are related to brain structure in schizophrenia and healthy controls in Latin America, where these factors are large and unequally distributed.
Methods: This is an MRI multi-center study in patients with schizophrenia and healthy controls from six Latin American cities: Buenos Aires, Medellin, Mexico City, Santiago, Sao Paulo and Porto Alegre. Total and voxel-level gray matter volumes obtained from T1-weighted MRI images and their relationship with income and homicide rates were analyzed using a general linear model.
Results: 334 patients with schizophrenia and 262 controls were included. Income was differentially related to total gray matter volume in the two groups (P=0.006). Controls showed a positive correlation between total gray matter volume and income (R=0.14, P=0.02). Surprisingly, this relationship was not present in schizophrenia (R=-0.076, P=0.17). Voxel-level analysis confirmed that this interaction was widespread across the cortex. After adjusting for global brain changes, income was positively related to prefrontal cortex volumes only in controls. Conversely, the hippocampus in patients, but not in controls, was relatively larger in affluent environments. There was no significant correlation between environmental violence and brain structure.
Discussion: Our results highlight the interplay between the environment, particularly poverty, and individual characteristics in psychosis. This is particularly important for harsh environments such as those from low and middle-income countries: potentially less brain vulnerability (less gray matter loss) is sufficient to become unwell in adverse (poor) environments. The development of algorithms exploring clinically-useful information from structural brain images in psychosis should include representative samples from low and middle-income countries.

T160. HIGH-RESOLUTION WHOLE BRAIN MR SPECTROSCOPIC IMAGING IN YOUTHS AT CLINICAL HIGH RISK FOR PSYCHOSIS: A PILOT STUDY

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Background: In general, MR spectroscopy (MRS) studies report alterations of both glutamatergic indices and NAA not only in first episode psychosis and established schizophrenia but also in high risk populations, suggesting that altered excitatory neurotransmission and loss of neuronal integrity are early pathophysiological processes. However, interpretation of these findings is limited by the region-of-interest approach of current MRS techniques, limiting the measurement of metabolites to delimited cerebral volumes, selected by a priori hypotheses. In that context, we developed and implemented a new technique including specific MR sequence and data reconstruction that allows for whole brain high-resolution MRS imaging (MRSI) in two or three dimensions. The results enable the mapping of main metabolites in all brain regions (cortex, white matter, deep grey matter) of youths at clinical high risk for psychosis (CHR-P).
Methods: An FID-MRSI (Henning et al. NMR Biomed 2009) sequence with a 3D phase encoding accelerated by compressed-sensing was implemented on a 3T Prisma fit MRI (Siemens, Erlangen, Germany). The echo time (TE) was 0.65 ms, repetition time (TR) was 355 ms and the flip angle 35 degree. FID was acquired with 4 kHz bandwidth. The size of the excited Volume of Interest (VOI) was (A/P-R/L-H/F) 210 mm by 160 mm by 95 mm with a matrix of 42 x 32 x 20 resulting in 5 mm isotropic resolution. After reconstruction (Klauser A et al. Magn Reson Med. 2018), 3D MRSI data were quantified with LCModel to produce 3D metabolite maps. Concentration for total N-acetyl aspartate (tNAA), total creatinine (tCre), choline-containing compounds (Cho), myo-inositol (Ins), glutamate and glutamine (Glx) were calculated in every single voxel. A T1-weighted MPRAGE anatomical scan was acquired for positioning of the 3D MRSI and for the segmentation of the brain. For each participant, brain tissue was segmented into gray and white matter. Cerebral lobes and deep grey mater structures were also delineated using Freesurfer software package.
CHR-P individuals were recruited in the service of child and adolescent psychiatry and in the service of general psychiatry, department of psychiatry at Lausanne university hospital. They were help-seeking adolescents and young adults aged between 14 and 35, who presented a psychosis-risk syndrome or basic symptoms as assessed by the Structured Interview for Psychosis-Risk Syndromes (SIPS) and the Schizophrenia Proneness Instrument, Adult (SPI-A) or Child & Youth version (SPI-CY). Healthy controls matched for age and sex were recruited in the general population.
Results: Three-dimension MRSI provides spatial specificity by allowing main metabolites (i.e., tNAA, tCre, Cho, Ins and Glx) to be reliably mapped in the volume of the entire brain. The resulting contrast allows the recognition of brain compartments and subcortical structures. Individual brain segments, cerebral lobes and subcortical structures were registered to 3D MRSI data and the mean concentration in each structure was computed to allow group comparisons between CHR-P and HC.
Discussion: In general, there is a strong need to develop new tools for the identification and stratification of CHR-P populations. Alterations of gross brain anatomy are relatively late events but early and subtle neurochemical changes and especially those reflecting oxidative stress and concomitant synaptic remodeling are promising candidates. This pilot study illustrates the potential of three-dimension MRSI to detect such alterations in the whole brain and with a good spatial resolution.

