a decrease in the effect of executive control over emotional interference. In line with our hypothesis oxytocin significantly affected the interaction between emotion and executive control. Specifically, under oxytocin recruitment of executive control did not mitigate emotional interference; and compared to placebo, the attenuation of emotion due to executive control was significantly reduced. However, unexpectedly, oxytocin did not affect emotional experience and perception.

These results suggest that oxytocin plays a role in modulating the connection between emotion and executive control, influencing the utilization of executive control as a means of emotion regulation, but it does not directly affect emotional processing. These current findings can be explained by oxytocin's role in increasing approach/decreasing avoidance motivation subserved by frontal-limbic interactions. Accordingly, oxytocin intake might lead to changes in frontal-limbic connectivity, resulting in an impaired ability to regulate emotional response through executive control. Given the crucial role of emotional processing and regulation in healthy population and in various psychopathologies, understanding its mechanism is of utmost importance.

Deferiprone and N-Acetyl Cysteine combination as a treatment in Ketamine induced psychosis

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Schizophrenia is a mental illness affecting 1% of society and has both a social and economic burden on society. Treatments for this disorder help only with part of the positive symptoms, and up to 30% of patients show some to complete resistance to treatments. A main reason no breakthrough was made during these years is lack of understanding of brain mechanisms underlying the disorder. The hypothesis that labile iron levels in the brain are involved in the pathophysiology of schizophrenia was first introduced over 25 years ago but has been largely overlooked. Recently, a study in our lab showed that deferiprone (DFP), an FDA approved iron chelator, decreases psychotic-like behaviors in mice. The present study was designed to gain further improvement in these behaviors by combining DFP treatment with oral administration of N-Acetyl Cysteine (NAC). NAC is an antioxidant that precursors L-cysteine, which results in glutathione elevation biosynthesis. In the present study, mice were given access to either plain drinking water or NAC dissolved in water (100mg/kg/day) for at least 3 days before and were administrated with ketamine (50 mg/kg i.p., N=68) 2 hours prior to deferiprone administration (100 mg/kg i.p., N=68). We then performed an Open Field Test (OFT), where ketamine induced hyperlocomotion whereas the combination of NAC and DFP significantly attenuated this effect. Finally, we used an ICP-MS analysis to detect changes in iron levels in specimens from the PFC, basal ganglia, and Hippocampus. We did not find any significant change in iron levels between treated and untreated groups and aim to further investigate this finding using metabolome analysis. Altogether, we hope that our findings will improve the biological understanding of psychotic-like abnormal behaviors and the mechanisms behind them, as well as enable the use of this DFP and NAC combination as a treatment in the future.

The Role of parental accommodation in the association between parent and child anxiety in times of terror

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Parental anxiety and related behaviors are pivotal in the onset and maintenance of anxiety disorders in children (Murray et al., 2009). Parental accommodation refers to various strategies parents employ to reduce a child's anxiety, such as modifying family routines, offering excessive reassurance, and encouraging avoidance of stress-inducing situations (Jones et al., 2015). Although these actions are intended to alleviate immediate distress, they can inadvertently escalate and intensify the child's anxiety over time.

In this study we investigated the moderating role of parental accommodation on the association between parent and child anxiety during acute stress. Additionally, we examined other relevant child outcomes, including perceived stress, emotional difficulties and the use of avoidance coping strategies. We explored these associations in the context of the unprecedented terror attack by Hamas on Israel on October 7 and the subsequent war.

Seventy adolescents aged 12-17 years, half of whom were diagnosed with anxiety disorders, participated in the study. Adolescents and their parents completed self-report clinical questionnaires at two timepoints: the first, t0, was completed in the laboratory during the year preceding the commencement of the events, and the second, t1,occurred during the first two weeks of the war, following the October 7th massacre.

Preliminary findings indicate that the tendency for parental accommodation, measured at t0, significantly moderated the association between parent and child anxiety symptoms ($R2$=.552, p=.005), as well as the link between parent anxiety and the child perceived stress ($R2$=.422, p=.037), emotional difficulties ($R2$=.514, p=.007), and use of avoidant emotional regulation coping strategies at t1 ($R2$=.469, p=.000).

These findings provide additional empirical support for the important role of parental accommodation on children's psychological well-being, suggesting that parental anxiety may predict increased challenges for children in coping with stressful and traumatic events. This effect is particularly pronounced in families prone to higher levels of accommodation.

Light and food: body image moderates the effects of chronotype on the risk to develop eating disorders

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Background: Chronotype, indicative of an individual's preference for morningness or eveningness throughout a 24-hour period, assumes a pivotal role in regulating diverse physiological and behavioral processes. Existing research has delineated substantial differences between evening types (ET) and morning types (MT) concerning personality traits, health outcomes, and overall well-being. In that context, the current study was designed to explore possible relationship between chronotypes and the susceptibility to developing an eating disorder (ED). Methods: the study included a convenience sample of 165 participants (mean age = 35.45±11.89). Participants were asked to answer online questionnaires including the Morningness-Eveningness Questionnaire (MEQ), Body Shape Questionnaire (BSQ), and Eating Attitudes Test-26 (EAT-26).
Results: results elucidate (1) a significant correlation between MEQ and the propensity for ED development (EAT-26), with evening types exhibiting a heightened risk. (2) a significant association between body image (BSQ) and ED risk (EAT-26), indicating that negative perception of body image is associated with a higher likelihood of ED occurrence. (3) A moderation effect of body image on the relationship between chronotype and ED risk.
Discussion: The moderation analysis emphasizes the amplification of the association between chronotype and ED risk as negative body image becomes more pronounced. These findings accentuate the significance of simultaneously considering sleep preferences and body image perceptions when comprehending the risk factors associated with ED. Prospective interventions aimed at mitigating ED risk may gain efficacy by targeting both ET and the existence of negative perceptions of one's body image.

Intergenerational binge eating-like behavior and stress in adolescence

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Binge eating (BE) is consuming large amounts of food in a short time, while experiencing loss of control over eating behaviour. BE has a hereditary component and stress in adolescence may contribute to its onset and/or severity. We examined the impact of juvenile stress (JS) on BE-like behavior in adulthood, in an animal model of intergenerational BE. 24 randomly assigned female Wistar rats (*F0*) received 2-hour access to palatable food (PF; Oreo Cookies) 3 or 5 times a week (3TW or 5TW) for 4 weeks. Afterwards, rats underwent the open field test (OFT), and hair samples were collected. Compared to 5TW, 3TW had a greater binge size and more anxiety-like behaviours in the open field test (OFT), but hair corticosterone (CORT) levels did not differ between the groups. At postnatal day (PND)27-29, the offspring (*F1*; 124 females) either underwent JS (O-JSC) or not (control, CC). At PND51-53, all offspring were tested in the OFT, dark/light box (DLB), and elevated plus maze (EPM) to assess stress/coping levels. At PND70-85, offspring received 2-hour access to PF three times a week to assess their tendency to engage in BE-like behavior. Offspring's hair samples were collected afterwards. In the EPM, only in O-JSC, offspring of 3TW (O-3TW) spent less time in the open arms than O-5TW. In the DLB, only in O-JSC, O-3TW spent less time in the lit area than O-5TW. O-3TW consumed more PF than O-5TW (intergenerational transfer), and O-JSC consumed more than O-CC (JS effect). O-3TW JSC showed the largest PF intake (additive effect). In O-CC, O-3TW had lower hair CORT levels compared to O-5TW. This novel animal model highlights the complex interplay between parental and offspring's experience underlying psychopathology.

