the base of each sulcal basin and aligned along the bottom sulcal lines [1]. Sulcal pits begin to form prenatally, alongside the first cortical folds, and expand throughout gestation and early childhood remaining stable across lifespan. Their consistency across individuals makes them highly reproducible and supports their potential as reliable markers of early neurodevelopmental processes [1].
Neurodevelopmental disorders such as autism, bipolar disorder, and schizophrenia have been associated with quantitative variations in sulcal pits [2–4]. However, the geometrical patterns of sulcal pits in these disorders remain underexplored. In this study, from a sex specific approach, we aimed: i) to investigate the sulcal patterns in schizophrenia patients in comparison with healthy controls (HC); and ii) to explore the association of the sulcal patterns with clinical symptoms.
Methods: The sample comprised 189 HC and 237 age-matched schizophrenia patients with T1-weighted MRIs. Sulcal pits were identified from white matter surfaces generated by FreeSurfer. Graphs were created for each hemisphere and lobe, treating sulcal pits as nodes and their connections as edges, and were compared based on area, sulcal pit depth, sulcal pit position, graph topology, and all previous combined features (global pattern) [5]. Similarity scores were calculated for each individual and between-group comparisons conducted. On those regions in which the sulcal pattern of patients was significantly different from that of HC, the correlation between the similarity scores of patients and the scale of Positive and Negative symptoms (PANSS) was tested.
Results: In males, patients with schizophrenia displayed a global differential sulcal pits pattern in the left frontal lobe compared to HC ($t = 4.22$; $p_{FDR} = 0.001$; $d = -0.54$). Furthermore, the similarity scores of SZ patients in this region were negatively associated with the general psychopathology subscale of PANSS ($p_{nom} = 0.017$; $r = -0.19$), remaining marginally significant after multiple comparisons correction ($p_{FDR} = 0.052$).
In females, patients with schizophrenia showed differences in the graph topology of the sulcal pits pattern in the right parietal lobe compared to HC ($t = 3.92$; $p_{FDR} = 0.006$; $d = -0.63$). In this case, no association with clinical symptoms was detected.
Conclusions: This study reveals sex-specific sulcal alterations in schizophrenia, with males showing differences in the global pattern of the left frontal lobe (including all the features such as depth, position, area and graph topology). On the other hand, females presented differences restricted to the graph topology of the right parietal lobe. Also, these patterns suggested a distinct association with symptomatology indicating a relationship of sulcal pits patterns with clinical severity only in males.
The results underscore the role of sulcal pits and their geometrical patterns as potential neurodevelopmental markers for schizophrenia, linking sex-specific processes related to cortical folding and sulcal organisation to the psychopathology of the disorder.
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WHY DO PSYCHOSIS PATIENTS DISCONTINUE THEIR ANTIPSYCHOTICS? USING AI TO UNRAVEL THE ROLES OF EFFICACY AND SIDE EFFECTS.

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Although most people with First Episode Psychosis show some improvement after their first antipsychotic treatment, 73-77% discontinue their first antipsychotic [1]. This discontinuation is associated with more frequent and longer psychiatric admissions [2]. Two key reasons that patients discontinue their medication are lack of efficacy or intolerable side effects [3]. Although several factors have been found to be associated with time to treatment discontinuation [4], it is not yet possible to determine which patients are at the greatest risk of discontinuing their treatment. It would be beneficial to predict the likelihood of a patient discontinuing their antipsychotic medication prior to treatment onset to guide clinical decision-making and find the most appropriate treatment. Artificial intelligence methodologies have the potential to solve this problem by finding multivariate patterns in data collected pre-treatment that can predict treatment discontinuation at the individual level. The aim of this research is to develop AI-based prediction tools for treatment discontinuation. We will first predict all-cause discontinuation and then see whether this prediction can be improved by separating the two groups into discontinuation due to tolerability and discontinuation due to efficacy.
The sample consists of 364 individuals with a diagnosis of a psychotic disorder for up to 7 years from the European Long-acting Antipsychotics in Schizophrenia Trial (EULAST) [5]. Participants in this trial were randomised to either long-acting injectable (LAI) paliperidone, LAI aripiprazole, or the respective oral formulations of these antipsychotics and were followed up for 18 months. We trained support vector machine learning models within a 10-by-10 repeated nested cross-validation on the whole sample using psychopathology, socio-demographic, education and employment, and substance use data. The chosen outcomes were all-cause discontinuation, symptomatic remission at one month after baseline measured by the Positive and Negative Syndrome Scale PANSS) as a proxy for discontinuation for efficacy reasons, and movement side effects at once month after baseline measured by the Abnormal Involuntary Movement Scale (AIMS) as a proxy for discontinuation for tolerability reasons. Model performances were given in Balanced Accuracy (BAC). We covaried for inpatient status as baseline because patients in hospitals would receive very different treatment to outpatient care.
The rate of all-cause discontinuation was 54.3% in our sample: this outcome was poorly predicted (BAC=52.2%). Symptomatic remission was successfully predicted with a much higher performance with a BAC of 67%. Movement side effects were predicted poorly by the clinical data with a BAC of 55.4%. Here we present the first evidence that all-cause discontinuation is a poor label for prediction modelling, and that this may represent too broad of an outcome for accurate prediction. This is supported by the fact that symptomatic remission can be well predicted in the same sample. Further analyses will investigate whether blood biomarkers will improve prediction, whether metabolic side effects can be predicted, and how treatment modifies model performance.
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P66SHC GENE KNOCK-OUT PROTECTS FROM LONG-TERM METABOLIC AND EMOTIONAL DERANGEMENTS INDUCED BY MATERNAL OBESITY IN MICE

