biomarkers are investigated with a meta-research approach, by providing a critical appraisal of the terms and definitions of mental pain, the studies' hypotheses, the experimental paradigms used to induce or mimic mental pain and the measurement instruments used to measure mental pain.
Methods: We conducted a systematic review (compliant with PRISMA guidelines) of all primary research reporting to investigate candidate biomarkers of mental pain in human subjects as stated by the authors. We searched from inception to June 23rd, 2022, the 3 databases MEDLINE, Web of Science and EMBASE. We extracted the study characteristics (e.g., year of publication, population, etc.), the terms used for meaning mental pain, the definition of mental pain, the method to induce mental pain and its rational, the hypotheses and aims, the measurement instruments of mental pain, the candidate biomarkers, and their method of investigation. We performed descriptive statistics of the sample's characteristics and the extracted data, a qualitative analysis of the definitions, hypothesis, aims and experimental paradigms, and a data visualization linking candidate biomarkers, experimental paradigms, and their investigation methods.
Results: The search retrieved 5685 papers of which we included 72 primary research publications constituting 78 distinct research studies. Only 37.5% of studies reported a definition of mental pain. 11.5% of studies did not show a measurement instrument of mental pain. The Cyberball (a social exclusion paradigm) was the most frequently used paradigm in experimental studies (62.7%). The cingulate cortex was the most frequently investigated biomarker category (15.3% of all candidate biomarkers), with fMRI as the most frequent investigation method (53.7% of all investigation methods).
Conclusions: The field of biological investigations on mental pain shows a marked heterogeneity of definitions, terms, hypotheses, experimental paradigms, and measurement instruments, with an over-representation of the construct of social pain and the Cyberball. These could compromise the comparison and combination of studies results in evidence synthesis and their translation into clinical practice.

Disclosure of Interest: None Declared

Neuroimaging

EPP0421

Exploring Associations between Grey Matter Volume and Clinical High-Risk for Psychosis: A Transdiagnostic Study Utilizing the NAPLS-2 Risk Calculator in the PRONIA Cohort

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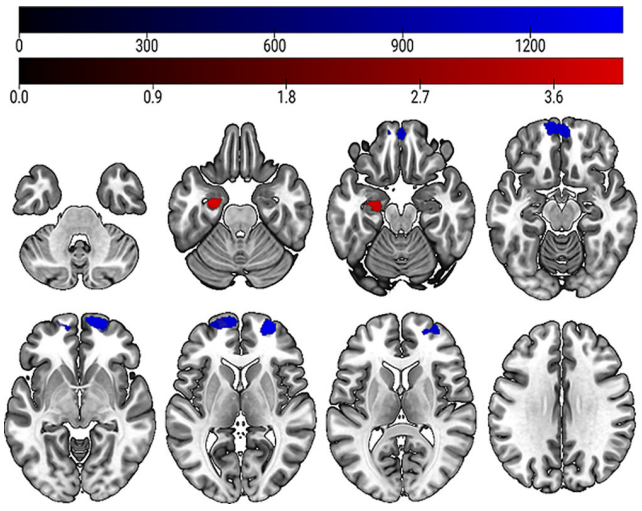
Introduction: The clinical high-risk state for psychosis (CHR) is associated with alterations in grey matter volume (GMV) in various regions such as the hippocampus (Vissink *et al.* BP:GOS 2022; 2(2) 147-152). Within the scope of the North American Prodrome Longitudinal Study (NAPLS-2; Cannon *et al.* AM J Psychiatry 2016; 173(10), 980-988), a publicly available risk calculator based on clinical variables was developed to assess the likelihood of individuals to transition to psychosis within a 2-year period.
Objectives: In the current study, we aim to examine the association between GMV and NAPLS-2 risk scores calculated for individuals with CHR and recent-onset depression (ROD), taking a transdiagnostic approach on the transition to psychosis.
Methods: The sample consisted of 315 CHR (M = 23.85, SD = ± 5.64; female: 164) and 295 ROD (M = 25.11, SD = ± 6.21; female: 144) patients from the multi-site Personalised Prognostic Tools for Early Psychosis Management (PRONIA) Study (Koutsouleris *et al.* JAMA Psychiatry 2018; 57(11), 1156-1172). Risk scores were calculated using the six clinical and neurocognitive variables included in the NAPLS-2 risk calculator that were significant for predicting psychosis. Further, we derived smoothed GMV maps from T1-weighted structural magnetic resonance imaging using a full width at half maximum kernel size of 8 mm. We employed a multiple regression design in SPM12 to examine associations between risk scores and GMV. On the whole-brain level, we calculated permutation-based threshold-free cluster enhancement (TFCE) contrasts using the TFCE toolbox. Additionally, we calculated t-contrasts within a region-of-interest (ROI) analysis encompassing the hippocampus. All results were thresholded at $p < 0.05$ with family wise error correction to address multiple comparisons.
Results: Our analysis revealed that linear GMV increases in the right middle and superior frontal gyrus (k_E= 2726 voxels) were significantly associated with higher risk for psychosis transition within two years (see figure 1, highlighted in blue). In the ROI analysis, we found a significant negative linear association between GMV decreases in the left hippocampus (k_E = 353 voxels) and higher risk for psychosis transition (see figure 1, highlighted in red).

