Background: Most individuals with schizophrenia experience relapse over the course of the illness, yet unfortunately the mechanisms of this phenomenon are poorly understood. This research is often confounded by non-adherence with antipsychotic drugs. We propose to study relapse in individuals treated with long acting injectable antipsychotics (LAIs), for whom treatment adherence is confirmed. Since striatal resting state functional connectivity (RSFC) has been shown to reflect pathophysiological aspects of antipsychotic treatment response, we aim to study striatal RSFC in relapse in individuals treated with LAIs to identify potential mechanisms. In particular, we will compare striatal RSFC between individuals who relapse while treated with LAIs, individuals who are not on LAIs and are non-adherent with antipsychotics at the time of relapse, and healthy controls, to generate a hypothesis about the role of striatal functioning in psychosis relapse.

Methods: Subjects with a psychotic disorder treated with LAI antipsychotics and history of clinical response to that trial confirmed by collateral, presenting with acute psychotic symptoms at the time of the scan (defined as ≥4 in BPRS) in at least one of the psychotic items) (n=16) were compared with subjects also with a psychotic disorder presenting with acute psychotic symptoms who were non-adherent with antipsychotic drugs demonstrated by negative plasma level (n=16), and healthy controls (n=18). Participants were scanned using fMRI and data was pre-processed using the HCP pipeline with the ICA-FIX procedure, removing motion artifacts and nuisance variables. Connectivity maps were generated for 6 bilateral (12 total) striatal regions of interest as in Di Martino et al. 2007, which were compared between groups (cluster threshold p<.05, voxel threshold p<.001 uncorrected). In addition, we calculated striatal connectivity indices (SCI) as in Sarpal et al. 2014, as this metric reflecting RSFC between the striatum and 91 other regions of interest has been shown to have high precision in predicting response to antipsychotics in patients with first episode psychosis.

Results: We found no significant differences in sex or age between any of the 2 patient groups or the healthy controls, nor of psychopathology between the patient groups. For patients treated with LAIs upon relapse, striatal RSFC was significantly lower in an area in posterior cingulate, whereas it was higher in another area in the middle temporal gyrus, inferior temporal gyrus, and precentral gyrus, compared with healthy controls. When the LAI-treated individuals' striatal RSFC was compared with that of individuals who were non-adherent with antipsychotic drugs at the time of relapse, it was significantly higher in the posterior parietal cortex, whereas it was lower in the pulvinar (thalamus) and primary and associative cortex. SCI values for individuals who relapsed despite assured antipsychotic exposure were significantly lower than for non-LAI individuals who had relapsed due to non-adherence (p=0.049), and than healthy controls (p=0.01).

Discussion: Despite a relatively small sample, these results indicate differences in striatal functional connectivity depending on antipsychotic exposure at the time of relapse. The finding of significantly lower SCI values for LAI treated individuals at the time of relapse compared with non-adherent individuals with relapse and healthy controls suggests the hypothesis that relapse occurring despite assured antipsychotic exposure may result from aberrant striatal functional connectivity which is insufficiently engaged by antipsychotic drugs.
Methods: Multicenter (four-site) two-year follow-up case-control brain magnetic resonance imaging study; 74 patients with a FEP of less than 12 months’ duration, and 64 healthy controls (matched for age, sex, parental socioeconomic status and handedness) were scanned twice (median time between baseline and follow-up scan 24 months, range [16 – 32]). We computed percentage changes (PC) over follow-up in thickness/area/ volume for frontal, temporal, parietal and occipital lobes. We included diagnosis (patient vs. control), age at baseline scan, sex, TBV and site as potential confounders. We conducted post-hoc comparisons for young (<19y) and adult (>19y) diagnostic pairs (FEP vs healthy controls).

Results: A significant age-by-diagnosis interaction was only found for temporal lobe cortical thickness (CT)-PC (d = -0.54, p = .002). Within this lobe, the largest effects for the age x diagnosis interaction were found in the middle (d = -0.43, p = .01) and inferior (d = -0.48, p = .007) temporal gyrius CT-PC. The younger the patient group, the greater temporal thinning relative to their age-matched control group. The most extreme patient vs. control PC difference (i.e. the largest effect size) was found at an age cut-off of 19 years (d=0.9, p=.01).

Discussion: In individuals with psychosis, the two-year cortical changes that follow the FEP are dependent of age at first episode, with those with an earlier onset showing more severe cortical thinning in the temporal lobe.