"Empathic Immunity" - How we feel about others may contribute to how well we feel. Behavioral and biological preliminary results

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Empathy is a multi-component process involving at least two components: an emotional component referred to as state-matching or affective sharing, and a more cognitive component called perspective-taking (Shamay-Tsoory, 2011). Here we examine whether the immune system plays a role in empathy. We coin the term 'empathic immunity' representing the inclination to adjust one's immune reaction in response to another individual's state and can be conceptualized as a feedback-loop involving an infected target and an observer. To test this hypothesis, we exposed participants (N=60) to short films of targets diagnosed with flu or covid 19, describing their symptoms and to control films. In addition, participants provided one saliva sample before watching the videos and two after (following exposure to the films, and 30 minutes following exposure), to assess the activation of the immune system through the measurement of proteins called cytokine. The results indicated that, compared to control films, exposure to films featuring infected individuals led to increased ratings of empathic concern and personal distress scales. Observing the films was also associated with increased reports of symptoms (mostly muscle aches, sore throat and phlegm), indicating that participants may internally imitate the observed symptoms. Importantly, preliminary results (N=7) indicated a significant increase in IL-1β (P=0.039) and changes in IL-6 were marginally significant (P=0.068). Although the sample is small, it represents initial evidence that observing sickness triggers empathy and is associated with changes in cytokines levels.

Sleep irregularity in preadolescent children is associated with child's chronotype and sleep duration and mother's sleep schedules

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Sleep regularity plays an essential role in children's well-being. Social Jetlag (SJL) quantifies sleep regularity as the difference between mid-sleep times on work/school days and free days. Little is known about associations between SJL in preadolescent children with their habitual sleep duration and chronotype, and mother's sleep schedules.

An internet-based Mom-Child 24/7 (MCH24/7) survey queried sleep-wake behaviors on work/school and free days of mothers and their children (4-10 years of age) using the ultra-short Munich ChronoType Questionnaire (µMCTQ). Between February 2022 – March 2023, 1951 Israeli women anonymously filled the MCH24/7 survey. After exclusions, 983 mother-child pairs comprised the analytic sample (mean age: mothers – 37.1±5.7, children - 5.8±1.7, 47.7% of children were girls).

Mothers reported that on average they sleep 7.3±0.9h and their children sleep 10.4±1.1h (SDmean – weighted sleep duration during work/school days and free days). The chronotype (MSFsc, local time, mid-sleep time on free days corrected for sleep debt) of mothers was 3:12±1:18, while children had on average earlier chronotypes - 2:30±1:04. The mean social jetlag (SJL, min), was 46.6±52.9min in mothers, while children unexpectedly presented a higher SJL - 64.9±47.7min. Pearson correlation analysis showed that the SJL and the MSFsc of mothers and children significantly correlated (ρ=0.23**, 0.20**, respectively), but the SDmean did not. Among children, higher SJL was associated with shorter sleep duration (SDmean, ρ=-0.30**) and later chronotype (MSFsc, ρ=0.28**), **-p<0.05.

Although sleep duration of children was within age-norms, they presented high SJL, reflecting habitual irregularity in sleep timing between school and free days. Higher child SJL was associated with later chronotypes and shorter sleep duration, but also with higher SJL of their mothers, providing insights into the contribution of family context to sleep irregularity in children. Further exploration of these associations is warranted to promote sleep health of both children and mothers.

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Significant contribution of chronotypes to the emotional well-being in a general population cohort in Hungary

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Background: relationship between chronotypes and emotional well-being (EWB) is an intriguing area of study. Chronotypes represent individuals' predisposition to be more alert and active during specific times of the day, often categorized as morning chronotype (MT), evening chronotype (ET), and intermediate chronotype (IT). Studies show that ETs often struggle with morning activities and experience increased stress, and a negative impact on overall mental and physical health. Understanding the relationship between chronotypes and EWB has significant implications for life and can inform decisions about work schedules, social activities, and even clinical interventions for mood disorders. Circadian-related interventions can enhance physical and mental well-being. In that context, this study explored the contribution of chronotypes to EWB in a large cohort of from the general population in Hungary.
Methods: 1120 participants (773 females, 347 males, age 31.5±0.3 years) answered questionnaires regarding (1) demographics, health, and mental health status; (2) EWB, including the Brief Symptoms Inventory, Zung self-rating Depression Scale, State and Trait Anxiety Index, Back Helplessness Scale, and (3) chronotypes using the Morningness/Eveningness Questionnaire. Data for the EWB-related questionnaires were transformed using Z-scores and combined to generate a comprehensive EWB variable. Pearson's correlations, t-tests and ANOVAs were used to evaluate possible relationship between demographic factors and chronotypes and EWB. Variables with significant relationship with EWD were included in a comprehensive regression analysis exploring the partial contribution of these factors to EWB.
Results: gender, marital status, children, finance, health, and mental health were associated with EWB. Chronotype was associated with EWB with higher EWB in MTs compared to others, and higher EWB in ITs compared with ETs. Regression model was significant with a significant contribution of chronotype [r=0.28, p=0.002].
Conclusion: the study supports chronotypes as significant contributors to EWB. This knowledge leads to possible chronotherapy interventions to assist individuals with ET achieve better EWB.

A novel juvenile phenotype in SAPAP3 knockout mice: Potential role of psilocybin treatment

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Background: SAPAP3 knockout (KO) mice exhibit OCD-like behaviors such as excessive grooming to the point of self-injury. There has been growing research into psychedelic drugs such as psilocybin to treat psychiatric disorders including OCD. We evaluated behavioral phenotypes in SAPAP3 KO juvenile mice that do not yet manifest the full adult phenotype and the effect of psilocybin on these juvenile behavioral phenotypes.
Methods: We studied 141 juvenile (10-12 weeks) homozygous, heterozygous and wildtype SAPAP3 KO mice. The mice underwent a series of behavioral tests to examine depressive, anxious, and obsessive-like features and cognition. To examine the effects of psilocybin on the juvenile phenotype we used 42 juvenile homozygous and wildtype SAPAP3 KO mice, treated with psilocybin or saline.
Results: On the Marble-Burying Test, juvenile homozygous SAPAP3 KO Mice mice buried significantly fewer marbles than heterozygous and wildtype mice ($p<0.001$). In the Open-Field Test, distance covered was significantly lower for homozygous mice ($p<0.01$). On the Elevated-Plus-Maze, homozygous mice showed significantly more anxiety ($p<0.01$). On the Buried-Oreo-Test homozygous mice exhibited significant anhedonic-like behavior, showing no interest in the cookies while heterozygous mice uncovered the cookies but did not eat them. On the Tube-Dominance Test male homozygous mice showed a significantly higher win percentage. There was no significant effect of psilocybin (4.4mg/kg) on performance on these behavioral tests.
Conclusions: Juvenile SAPAP3 KO mice present behavioral phenotype that is not entirely consistent with OCD-related behavior, in particular a lower level of marble burying. The KO mice are significantly less active in the open field and the males show greater dominance on the tube-test. On the EPM, the KO mice show greater levels of anxiety. The highly significant results of the Oreo-test suggest an anhedonic component. Administration of psilocybin does not have significant behavioral effects in juvenile SAPAP3 KO mice.

Metabolic Impacts of Psychedelics: Exploring Short-term and Long-term Effects

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Background: While psychedelics show promise in neuropsychiatric diseases, their neurochemical mechanisms remain unclear. Global untargeted metabolomics provides a powerful approach to elucidate pharmacological mechanisms by mapping biochemical alterations induced by these compounds.

Methods: We employed ultra-high-performance liquid chromatography coupled with high-resolution tandem mass spectrometry-based metabolomics to characterize acute metabolic changes at the head twitch response (HTR) peak (approx. 4 min.) and collected tissue 12 days post a single dose for the long-term effect. Administered intraperitoneally at behaviourally active doses, the compounds tested included psilocybin (PSIL), psychedelic mushroom extract (PME), dimethyltryptamine (DMT), 5-MeO-DMT, and serotonin precursor 5-HTP in the frontal cortex of adult male C57BL/6J mice.