Image:



Conclusions: GMV reductions in the hippocampus have frequently been observed in CHR and psychosis patients (Vissink *et al.* BP:GOS 2022; 2(2) 147-152), therefore our results further highlight the crucial role of this region in the progression of the disease. There is limited evidence on GMV increases in CHR patients. However, the GMV increase we found in the frontal pole may reflect compensatory mechanisms of the brain in the development of psychosis. In addition, we were able to provide biological validation of the NAPLS-2 risk calculator and its assessment of risk for transition to psychosis.

Disclosure of Interest: None Declared

EPP0422

Multivariate associations between psychiatric drug intake and grey matter volume changes in individuals at early stages of psychosis and depression

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Introduction: Psychiatric drugs, including antipsychotics and antidepressants, are widely prescribed, even in young and adolescent populations at early or subthreshold disease stages. However, their impact on brain structure remains elusive. Elucidating the relationship between psychotropic medication and structural brain changes could enhance the understanding of the potential benefits and risks associated with such treatment.
Objectives: Investigation of the associations between psychiatric drug intake and longitudinal grey matter volume (GMV) changes in a transdiagnostic sample of young individuals at early stages of psychosis or depression using an unbiased data-driven approach.
Methods: The study sample comprised 247 participants (mean [SD] age = 25.06 [6.13] years, 50.61% male), consisting of young, minimally medicated individuals at clinical high-risk states for psychosis, individuals with recent-onset depression or psychosis, and healthy control individuals. Structural magnetic resonance imaging was used to obtain whole-brain voxel-wise GMV for all participants at two timepoints (mean [SD] time between scans = 11.15 [4.93] months). The multivariate sparse partial least squares (SPLS) algorithm (Monteiro *et al.* JNMEDT 2016; 271:182-194) was embedded in a nested cross-validation framework to identify parsimonious associations between the cumulative intake of psychiatric drugs, including commonly prescribed antipsychotics and antidepressants, and change in GMV between both timepoints, while additionally factoring in age, sex, and diagnosis. Furthermore, we correlated the retrieved SPLS results to personality domains (NEO-FFI) and childhood trauma (CTQ).
Results: SPLS analysis revealed significant associations between the antipsychotic classes of benzamides, butyrophenones and thioxanthenes and longitudinal GMV decreases in cortical regions including the insula, posterior superior temporal sulcus as well as cingulate, postcentral, precentral, orbital and frontal gyri (Figure 1A-C). These brain regions corresponded most closely to the dorsal and ventral attention, somatomotor, salience and default network (Figure 1D). Furthermore, the medication signature was negatively associated with the personality domains extraversion, agreeableness and conscientiousness and positively associated with the CTQ domains emotional and physical neglect.