T161. THE RELATIONSHIP BETWEEN FRONTAL CORTICAL VOLUME AND STRIATAL DOPAMINE SYNTHESIS CAPACITY IN PSYCHOSIS

Abstract not included.

T162. THICKER PREFRONTAL CORTEX IS ASSOCIATED WITH SUBCLINICAL NEGATIVE SYMPTOMS IN SCHIZOTYPY - AN ENIGMA CONSORTIUM META-ANALYSIS

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Background: Negative symptoms can be seen to represent a continuum from subclinical manifestations in the general population to severe symptoms in

schizophrenia. Neuroanatomical studies show evidence of fronto-striatal structural abnormalities linked to negative symptoms in patients with schizophrenia (Walton et al. 2018). However, it remains an open question whether these structural associations are also observed in ostensibly healthy individuals reporting subclinical negative symptoms. The present study used structural T1-weighted brain imaging data from the ENIGMA Schizotypy Working Group to investigate the relationship between subclinical negative symptoms and fronto-striatal structural measures.

Methods: We included 2,235 healthy unmedicated individuals with varying levels of schizotypy from 17 centers around the world. The complete sample had a weighted mean (range) age of 29.2 (15.9–39.6) and 59.4% (51–100) were male. Subclinical negative symptoms were assessed at each site separately using factor scores from self-report schizotypy questionnaires (i.e., the Community Assessment of Psychic Experiences, the Oxford-Liverpool Inventory of Feelings and Experiences, or the Schizotypal Personality Questionnaire). Based on prior studies in schizophrenia, we obtained cortical thickness from 22 frontal regions-of-interest (ROIs) and subcortical volumes from 6 striatal ROIs using FreeSurfer. We performed meta-analyses of effect sizes (standardized regression coefficients) from a model predicting mean cortical thickness by subclinical negative symptom scores, adjusting for age, sex, and site. The same analysis was repeated for subcortical volumes including intracranial volume as additional covariate.

Results: Meta-analyses revealed significant positive associations between subclinical negative symptoms and cortical thickness of the left frontal pole (βstd=0.091; pFDR=0.009), right medial orbitofrontal cortex (βstd=0.083; pFDR=0.009) and right anterior cingulate cortex (βstd=0.07; pFDR=0.011).

Discussion: Using a large sample of healthy unmedicated individuals with varying levels of schizotypal personality traits, this ENIGMA meta-analysis showed that subclinical negative symptoms are associated with thicker prefrontal cortex. The present data are contrary to previous findings in schizophrenia, which demonstrates a relationship between negative symptoms and lower prefrontal cortical thickness (Walton et al. 2018). These divergent neural correlates suggest that thicker cortex could be a potential compensatory mechanism preventing individuals with schizotypy from the clinical manifestation of severe negative symptoms. Alternatively, greater prefrontal cortical thickness could also be associated with pathological processes along the negative symptom continuum prior to clinical manifestation.