Results: In the short term, all compounds exhibited metabolic similarities to vehicles, yet each uniquely upregulated nonanoic acid, suggesting potential lipid metabolism modulation. Long-term DMT exposure induced specific metabolic changes compared to 5-MeO-DMT and vehicle-treated mice, as indicated by improved discrimination in OPLS-DA models. Significant differences in PME and Vehicle groups were driven by specific metabolites, including a progressive decline in purines from vehicle to PSIL to FSME. Enrichment in thiamine metabolism, fatty acid metabolism, and nucleotide sugars metabolism persisted after multiple testing corrections. In the comparison of 5HTP to the vehicle, PCA demonstrated a distinct separation, with serotonin (expected) and nonanoic acid significantly overexpressed, along with other non-significant elevations (e.g. palmitoleic acid and 6-methoxyquinoline).

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Differences between effects of psychedelic compounds and their modulators on head twitch response (HTR) and on immediate early gene expression

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Background: Immediate Early Genes (IEG) *cfos erg1 and erg2* are transiently activated by psychedelic drugs. We studied the relationship between psilocybin and 5-HTP effects on head twitch response (HTR), a rodent model of psychedelic effects, and brain IEG expression and also of serotonin and TAAR1 receptor modulators on psilocybin-induced HTR and IEG expression. In another experiment we evaluated the effects of the psychedelic drugs DMT and 5-MeO-DMT on IEG expression.

Methods: Male C57Bl/6j mice were injected with psilocybin 4.4 mg/kg i.p, 5-HTP 200 mg/kg or combinations of psilocybin with serotonergic or TAAR1 receptor modulators. Immediately after injection, HTR was measured for 30 minutes in a magnetometer. One hour after injection animals were sacrificed; total RNA was extracted from somatosensory cortices. IEG mRNA expression was determined by real time qPCR. Effects of 5-MeO-DMT10mg/kg or DMT 5mg/kg were measured using the same methodology.

Results: Psilocybin significantly increased expression of all three IEGs ($p<0.01$). Co-administration of the 5-HT1A agonist, 8-hydroxy-DPAT, reduced psilocybin-induced HTR but did not alter IEG expression (same for TAAR-1 antagonist). The 5-HT2A antagonist, M107200, blocked psilocybin induce HTR and significantly reduced psilocybin-induced *egr2* but not *cfos* and *erg1* expression. The 5-HT2C antagonist, RS102221, significantly enhanced psilocybin induced HTR, also increased egr*2* expression but did not affect psilocybin-induced *erg1* or *cfos* expression. 5-HTP, at a dose sufficient to induce significant HTR (200mg/kg), did not affect any of the three IEGs. DMT caused increases in cfos and erg 1 levels, but not *egr2*. 5-MeO-DMT increased expression of the 3 IEG's, and more significantly then DMT, *egr* 2 and *cfos*.

Conclusions: Effects of psychedelic compounds alone or co-administered with modulators on HTR and IEG's expression levels are not identical. *Egr2* seems to be more directly associated with HTR enhancement. 5-MeO-DMT is more potent than DMT in causing increase of IEG expression.

The efficacy of supportive vs. supportive-expressive treatment for patients with high narcissistic personality disorder

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Background: Narcissistic Personality Disorder (NPD) is characterized by a pervasive pattern of grandiosity, a need for admiration, interpersonal exploitativeness, and a lack of empathy. This pattern typically emerges in early adulthood and manifests in various contexts. Current treatments for narcissistic personality disorder have limitations, and show poor prognosis. There is an ongoing clinical debate on whether supportive or supportive-expressive treatment is more effective for patients with higher levels of narcissistic personality disorder.
The present study aimed to compare efficacy of supportive vs. supportive-expressive treatments for Major Depressive Disorder (MDD) for patients high vs. low on NPD.
Method: This study is part of a completed Randomized Controlled Trial (RCT) involving Supportive-Expressive Therapy for depression, conducted at the University of Haifa. Participants were 100 patients aged 18-60 diagnosed with Major Depressive Disorder. Treatment efficacy was evaluated using the Hamilton Rating Scale for Depression (HRSD) as completed before every session. NPD was evaluated using structured Interview for DSM Personality Disorders. All data has been collected, and analysis is currently underway.
Conclusions: This study aims to illuminate the efficacy of treatment for individuals with high narcissistic traits. Additionally, we seek to determine whether patients with Narcissistic Personality Disorder may benefit more from Supportive-Expressive treatment vs. Supportive Therapy.

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Estrogen as a Protective Factor? Executive functions and symptoms among trauma-exposed women across the menstrual cycle

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Background: Women are at heightened risk of developing posttraumatic stress symptoms (PTSS) after trauma exposure. The underlying mechanisms are still not fully understood. Executive Functions (EF) are critical cognitive functions which may be disturbed or enhanced by stress. Estrogens appear to play a role both in PTSS and EF. However, the relationship between the three has not been elucidated.

Methods: This study includes preliminary data from nine naturally cycling women (ages 23-41) with traumatic history recruited within a larger study. They were evaluated in one of two hormonal phases (high/low Estrogen), as individually assessed vis-à-vis ovulation and cycle length. Participants completed self-reporting questionnaires on EF and PTSS (Behavior Rating Inventory of Executive Functions-Adult version [BRIEFA] and PTSD Diagnostic Scale [PDS]) and EF computerized tasks (Wisconsin Card Sorting Test [WCST] and Sustained Attention to Response Test [SART]). ANOVA was used to compare scores between menstrual cycle phases.

Results: Compared to low estrogen phase, during high estrogen phase, women reported reduced PTSS severity ($F(1,7)=7.59$, $P=0.028$, $h2= 0.52$) and higher performances on several BRIEFA scales, including Inhibition ($F(1,7)=7.67$, $P=0.028$, $h2=0.52$), Initiating ($F(1,7)=7.94$, $P=0.026$, $h2=0.53$), Working memory ($F(1,7)=18.28$, $P=0.004$, $h2=0.72$), Planning and Organizing ($F(1,7)=11.75$, $P=0.011$, $h2=0.63$), Task Monitoring ($F(1,7)=20.26$, $P=0.003$, $h2=0.74$), Global Executive Composite ($F(1,7)=14.79$, $P=0.006$, $h2=0.68$), and metacognitive Index ($F(1,7)=18.68$, $P=0.003$, $h2=0.73$). Phase effects on BRIEFA remained when PTSS was controlled for. No significant between phase differences were found on computerized tasks.

Conclusions: These results show self-reports of higher EF and lower PTSS during the high estrogen phase. Phase effects on EF are not explained by variability in PTSS, but not replicated in behavioral tasks. This suggests protective effects of estrogen among women with a history of trauma. Future studies may decouple estrogen effects on self-report and behavioral measures of EF and test potential for harnessing the high estrogen hormonal phases in supporting interventions.

Driving under stress: Psycho-physiological recovery in realistic driving scenario as a marker of stress resilience

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Background: Exposure to stress has a wide impact across various psychological, physiological and behavioral functional domains. One such domain is driving, with extensive evidence pointing to dangerous and reckless driving behavior while under stress. Individuals greatly vary with respect to the impact of stress on their overall functioning, with resilience representing the ability to recover following stress. Whether and how resilience is expressed in the context of recovery of driving behavior post stress, and what is its physiological underlay has yet to be assessed.
Methods: 25 healthy adult participants completed three simulated driving scenarios in a driving simulator before, during, and after acute stress induction. Stress was induced using a modified version of the Maastricht Acute Stress Task [MAST], that included a distinct relief component after stress. Physiological (heart-rate variability) and psychological (positive and negative affect) responses were measured at each time point. Participants also completed stress resilience questionnaires.
Results: Contrary to expectation, participants improved their driving performance during stress, in terms of over-speeding (they drove less time and less overall distance over the speed limit compared to their driving before stress and after relief). Acute stress did induce the expected psychological effect, with reduced positive affect and increased negative affect during stress compared to before and after.
Discussion: Our preliminary findings underscore that acute stress leads to more cautious driving. These findings may be explained by our stress manipulation, that includes a strong social-evaluative pressure of negative feedback. Consequently, participants seem inclined to perform actions that are oriented towards pleasing others, specifically through increased compliance with traffic laws. Ongoing analyses are focused on physiological responses to stress and their association with driving performance as well as with variability in stress resilience.

