# Changes in functional connectome after one year from the onset of psychosis: rsfMRI longitudinal study

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## Introduction

Schizophrenia is considered as chronic disease with heterogeneous outcomes. The latest research in schizophrenia mainly focuses on the period before the onset of psychosis and after the first occurence of psychotic symptoms. Takahashi (Takahashi et al 2018) indicated most progressive reduction of gray matter is in period of transition from prodromal state to psychosis and the initial period after the onset , if compared to chronic patients. During the first episode and after that, the brain goes through structural changes and this could be possibly mirrored in functional connectivity of the brain. Resting state functional MRI is now widely used for exploring neurobiology of psychiatric diseases. Thus, **the aim of our study was: firstly, to compare resting state connectome in patients with first episode of psychosis and healthy controls; secondly, to explore functional resting state connectome in patients with psychosis and healthy controls longitudinally, scanning both groups at baseline and one year after**. We hypothesized a greater disruptions in resting state functional connectivity in patients one year after the onset.

## Methods

We obtained the resting state functional and structural scans of first episode psychosis patients (FEP) N=25 (M=12; Age 28,24+/- 7,7) and healthy controls (HC) N=26 (M=14,Age 29,23+/-5,70 ) matched by age and sex. But groups differ in education see Table 1 Both groups underwent 2 scanning sessions: right after the onset (patients' group) and for both groups in one year follow-up. We have explored the functional connectome of both groups at baseline and after one year follow up. For comparison, we chose 32 seeds that represented functional networks. Functional connectivity analysis was performed using Conn Toolbox, and thresholded at p>0,05 FDR.

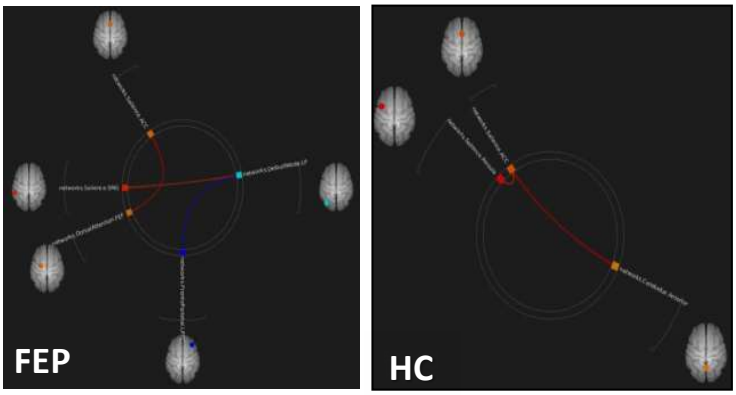
| | FEP n=25 | HC n=26 | P-values |
|---|---|---|---|
| Sex | 12M/13F | 14M/12F | p=0.676 |
| Age | 28,24 (7,77) | 29,27 (5,77) | p=0,687 |
| Education (years) | 14,84(3,36) | 18,35(3,42) | p=0,001 |

## Results

We found no differences in functional connectome comparing patients and controls neither at the baseline, nor after one year follow-up. The comparison in FEP group at baseline and one year after revealed a hyperconnectivity between posterior part of the Default Mode Network (left parietal lobule) and Salience Network (left supramarginal gyrus ) (p=0.022 FDR corr.), a hyperconnectivity between Salience Network (anterior cingulate, ACC) and Dorsal Attention Network (part of the frontal eye field) (p=0.028 FDR corr.) and a hypoconnectivity between posterior part of the Default Mode Network(parietal lobule L) and Frontal Parietal Network (left prefrontal cortex) ( (p=0.046 FDR corr.). After one year follow-up we found differences in control group as well. We observed a hyperconnectivity between Salience Network (ACC) and Cerebellar Anterior Network (p=0.020 FDR corr.), and between anterior and posterior parts of the Salience Network,- ACC and anterior insula region. (p=0.040 FDR corr.)

## Conclusion

While majority of published studies (for meta-analysis see.Li et al 2016) showed differences in resting state network connectivity between patients with psychosis and healthy controls, **our study did not show any differences neither at the baseline, nor after one year follow-up.** This is,however in line with a recent study (Ganella et al. 2018) that suggested no differences in resting state connectome between healthy controls and patients with psychosis. On the other hand, our follow-up results showed differences in both groups. Changes in HC in the follow-up are rather unexpected given the proposal of Gratton (Gratton et al 2018 who showed that resting state networks were best suited to measuring stable characteristics. However the same study debated if resting state networks are suitable for group analysis. In our study, **the differences were found mainly in so called large scale networks, that are responsible for cognitive control and saliency**. Effects of individual identity are more pronounced in these control networks rather than in processing networks (Gratton et. al 2018). **In patients group, dysconnectivity were explored prominently in default mode network (DMN) regions**. Connectivity of DMN is widely accepted to be abberant in patients with psychosis (Garrity et al. 2007, Du et al 2016). Our results must be confirmed in a larger sample.




| Connections in First Episode Psychosis Group | T-statistics | P-value FDR corr |
|---|---|---|
| Salience SMG – DMN LP | T(24) = -3.87 | 0.022 |
| Salience ACC-DAN FEF | T(24) = 3.78 | 0.028 |
| FrontalParietal L- DMN LP | T(24) = -3.30 | 0.046 |

| Connections in Healthy Controls Group | T-statistics | P-value FDR corr |
|---|---|---|
| Salience ACC – Cerebellar | T(25) = -3.89 | 0.020 |
| Salience Insula - Cerebellar | T(25) = -3.34 | 0.040 |

Abbreviations: SMG – Supramarginal Gyrus, DAN FEF – Dorsal Attention Network frontal eye field, ,ACC - Anterior Cingulate Cortex, DMN – Default Mode Network LP – Left Parietal Lobule

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