T163. STRUCTURAL AND CONNECTIVITY CHANGES IN THE CEREBELLUM CONTRIBUTE TO EXPERIENCING AUDITORY VERBAL HALLUCINATIONS

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Background: Auditory verbal hallucinations (AVH) have been explained in the context of the forward model, giving the cerebellum a prominent role. However, research utilizing multiple neuroimaging modalities has rendered results on the specificity of cerebellar contribution to AVH unclear.

Methods: To examine the reliability and regional specificity of cerebellar changes in AVH, a systematic search of electronic databases through October 2019 was conducted to identify neuroimaging studies of the cerebellum in psychotic patients or nonclinical participants reporting AVH, focusing on structural MRI, diffusion tensor imaging, and resting state functional connectivity studies. Twenty-two studies were selected, including 892 participants with AVH (792 psychotic patients; 100 at-risk subjects) and 775 healthy controls. Activation likelihood estimate analysis (ALE) examined the reported coordinates for reduced volume, fractional anisotropy (FA) or connectivity (control participants > participants with AVH) and increased volume, FA or connectivity (participants with AVH > control participants). The consistency of cerebellar changes and their relationship with sociodemographic and clinical measures were meta-analyzed.

Results: The ALE meta-analysis revealed changes in both anterior and posterior cerebellar lobes, with opposite patterns: whereas decreased volume or connectivity was identified in the right anterior cerebellum (lobule IV/V), increased volume or connectivity was identified in the bilateral posterior cerebellum (Crus I and II). A random-effects model with small sample corrections identified consistent changes in both volume and functional connectivity of the cerebellum in participants with AVH (g = .84; SE = .24, 95% CI [.33, 1.34]), which were enhanced in Crus I (g = 1.52, SE = .28, p = .006, 95% CI [.73, 2.31]) but not moderated by age, sex, medication, or illness duration.

Discussion: The ALE meta-analysis confirms cerebellar structural and connectivity changes in psychotic and nonclinical participants reporting AVH. These changes may contribute to AVH due to altered sensory feedback and consequently to erratic prediction as described by the forward model. The current findings also indicate that not all cerebellar regions are equally affected by AVH: the most pronounced changes were observed in Crus I. Specifically, altered communication between Crus I and neocortical network nodes, including the prefrontal cortex, may contribute to ineffective cognitive control in AVH, leading to external misattributions of auditory feedback and a reduced sense of control over events in the environment.

T164. NETWORK CONNECTIVITY SUPPORTING REWARD LEARNING DIFFERENTIALLY DISRUPTED IN TREATMENT RESISTANT SCHIZOPHRENIA

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Background: It is estimated that one third of patients with schizophrenia fail to adequately respond to antipsychotic medication, termed 'treatment-resistance'. This occurs despite adequate blockade of D2 receptors in the brain. The parsimonious options are that treatment resistance could arise through a failure of cognitive control over the dopaminergic dysfunction in the striatum; or has a different primary non-dopaminergic mechanism that isn't targeted by current antipsychotics. Contemporary models suggest that schizophrenia is associated with reduced reward prediction errors (RPE) and consequent aberrant salience driven by increased dopamine levels that 'drown out' phasic signals. This causes positive symptoms and impaired reward learning. However, RPE signalling in treatment-resistant patients appears intact despite sub-optimal behavioural performance. It is therefore unclear how reward learning is impaired in these patients.

Methods: We investigated how reward learning is disrupted at the network level in 21 medicated treatment-responsive and 20 medicated treatment-resistant patients with schizophrenia compared with 24 healthy controls (HC). Participants learnt to associate one of two emotional faces with a reward during a reinforcement learning task in an MRI scanner. Functional MRI BOLD signal was extracted from four brain regions (fusiform cortex, amygdala, caudate and anterior cingulate cortex (ACC)) activated in response to face cues and RPEs. These formed a network of interacting brain regions supporting reward learning. Dynamic Causal Modelling assessed how effective connectivity between regions in this cortico-striatal-limbic network is disrupted in each patient group compared to HC. Connectivity was also examined with respect to symptoms and salience. Finally, cognitive control and the role of glutamate were assessed by relating top-down

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