Ethnic variations in violent suicidality: A comparative study of Israeli Jews and Arabs

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Background: In suicide attempts, the level of violence is a crucial factor influencing outcomes, with variations noted in age, gender, and ethnicity. However, the influence of demographic variables and specifically ethnicity on violent suicide attempts (VSA) in Israel has yet to be characterized.
Objective: To evaluate the ethnic and demographic predictors of VSA observed in the emergency department (ED).
Methods: We analyzed ED visits at Rambam Health Care Campus following suicide attempts carried out by adults between 2017 and 2022. Two logistic regression models were built to examine whether patients' demographic variables can predict VSA and their effects on the need for medical hospitalization.
Results: We examined 791 suicide attempts (498 women [62.96%]; 596 Jewish [75.35%]), with the majority being non-violent attempts (716 [90.52%]). Demographic variables significantly predicted VSA, indicating an increased prevalence of VSA among Israeli Arabs, especially among younger individuals. Additional analysis revealed that VSA are associated with increased rates of medical hospitalization, independent of ethnicity.
Conclusions: The findings highlight the role of ethnicity in selection of suicide method and identify young Israeli Arabs as a risk group for violent suicide. This underscores the importance of culturally sensitive risk assessment and suicide prevention in minority groups.

Trauma under psychedelics: Protective effects of MDMA during the peritraumatic period

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On 7/10/23, the Nova festival was a main target of a large-scale terror attack. Survivors experienced life-threatening traumatic events (TEs) and thus are at high risk of suffering post-traumatic stress disorder (PTSD). Uniquely, many attendees experienced the TE under the influence of mind-altering substances which poses an unknown challenge to survivors' recovery trajectory. Here, we evaluate the processing of trauma experienced under the influence of psychedelics, and specifically, early symptoms investigation during the peritraumatic period, which is highly predictive of trauma recovery trajectories.

Participants were recruited from the cohort of the Nova festival terror attack survivors. Participants completed online self-report questionnaires in the peritraumatic period, 4-12 weeks following the TE, to assess demographics, substance use during the festival, and constructs relevant to trauma processing (e.g., social interactions). Participants also completed established scales to assess distress (K6) and PTSD symptom severity (PCL-5).

Results: (n=671) indicate that 69% of participants were under the influence of mind-altering substances during the TE. Analyses revealed that distress (K6) ($F(2,248)=6.025, p=0.003$) and PTSD symptoms (PCL-5) ($F(2,232)=4.443, p=0.013$) differed between groups of survivors that were under the effect of 3,4,-methylenedioxmethamphetamine (MDMA), light-drugs (Cannabis/Alcohol) or not under the influence of substances during the TE. This was driven by lower PCL-5 and K6 scores in the MDMA group than the light-drugs group. Additionally, these groups differed in reported feeling of support from the environment ($F(2,410)=8.845, p<0.001$) and social interactions ($F(2,410)=3.868, p=0.022$), driven by elevated levels of these constructs in the MDMA group compared to the other groups. These results suggest that traumatic exposure under the influence of MDMA may yield improved clinical outcomes in the peritraumatic period. This early protective effect of MDMA seems to be long-lasting, spanning across weeks and months following the trauma. Further research is needed to understand the mechanisms underlying this effect and its influence on survivors' recovery.

Induced Theta Oscillations (4-7 Hz) Predict Heightened Acute Stress and GAD Symptoms Among Adolescents Exposed to War-Related Stress

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Mediofrontal error-related theta (4−7 Hz) oscillations are thought to reflect a neural mechanism that supports cognitive control and adaptation of goal-directed behaviors (Cavanagh and Frank, 2014; Beatty et al., 2020). Studies examining the effect of theta activity on anxiety and excessive worry have yielded equivocal findings. In a recent study, we demonstrated that induced theta activity was associated with lower anxiety and worry among 8–13-year-old children during the first COVID-19 lock down (Shner-Livne et al., 2023). Conversely, a different study reported that adults with generalized anxiety disorder (GAD) exhibited higher error-related theta compared to a control group (Cavanagh et al., 2017). These discrepancies may arise from age-related differences.

In this longitudinal study, we examined the association between induced theta and anxiety in the context of a unique real-life stress event, focusing on adolescents. We first measured error-related induced theta activity during a laboratory based behavioral task, and then examined its association with anxiety symptoms and acute stress during the Israel-Hamas war. In the first time point (T0), participants aged 12-18 years, completed a Flanker task (Eriksen & Eriksen, 1974) while EEG was recorded. Data for the second (T1) and third (T2) time points were collected through online clinical questionnaires a few months later (Mean(time)=5.48 months, SD=3.51), during the first two weeks and a month following the commencement of the war.

Results showed that stronger response-related induced theta power following an error (T0) predicted more GAD symptoms across all three time points (p=.033). Moreover, induced error-related theta activity moderated the link between subjective exposure to the war and levels of acute stress in T1 (p=.027). These results are generally in line with findings obtained in previous studies with adults, contributing to our knowledge of the developmental mechanisms and neural biomarkers of risk for anxiety.

The biological mechanism behind the anti-depressant effect of Shan Zha in mice

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Depression and anxiety pose significant challenges to mental health globally. While Selective Serotonin Reuptake Inhibitors (SSRIs) have been the conventional choice for antidepressant treatment, they often exhibit limited efficacy and undesirable side effects, including weight changes and decreased libido. Seeking alternative solutions, this study delves into the antidepressant effects of Shan Zha, a traditional Chinese herb, aiming to understand its biological mechanism in comparison to the commonly prescribed SSRIs.

Male ICR mice were subjected to four weeks of unpredictable chronic mild stress (UCMS) and treated daily for three weeks with either Shan Zha or SSRI (Citalopram). Behaviorally, Shan-Zha produced similar anti-depressive and anxiolytic effects compared to Citalopram. Notably, in contrast to Citalopram, Shan Zha-treated mice did not exhibit sexual or weight-related side effects. To uncover the biological mechanisms underlying Shan Zha's effects, we quantified monoamines (dopamine, norepinephrine, and serotonin), their metabolites, and monoamine receptor expression in the hippocampus and prefrontal cortex using HPLC and qPCR, respectively. The results demonstrate that Shan Zha exerts unique and novel effects on the monoamine system, that are distinct from conventional antidepressants. These effects might be related to Shan-Zha treatment's lack of side effects. Overall, our data show that Shan Zha produces robust antidepressant and anxiolytic efficacy similar to Citalopram but without associated side effects, possibly by differentially modulating monoaminergic neurotransmission.

The study offers a holistic understanding of Shan Zha's antidepressant mechanism, shedding light on alternative pathways for antidepressant interventions and contributing to a more comprehensive understanding of its effectiveness and mechanisms.