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The p66Shc gene encodes for a mitochondrial protein that, by increasing oxidative stress (OS), accelerates aging by favouring fat deposition and fat-related disorders [1,2]. Maternal obesity has been shown to derange foetal developmental programming by increasing inflammation and OS in the womb, setting the stage for adverse health outcomes during aging [3,4]. In this study we hypothesized that reduced levels of OS, characterising p66Shc-/- knock-out (KO) mice might protect the offspring from the long-term negative effects of a maternal high-fat diet (mHFD), especially during aging.
To induce maternal obesity, wild-type (WT) and KO female mice were fed a HFD starting 10 weeks before breeding, until delivery. The metabolic, emotional and cognitive profiles were assessed in 18-months-old male (M) and female (F) offspring. In particular, the animals underwent: a) a glucose tolerance test (GTT); b) the elevated plus-maze (EPM) test and c) the novel object recognition (NOR) test. A three-way ANOVA was used with sex, genotype and diet as between- and time as within-subjects' factors when appropriate. Regression analysis was used to evaluate the association between cognitive performances and hippocampal levels of brain-derived neurotrophic factor (BDNF), a neurotrophin involved in brain plasticity and emotional as well as metabolic regulation.
Results indicate a clear negative effect of mHFD on the metabolic and emotional phenotype that was prevented by p66Shc deletion. KO mice were overall protected from age-related cognitive decline. In detail, following the GTT, mHFD resulted in a greater peak in glycaemia levels in WT-F while the deletion of the p66Shc gene prevented this effect (F-KO-HFD vs. F-WT-HFD: p=0.0208). As far as the emotional profile is concerned, males spent more time in the open arms of the EPM (M vs. F: p=0.0005), a result that might indicate a reduced ability to perceive the anxiogenic EPM context. Interestingly, in all subjects mHFD reduced exploration and increased self-grooming while the KO condition counteracted such effects (WT-HFD vs. WT-CD and KO-HFD: p=0.0122 for head-dipping and p=0.0224 for grooming frequency). When tested in the NOR, KO mice showed a reduced latency to touch the novel object (KO vs. WT: p=0.0002) and a higher recognition index (RI%; KO vs. WT: p=0.0133) suggesting that a reduced exposure to OS throughout life may be protective for aging-related cognitive decline. Hippocampal levels of BDNF were higher in all females (F vs. M: p=0.0397) and were positively related with the NOR-RI% (F: R^2=0.5688, p=0.0029; M: R^2=0.0567, p=0.5073), possibly indicating a protective effect of this neurotrophin specifically in females. Our results suggest that mHFD interferes negatively with the foetal developmental programming, affecting the aging process, leading to altered metabolic and emotional profile of the aged offspring in a sex-dependent fashion. Deletion of the p66Shc gene, by reducing OS, protects the offspring from early life metabolic insults, leading to a healthier phenotype during aging. Overall, these data strengthen the notion that OS is a key mechanism involved in the embedding of maternal obesity in long-term health outcomes in the offspring.
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EMOTIONAL DYSREGULATION IN ADHD: PRELIMINARY INSIGHTS INTO INTERNALIZING SYMPTOMS, PARENTAL FACTORS, AND EMBODIMENT

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Introduction: Emotional dysregulation (ED) is a central aspect of ADHD in adolescents, contributing to emotional, social, and academic challenges alongside core symptoms such as inattention and hyperactivity. This study aims to investigate the determinants of ED in ADHD with a focus on parental resilience and emotional regulation, adolescent emotional embodiment and resilience, in addition to the internalizing symptoms.
Methods: Forty-eight adolescents aged 11-18 diagnosed with ADHD based on DSM-5 criteria were evaluated. Emotional dysregulation was measured using the Difficulties in Emotion Regulation Scale (DERS). ADHD core symptoms (inattention, hyperactivity, and impulsivity) were assessed using the DSM-5-based ADHD Symptom Checklist.Internalizing symptoms were assessed using the Revised Child Anxiety and Depression Scale (RCADS). Resilience was measured via the Connor-Davidson Resilience Scale (CD-RISC). Parents also filled DERS and CD-RISC for themselves.
Participants utilized the Turkish version of EMBODY, a MATLAB-based computer tool designed to generate somatic body maps (SBM) of emotions. They identified body regions where emotions were experienced by marking "activated" (red) and "deactivated" (blue) areas on body images. The maps were analyzed based on pixel count and intensity for a range of emotional states, including negative emotions (anger, fear, disgust, sadness, anxiety, depression, contempt, shame, envy) and positive emotions (happiness, pride, surprise). Additionally, participants mapped bodily responses to stress-inducing scenarios (fight, exam, bullying, homework) and relaxation states (break, game).
Results: No significant relationships were found between adolescents' DERS scores and the severity of ADHD core symptoms, nor between parental resilience and emotional regulation. Significant correlations were found between DERS total and RCADS total scores ($r = 0.634$, $p < 0.001$), indicating a strong association between emotional dysregulation and internalizing symptoms.
In terms of SBM correlations with DERS, the word 'depression' showed the strongest correlation for "activated" red pixels ($r = 0.311$, $p = 0.031$) and for total pixel count ($r = 0.413$, $p = 0.004$). Words such as defeat ($r = 0.335$, $p = 0.020$) and shame ($r = 0.339$, $p = 0.019$) showed trends toward significance. Both