Exploring the effectiveness of a sensory room in reducing seclusion, restraint and aggression at an acute psychiatric ward

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Background: In recent years there has been an increase in violence at mental health centers in Israel where seclusion and restraint were mostly applied. Recently, effort has been applied to reduce the use of these means, with the main alternative being medication 'as required' and de-escalation techniques, one of which is a sensory room.
Purpose: Exploring the effectiveness of a sensory room in reducing seclusion, restraint, and aggressive behavior in an acute psychiatric unit.
Method: This experimental longitudinal study included two phases: 1. without intervention (control group) 2. with intervention that also included qualitative research (study group). Each phase lasted 133 days. Participants comprised a convenience sample of eighty men hospitalized in an acute ward, aged 18-50, who signed a hospitalization consent. Throughout the two phases, data on restrictions and incidents of aggressive behavior performed in the ward were collected. In addition, second phase (research group) participants were interviewed regarding their experiences in the sensory room.
Results: A statistical decrease demonstrating medium effect in using 'as required' medication (Beta = -.30, p = .010), and a statistical decrease demonstrating high effect in the events of aggression (Beta = -.50, p < .001), were found. No statistically significant decrease and low effect were found in the use of seclusion and restraint (Beta = -.08, p = .527).
Conclusions: This study, the first of its kind, indicates the effectiveness of using a sensory room in reducing aggression and the use of 'as required' medication among men in an acute psychiatric ward. It is suggested that integrating a sensory room in a psychiatric ward may positively impact the ward climate.

Exploring ecological dynamic patterns in patients with major Depressive Disorder with vs. without Borderline Personality Disorder

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Background: Patients with borderline personality disorder (BPD) and major depressive disorder (MDD) experience a poorer prognosis when treated for MDD. The overarching goal of the current study is to investigate through a series of case studies the differences between patients with MDD, with vs. without BPD, in their resting heart rate (HR), and sleep and activity patterns at baseline (aim 1) and throughout treatment (aim 2). These parameters were measured ecologically using wearable devices.

Method: Sixteen patients recruited from an ongoing randomized controlled trial participated in the study. Data was collected using a Fitbit charge 3 wearable device during the week prior to treatment, a week at the middle of treatment and the last week of treatment.

Results: Preliminary results indicated a potential association between resting HR and severity of BPD symptoms at intake, and MDD scores throughout the week. Patients with more severe symptoms of BPD and MDD tend to experience increased resting HR. Further analyses are ongoing.

Discussion: The current study holds the potential to shed light on the differences underlying the poorer prognosis of patients with MDD and BPD compared to patients with MDD without BPD, using objective measures and thus limiting the burden on the patients. This is of high importance in patients with BPD, who tend to struggle to report accurately on their internal states. Uncovering these differences may be the first step towards advancing the personalization of MDD treatment for patients with BPD.

Effects of D-cycloserine (DCS) on psilocybin-induced head twitch response, MK-801-induced hyperlocomotion and synaptic proteins in ICR mice

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Background: Emerging evidence suggests that hallucinogenic effects of psilocybin may not be required for its therapeutic and neuroplastic effects. D-cycloserine (DCS) is an antibiotic that also acts as a partial agonist for NMDA receptors. We evaluated the effects of DCS on psilocybin-induced head twitch response (HTR), a rodent proxy for psychedelic effects; MK-801-induced hyperlocomotion, a test modeling positive symptoms of schizophrenia and synaptic proteins as a measure of synaptic plasticity.
Methods: To measure HTR, mice were injected intraperitoneally with psilocybin (4.4 mg/kg), DCS (320 mg/kg), a combination of both or saline, and were placed inside a magnetometer for 20 minutes. Post-mortem brain specimens (frontal cortex, hippocampus, amygdala, striatum) were obtained 12 days later. For MK-801 drug-induced hyperactivity, mice were injected with the same drugs, after 30 minutes MK-801 (0.5 mg/kg), and 30 minutes later were placed in the open-field for 60 minutes. Synaptic protein levels (GAP43, PSD95, Synaptophysin, SV2A) were measured by western-blots.
Results: Psilocybin significantly increased HTR ($p<0.0001$). DCS did not while psilocybin+DCS induced a significantly lower number of HTR ($p=0.0001$). MK-801 significantly increased mobility ($p=0.0063$). DCS or psilocybin did not affect MK-801-induced mobility, but the combination significantly reduced the hyperactivity ($p=0.0079$). Western blot analysis showed that psilocybin caused a significant increase in SV2A in the frontal cortex ($p=0.0094$), amygdala ($p=0.0456$), and hippocampus ($p=0.0119$); psilocybin+DCS caused a significant increase over all four synaptic proteins in the amygdala ($p=0.0117$)
Conclusions: The HTR analysis suggests that DCS has the potential to limit psilocybin-induced hallucinogenic effects. The open-field results show that psilocybin+DCS counteracts the effects of MK-801, suggesting antipsychotic potential. Enhancement by DCS of psilocybin effects on synaptic proteins in the amygdala indicates enhanced neuroplastic effects.

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Physiological and psychological resilience among healthcare workers in COVID-19 units - the protective role of religious beliefs

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The COVID-19 pandemic has profoundly impacted global health, with disproportionate
consequences for healthcare workers (HCWs). HCWs already have an elevated prevalence of mental health problems, including depression, anxiety, and insomnia, and it is crucial to identify protective factors. Religious practices have been suggested to improve emotional health and build resilience by fostering community, finding a sense of purpose, and giving meaning to hardships. How religiosity impacts HCWs during a time of crisis is unclear. Therefore, we evaluated how religiosity contributes to resilience among HCWs who were routinely exposed to high levels of stress at work during the pandemic.

We performed a cross-sectional study to investigate resilience through a physiological measure (the Auditory Sustained Attention Test; ASAT) and psychological self-reports to assess whether being religious increases resilience among HCWs.

Forty-two HCWs were recruited from COVID-19 units and 44 HCWs from general internal medicine units, during June and July of 2022. COVID-19 HCWs showed significantly elevated emotional and attentional dysregulation with the ASAT, as measured by acoustic startle and PPI, that was undetectable with self-reported assessment tools. Furthermore, after dividing the HCWs into a 'high' and 'low' religiosity group, those with lower religiosity scores showed higher emotional and attentional dysregulation with the ASAT.

The findings suggest that the ASAT may have greater sensitivity at detecting emotional and attentional dysregulations than self-reports. Moderate or high religiosity may be protective against poorer performance on the ASAT which could suggest greater resilience to mental health problems in the face of a crisis.

Dynamics in the physiological trajectories of response to acute stress: Uncovering latent variability

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Background: Exposure to acute stress is omnipresent in everyday life and may significantly impact physical and mental health. Physiological responses to acute stress involve sympathetic activation, expressed via fluctuations in heart rate variability (HRV). To date, majority of studies have captured HRV as a single, static measure during the entire acute stress period, disregarding putative dynamics in its response trajectories. In here, we propose that characterization of the dynamics in the physiological trajectories of response to acute stress may uncover latent variability that in turn could relate to subjective stress outcomes.
Methods: One-hundred and two (102) healthy female participants underwent a 10-min long acute stress induction. Physiological (HRV) and subjective (positive and negative affect) responses were continuously measured throughout the experimental session. HRV response trajectories were quantified by dividing the stress induction period into three subsequent segments of 3.3 min and calculating their root mean square of successive differences between heartbeats (RMSSD). These segments, alongside physiological recording of equal length from before and after the stress were analyzed using latent class mixture modelling.
Results: Three different HRV RMSSD acute stress response trajectories emerged, depicting no change in HRV over time, an expected decrease in HRV in response to acute stress, or an unexpected increase in HRV. Post-hoc analysis revealed that individuals that exhibited the response trajectory of an increase in HRV also depicted sharper decline in positive affect in response to stress and reduced ability to recover their positive affect post-stress.
Discussion: Findings point towards a novel form of variability in physiological response to acute stress, expressed via different physiological dynamics. Interestingly, these patterns were associated with and may have contributed to variability in subjective response to stress. Upon completion, this study may shed light on a novel source of variability in acute stress responsivity that may characterize stress vulnerability.

Involvement of the Na+ , K+ -ATPase α1 Isoform and endogenous cardiac steroids in depression- and manic-like behaviors

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Bipolar disorder (BD) is a severe and common chronic mental illness characterized by recurrent mood swings between depression and mania. The biological basis of the disease is poorly understood, and its treatment is unsatisfactory. Na+ , K+ -ATPase is a major plasma membrane transporter and signal transducer. The catalytic α subunit of this enzyme is the binding site for cardiac steroids. Three α isoforms of the Na+ , K+ -ATPase are present in the brain. Previous studies have supported the involvement of the Na+ , K+ -ATPase and endogenous cardiac steroids (ECS) in the etiology of BD. Decreased brain ECS has been found to elicit anti-manic and anti-depressive-like behaviors in mice and rats. However, the identity of the specific α isoform involved in these behavioral effects is unknown. Here, we demonstrated that decreasing ECS through intracerebroventricular (i.c.v.) administration of anti-ouabain antibodies (anti-Ou-Ab) decreased the activity of α1 +/− mice in forced swimming tests but did not change the activity in wild type (wt) mice. This treatment also affected exploratory and anxiety behaviors in α1 +/− but not wt mice, as measured in open field tests. The i.c.v. administration of anti-Ou-Ab decreased brain ECS and increased brain Na+ , K+ -ATPase activity in wt and α1 +/− mice. The serum ECS was lower in α1 +/− than wt mice. In addition, a study in human participants demonstrated that serum ECS significantly decreased after treatment. These results suggest that the Na+ , K+ -ATPase α1 isoform is involved in depressive- and manic-like behaviors and support that the Na+ , K+ -ATPase/ECS system participates in the etiology of BD.

The effect of Intranasal Oxytocin on Social Cognition and theory of mind in children with attention deficit hyperactivity disorder – A pilot study

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Introduction: Attention deficit hyperactive disorder (ADHD) associated with impairments in social cognition and theory of mind (ToM), tends to improve following treatment with Methylphenidate (MPH). Changes in reactivity of Oxytocin (OT) to interpersonal situation might improve these deficits in children with ADHD taking MPH.

Aim of study: Validate the feasibility of a double-blind placebo control study, to assess the effect of a single dose of IN-OT on ToM and social cognition functions in children and adolescents with ADHD, with and without MPH.

Methods: Two-stage prospective study. First stage - children diagnosed with ADHD treated with stimulants, were randomized in a 1:1 ratio into two groups - OT group and control group. Without taking stimulants on the morning of the study, the active treatment group received a single IN-OT dose. Control group received placebo solution. We compared the performance in a cognitive tasks battery - Penn Web-Based Computerized Neurocognitive Battery. We conduct Faux Pas recognition task. Second stage, participants of control group received IN-OT without prior administration of stimulants. Active treatment group received their regular stimulants' therapy and were administered with IN-OT. Both groups completed similar tasks to those of the first stage.

Results: Six boys and two girls, ages 9-16 years old were recruited to the pilot study, all of whom were diagnosed with ADHD without co-morbidity and treated daily with stimulants. Six children (75%) completed the study and the other two completed only the first stage. Preliminary results and conclusions regarding the feasibility of the study, strong suits and weak aspects will be presented.

Significance: This study will help establish some of the biological underpinning of ToM and social cognition impairments in children with ADHD, as well as the feasibility of a larger scale study aimed at evaluating the beneficial role of IN-OT on these functions in those children.

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Identifying a biochemical biomarker of fibromyalgia based on exhaled breath

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Background: Fibromyalgia (FM) is a common illness characterized by chronic widespread pain, sleep problems, physical exhaustion, cognitive difficulties and strong comorbidities with mental health. FM diagnosis is currently based on subjective reports of symptoms. In clinical practice, FM is diagnosed after ruling out other possible neurological or rheumatic diseases, a process that usually lasts for years. Previous research tried to establish neurophysiological biomarkers of FM. However, this approach is costly and mostly not feasible for clinical settings. Several studies have investigated the relationship between FM and stress, but this issue is still not fully understood. Notably, some research has identified volatolomic signatures—detectable in volatile organic compounds (VOCs)—as effective diagnostic markers for different health conditions. This study aims to develop a new objective biomarker for FM diagnosis based on exhaled VOCs.
Methods: The study was conducted to develop a new diagnostic tool for detecting FM based on exhaled VOCs collected under both baseline and stress. VOC exhaled measurements were conducted using a Sniffphone device from 37 FM patients and 30 healthy controls. We employed machine learning approaches, specifically Support Vector Machine and Decision Tree models, to analyze the exhaled VOCs and differentiate between FM patients and controls.
Results: Under baseline conditions, both the Support Vector Machine and Decision Tree models showed an accuracy of 72.73% in predicting fibromyalgia based on exhaled VOCs. However, in stress conditions, the SVM model maintained the same accuracy level at 72.73%, while the DT model showed a significant increase in accuracy, reaching 90.91%. Interpretability analysis revealed mechanistic characteristics of the model.
Conclusion: This study makes a significant contribution to fibromyalgia diagnostics by demonstrating the potential of using exhaled VOCs as biomarkers, representing a significant step towards developing an easy-to-apply, objective tool for FM diagnosis, paving the way for more efficient healthcare solutions in managing this condition.

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Effect of chemically synthesized psilocybin and psychedelic mushroom extract on molecular and metabolic profiles in mouse brain

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Background: Anecdotal reports and limited rodent studies suggest that psychedelic effects of full spectrum, psilocybin-containing, psychedelic mushroom extract (PME) differ from those of synthesized psilocybin (PSIL) in nature and intensity. We compared the effect of PSIL to that of PME on head twitch response (HTR), neuroplasticity-related synaptic proteins and metabolomic signature profiling in male C57Bl/6j mice.

Methods: PSIL (Usona 98.75% purity) and PME (ParowBio, Psilocybe cubensis methanol extraction, psilocybin 1.5%) doses were calculated so that equal injection volumes of PSIL and PME contained equal concentrations of psilocybin. HTR was measured in a magnetometer-based system using ear-clip magnets. 11 days after treatment, dissected brain specimens (frontal cortex, hippocampus, amygdala, striatum) were frozen at -80˚C. Synaptophysin, GAP43, SV2A and PSD95 levels were measured by Western blots. Metabolomic analyses were performed on frontal cortex of 5 mice from each treatment group by the omega scan polar method.

Results: PME induced a slightly greater, not significantly different number of HTR's than PSIL. WB assays revealed a significant increase in each of the 4 proteins over all brain areas studied for PME versus vehicle control, while significant PSIL effects were observed only in the hippocampus and amygdala and were limited to PSD95 and SV2A. Metabolomics analyses revealed complete separation between PME and VEH groups, and PSIL having shared area associated with both groups. The purines guanosine, hypoxanthine and inosine, showed a progressive decline from VEH to PSIL to PME

Conclusions: Our findings suggest a potent effect of PME compared to synthetic psilocybin, particularly longer-term effects on synaptic proteins and by implication synaptogenesis. Our preliminary metabolomics data support a gradient of effects from inert vehicle via chemical psilocybin to PME and a greater intensity of processes associated with synaptogenesis in the brains of mice treated with PME.

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The influence of psychosocial stress on Sense of Agency across the psychosis continuum

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Background: Impaired Sense of Agency (SoA) is observed across the psychosis continuum, impacting the control and recognition of one's actions. Although tasks assessing SoA have moderately improved early psychosis identification, we propose enhancing this process by introducing psychosocial stress, akin to stress tests in general medicine. In the pre-registered 'Stress-sensitive Self' (https://osf.io/ubjeq), we examined the impact of psychosocial stress on SoA across the psychosis continuum.
Methods: To ecologically examine SoA, we designed the 'Virtual Hand' (VH) task in immersive virtual reality. In the task, participants assessed whether the VH's movement matched their actual movement. The task was conducted under neutral or stress conditions. A structured interview for psychosis-risk syndromes (SIPS) and a self-disturbance examination (EASE) were used to assess psychosis proneness. The study included three groups: at-risk for psychosis (CHR; N = 13), non-psychotic psychopathology (N = 29), and healthy controls (N = 47).
Results: Contrary to our expectations no significant correlation was found between SoA and psychosis proneness (r = .10, p = .35) or self-disturbances (r = .05, p = .9). Likewise, no significant differences were observed between groups in SoA (F(2,82) < 1, p = .78) and metacognition (F(2,82) = 1.3, p = .28). (2) Stress induced a significant change in participant criteria (t(82) = 3.2, p = .002, Cohen's d = 0.35), resulting in decreased self-attribution of actions. Yet there were no significant differences between groups in their criteria shift (F(2,82) = 1.4, p = .25).
Discussion: Unexpectedly, our findings challenge previous links between psychosis and self-cognition impairments, suggesting a more complex relation that may have been under-reported in the literature. The low number of CHR individuals in the sample and ongoing data collection on conversion to full-blown psychosis warrant cautious interpretation of these results.

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Resting Heart Rate Variability (HRV) is associated with levels of anxiety during war related stress

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Heart rate variability (HRV) measures the variation in time intervals between consecutive heartbeats. Higher HRV is associated with improved adaptive responses, while lower HRV may reflect a reduced ability to adjust to environmental changes (Heiss et al., 2021; Thayer & Lane, 2000). Although HRV has been extensively studied in laboratory settings, its implications during real-life stress events remain unexplored. Heart rates at rest and self-reported anxiety were assessed for 27 adults (M^{age}=27.48, SD=3.17) and 46 adolescents (M^{age}=14.88, SD=1.54) at T0. Approximately two years after initial assessments (T1), participants were surveyed online for stress and anxiety following the October 7th terror attack and the onset of the Israel-Hamas war. Based on the median root mean square of successive differences (RMSSD), a time-domain HRV metric, participants were categorized into groups with high and low resting HRV. Results indicated a two-way interaction between assessment time (T0, T1) and HRV group (High, Low) on anxiety as measured by the Screen for Child/Adults Anxiety Related Emotional Disorder (SCARED/SCAARED), F (1,78) = 4.348, p =.04. During the initial lab visit, participants in the lower HRV group reported elevated levels of anxiety (M=28.90, SD=13.23) compared to those in the higher HRV group (M=20.06, SD= 12.47); *t*(78)=3.070, p=.003. Moreover, participants in the higher HRV group exhibited an increase in anxiety levels between the two measurement time points (M=26.32, SD=15.49); *t*(39)=2.802, p=.008. Notably, the lower HRV group did not demonstrate a significant change in anxiety levels between the two time points. These results suggest HRV as a potential indicator of adaptive response to real-life situational demands, with lower HRV potentially indicating less capacity for environmental adjustment.

Measuring anxiety-like behavior in a mouse model of mTBI: assessment in standard and home cage assays

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Traumatic brain injury (TBI) is a primary global health concern and one of the most common causes of neurological impairments in people under 50. Mild TBI (mTBI) accounts for the majority of TBI cases. Anxiety is the most common complaint after mTBI in humans. This study aims to evaluate behavioral tests designed to assess anxiety-like phenotypes in a mice model of mTBI. ICR mice underwent mTBI using the weight-drop model. Seven days post-injury, mice were subjected to one of five different behavioral tests: Elevated Plus Maze (EPM), Open Field apparatus (OF), Marble Burying test (MBT), Light Dark Box (LDB), and the Light Spot test within the PhenoTyper home cage (LS). In the EPM and OF tests, there were no significant differences between the groups. During the 30-min test period of the MBT, mTBI mice buried significantly more marbles than control mice. In the LDB, mTBI mice spent significantly less time on the far side of the arena than control mice. In addition, the time it took for mTBI mice to get to the far side of the arena was significantly longer compared to controls. Results of LS show significant within-group mean differences for total distance traveled for mTBI mice but not for the control. Furthermore, injured mice moved significantly more than control mice. Accordingto the results, the anxiety traits exhibited by mTBI mice depend upon the time of exposure to the aversive stimulus, the apparatus, and the properties of the stressors used. Therefore, the characterization of anxiety-like behavior in mTBI mice is more complicated than was initially suggested. Based on our findings, we recommend incorporating a variety of stressors and test session lengths when assessing anxiety-like behavior in experimental models of mTBI.

Mindful Self-Compassion (MSC) intervention program for mental health professionals: Preliminary evidence for effectiveness

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Background: Self-compassion involves kindness toward oneself, mindfulness, and a sense of common humanity. Interventions such as the Mindful Self-Compassion (MSC) program have been developed to cultivate self-compassion and have been found effective in enhancing mental resilience in civilians as well as among general healthcare workers. Mental health professionals such as doctors, nurses, psychologists, and social workers are particularly vulnerable to stress and burnout due to the emotional demands of their work. This study aims to assess, for the first time, the effectiveness of mindfulness self-compassion training in improving well-being, reducing stress, and preventing burnout among mental health professionals.

Methods: Participants were recruited from the staff members at the Child and Adolescent Mental Health Center, Ziv Medical Center and were divided into four groups with 15-20 participants in each group. Three of the groups received the 8-session long MSC intervention consecutively, while the fourth group served as the control group. A battery of questionnaires was used to assess participants' well-being, stress, and burnout before the intervention, midway through the intervention, upon completion of the intervention and three months later.

Results: Mental health professionals that underwent the MSC intervention program exhibited a stronger increase in their self-compassion levels compared to the control group. The increase in self-compassion was related to a decrease in difficulties emotion regulation, burnout, and stress.

Conclusions: This study sheds light on the potential effectiveness of the MSC intervention program in mental health professionals, including enhanced self-compassion and decreased in difficulties emotion regulation, burnout, and stress. The positive impact of MSC training implies its potential for wider adoption in diverse healthcare settings, offering potential benefits to both mental health professionals and patients. Ongoing analysis are assessing whether this training program also boosted participants' resilience in the face of the October 7th terror attack.

Resting-state connectivity in healthy community-dwelling adults: a repeated measures EEG study

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Brain activity is organized by functional networks, defined by their spatiotemporal configuration and functional roles. Importantly, most studies on resting-state connectivity used functional-Magnetic-Resonance-Imaging (fMRI) and little is known about the stability of these networks over weeks/months. Using fMRI it was shown that age affected connectivity with increased between- and decreased within-network-connectivity (WNC) in older compared to younger adults. fMRI is costly and not highly accessible, hampering the ecological validity of these findings and calling for the development of additional tools to explore resting-state connectivity. Electroencephalography (EEG) offers one possible solution with recent developments enabling to yield spatial patterns consistent with neural-network organization as revealed by fMRI.

Here, we examined EEG resting-state network stability over weeks/months and age-related differences in WNC using a repeated-measures design. Following previous work in fMRI, we hypothesized that: 1) network stability will differ between top-down and primary processing systems; 2) compared to younger adults, older adults will show decreased WNC.

Forty-four healthy volunteers (25 women mean-age= 47±14.1), participated in this study at Stanford University. Each participant completed 6 sessions, once every two weeks. Recordings consisted of two resting-state measurements (eyes close/open), using a 128-channel EGI system. Data were cleaned and analyzed using EEGLab-toolbox following a previously published protocol. Network stability was calculated by intra-class-correlation, age-related trajectories were computed using correlations.

As expected, WNC decreased with age. Furthermore, we found differences in network stability over time with ventral and dorsal attention networks showing higher stability compared to the visual network. These results highlight the crucial role of repeated measurements in neuroscience and underscore the importance of insights about local information processing during aging.

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Case Study: The relation between emotional verbal expressions to postpartum psychiatric disorders in High-Risk hospitalized pregnant women

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Introduction: The postpartum period can be a time of vulnerability for some women[1]: Around 1.5%-6% are diagnosed with Postpartum Post-Traumatic Stress Disorder (PP-PTSD), and 10%-15% are diagnosed with Postpartum Depression (PPD) [2]. A higher prevalence of PPD is found in High-Risk pregnancies: 17.5% of women[3]. The current study examined whether emotional verbal expressions during pregnancy can predict the emergence of these psychiatric disorders.

Method: Emotional verbal expressions of 14 hospitalized women with High-Risk pregnancies were collected during the third trimester while they performed a battery consisting of 2 questionnaires (IU, STAI) and 3 cognitive tasks (2 attention-tasks, 1 interpretation-task). Two months after birth they completed 3 more questionnaires (EPDS, PCL, MAI). The texts were divided to themes and analyzed with the quantitative data of the study.

Results: The most common themes were related to identity and autobiography (50%), and stressed expressions that were in conflict with not so stressed expressions (28.6%). The relation between performance and the collected expressions in the questionnaires ("open" assignments) was contradictory and elicited fewer verbal expressions in comparison to the interpretation task where the relation was consistent, and the participants were more expressive. Participants who expressed themes related to disengagement and to difficulty with handling uncertainty scored the highest in the PP-PTSD and PPD questionnaires compared to those who didn't apply to these themes.

Discussion: This innovative study emphasizes the importance of speech analysis to the understanding of PPD and PP-PTSD underlying mechanisms and predictive factors. Deep examination of patients' narratives, that includes the combination of quantitive and qualitative data during the pregnancy's early stages, offers insights that can assist with accurate treatment, early identification, and prevention of postpartum psychiatric disorders.

Socio-Demographic predictors of hospitalization among patients with Borderline Personality Disorder

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Borderline Personality Disorder (BPD) is a complex psychopathology associated with high service utilization rates. In turn, the hospitalization of BPD patients is a controversial challenge for mental health professionals. Prior literature has identified certain socio-demographic factors as linked to an increased risk of BPD. In this study, we examined the possible connection between these socio-demographic factors and hospitalization duration. We analyzed 1077 hospitalization records of 200 BPD-diagnosed patients. Patients' gender, age, education level, employment and marital statuses, and living arrangement were statistically significantly linked with hospitalization duration. Specifically, female gender, age twenty or below, no high-school diploma (or, to a lesser extent, a diploma with no academic education), unemployment status and/or patients who live with parents are strongly associated with longer hospitalizations compared to male gender, older patients, more educated, married/divorced status and/or those who do not live with their parents. Additionally, the results point to a weak, albeit statistically significant, temporal pattern with more advanced hospitalizations generally aligning with the duration of their preceding ones, while being slightly shorter. In order to prevent potentially unnecessary prolonged and regressive hospitalizations, an estimation of the expected hospitalization duration should be explicitly considered when setting hospitalization goals and plans.

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Non-coding RNA changes in adolescent stress-exposed female rats and their offspring

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Objectives: Pre-reproductive stress (PRS) affects behavior, mRNA and microRNA expression in adolescent female rats and their offspring. Transfer RNAs (tRNAs), small non-coding RNAs consisting of 70-90 nucleotides, play a role in regulating adult brain function and behavior. Here, we asked whether PRS impacts the expression of tRNAs and its fragments (tRFs) in the prefrontal cortex (PFC) and blood of rats and their offspring, and explored their presence in the female germline.

Methods: Adolescent female rats underwent chronic mild stress, and PFC, blood, and oocytes were extracted at 4 days and 2 weeks later. PFC and blood were also collected from neonate offspring. tRNA, tRFs and miRNA levels were measured using YAMAT-seq and sncRNA-seq, and by RT-PCR.

Results: We found differences in the levels of tRNA isodecoders and tRFs in PFC at both time-points. Furthermore, PRS exposure altered miRNAs, but not tRFs profiles in blood and oocytes. Interestingly, PRS had no effect on the expression of isodecoders, but did affect miRNAs and tRFs expression, in offspring PFC.

Conclusions: Combined with our previous findings, these data raise the possibility that changes in non-coding RNA profiles act in concert with psychosocial mechanisms to mediate transgenerational transfer of stress effects.

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Complications of community-acquired pneumonia in Schizophrenia patients in a general hospital

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Background: Community-acquired pneumonia (CAP) is a high mortality disease. Schizophrenic patients have significantly higher mortality than the general population from pneumonia. So far, the complications and course of pneumonia in schizophrenia patients, hospitalized in general hospitals, have not been studied.
Hypotheses: Schizophrenia patients suffer from severe pneumonia at admission and develop more complications during hospitalization, compared to non-psychiatric patients.
Methods: A retrospective cohort study utilizing electronic medical records (EMR) from the departments of Internal medicine at a single medical center during 2013-2021. The study included 314 CAP patients and compared the 66 Schizophrenia patients with CAP (SPCAP) with 248 gender-and-age propensity score matched non-psychiatric CAP patients (NPCAPP). Pneumonia severity was assessed according to the CURB-65 score. Hospitalization complications were determined according to the following conditions: invasive ventilation, empyema, successive need of oxygen support, and 30-day mortality.
Results: The study population mean age was 67 (standard deviation 14) and ranges 27-95, with 39% females. Overall, the SPCAP and NPCAPP groups had similar age and gender distribution (P=0.7832 and P=0.7631). However, the study groups significantly differed in some other demographic backgrounds (marital status and number of children) as well as with some background diseases (CHF and arrhythmia) and severe Pneumonia (i.e., CURB-65≥2). After adjusting for these potential confounders, it was found that for SPCAP the odds for ventilation are 2.8 [95%CI: 1.4-5.6] times higher compared with SCAPP. For severe Pneumonia, after adjusting for the potential confounders, the result was borderline insignificant (adjusted Odds ratio = 1.73 [95%CI: 0.91-3.3]; P=0.0928). No association was found between the study groups and the rest of the outcomes.
Conclusions: Even though there was no significant difference in pneumonia severity between SPCAP and NPCAPP, the SPCAP required more ventilation support. Further studies are needed to establish preventive strategies to reduce pneumonia-related complications and death among schizophrenia patients.

Iron Chelation: a Novel Mechanistic Approach Targeting Drug-induced Psychosis

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This study explores the potential of deferiprone, an oral iron chelator, as a novel therapeutic approach in treating schizophrenia (SCZ) and acute psychosis. Schizophrenia and psychosis are complex heterogenous psychiatric disorders with significant personal, social, and healthcare implications. Traditional antipsychotic treatments primarily target dopamine and serotonin receptors to mitigate symptoms without addressing the underlying causes of neurotransmitter abnormalities. This research centers on the hypothesis that the oral iron chelator deferiprone (DFP) can modulate the synthesis of dopamine, serotonin, and glutamate by reducing the availability of iron required for iron-dependent enzymes involved in their production pathways. The principle findings of the study were that DFP rescued multiple psychosis-like phenotypes in 5 animal models. Specifically, DFP suppresses amphetamine-induced hyperlocomotion and stereotactic circling in 2 mouse strains. DFP attenuates ketamine-induced hyperlocomotion and circling in both strains as well. The addition of DFP to the antipsychotic Haldol doubles its therapeutic effect in the ketamine model. DFP is effective regardless of presence of elevated total brain iron. DFP attenuates head twitch response induced by 5-HTP. DFP rescues elevated metabolites in several relevant pathways, specifically the dopamine pathway. DFP does not bind to dopamine receptors or transporter or to Serotonin receptor 5HT2A. Unlike antipsychotics, deferiprone does not massively elevate serum prolactin. Pharmacological, biochemical, metabolomic, and electrochemical methods were used to repeatedly prove that the mechanism of this rescue is distinct from antipsychotics and not mediated by interference of post-synaptic signaling, but rather on upstream presynaptic pathways. The behavioral data was corroborated by complex metabolomics analysis using UHPLC-MS and DESI-MS as well as brain slice electrophysiology to further understand how DFP affects the kinetics of neurotransmission and demonstrate that the mechanism of DFP rescue is distinct from antipsychotics and not mediated by interference of post-synaptic signaling, but rather on upstream presynaptic pathways.