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P.307
Resting state MRI functional connectivity and negative symptoms in subjects with schizophrenia

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Introduction: Negative symptoms (NS) are a key aspect of schizophrenia due to their remarkable impact on real-life functioning in subjects suffering from this disorder [1]. These symptoms can be clustered in two domains: the avolition-apathy and the expressive deficit domains. Functional magnetic resonance imaging (fMRI) data have been extensively used to investigate the underlying neurobiological dysfunctions in subjects with schizophrenia (SCZs). A robust finding is the presence of faulty connections within and between neuronal networks, revealing also associations with NS [2]. The present study focuses on resting-state functional connectivity (RS-FC), an extremely useful fMRI method that analyses how anatomically-separated cerebral regions operate in functionally connected networks. Therefore, we aim to detect the presence of RS-FC abnormalities in SCZs and investigate any association between RS-FC values and NS severity.

Methods: fMRI data were acquired from 79 SCZs and 61 healthy controls (HCs), recruited within the Italian Network for Research on Psychoses. RS-FC values were extracted using a predefined parcellation of the cerebral surface into 7 functional networks [3]. 23 regional clusters were then set by detecting the highest RS-FC values across participants, within the 7 networks of interest. NS in SCZ were assessed with the Brief Negative Symptom Scale, a second-generation rating scale, and major confounders for secondary negative symptoms were assessed and controlled for. For data analysis, MANOVA test (followed by post-hoc comparisons, with Bonferroni correction) was used to compare RS-FC values between SCZs and HCs. In addition, Pearson's correlations (with Bonferroni correction) were performed to investigate the association between RS-FC and NS.

Results: SCZs, compared to HCs, showed a significant decrease ($F= 9.61$, $p= 0.002$) of the RS-FC in the left superior temporal gyrus (limbic network). Significant correlations were found between the RS-FC of the left superior parietal lobule, which is part of the dorsal attention network, and the total score of NS ($r=0.39$, $p<0.001$), as well as with the two NS domains, the Avolition-apathy ($r=0.35$, $p<0.01$) and the Expressive deficit ($r=0.42$, $p< 0.001$). These correlations remained significant after controlling for positive, depressive, disorganized symptoms, and global parkinsonism.

Conclusion: The results seem to suggest that schizophrenia is characterised by a decrease in functional connectivity within the limbic network, which is involved in emotions, auditory and language processing and social cognition. NS were associated with a hyperconnectivity within the dorsal attention network, which is devoted to early sensory processing and top-down deployment of attention. Deficits in this network have been previously detected in SCZs [4] and dysfunctions in early sensory processing have been linked to NS onset [5]. The dorsal attention network is also characterised by its interaction with a parallel anatomically-separated network counterpart, the ventral attention network [4]. This network is involved in motivation, attentional capture from salient stimuli and reward prediction. Aberrations in these processes are associated to some of the NS domains. As suggested by the present study, further investigations are needed to understand how abnormalities in the dorsal attention network, and possibly the subsequent disrupted interactions with the ventral attention network, could lead to NS appearance.

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Latent class growth modeling reveals two distinct pupillometric response profiles in a working memory task

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Cognitive impairments manifest in a wide range of psychiatric disorders [1] and have been proposed as a transdiagnostic endophenotype and risk factor [2]. In previous work, we showed that pupil size increases with increasing working memory load and is reliably correlated to activity in the fronto-parietal network (FPN) in healthy individuals. It is largely unknown whether pupillometry constitutes a valid marker for cognitive dysfunctionality. Here, we investigate pupil fluctuations and its neural correlates in a working memory task in a dimensional cross-diagnostic approach.

The sample consisted of 197 healthy subjects and patients with various degrees of affective/anxiety symptomatology (Mage = 34.5, SDage = 11.9, 132 female) who completed the N-back task with four conditions (fixation, 0-back, 1-back, and 2-back) during functional magnetic resonance imaging (fMRI) and simultaneous pupillometry. We modelled mean pupil size per condition into general linear models in SPM12. We used latent class growth modeling (LCGM) to detect groups with different pupillometric response profiles. The model with the best fit according to the Bayesian Information Criterion was chosen and its mean pupil values were entered into additional first level analyses. For the group comparison on the second-level we used propensity score matching in order to obtain an age and sex matched control group without any current diagnosis to one of the resulting subclasses. Moreover, we examined pupillometry and fMRI in classical group comparisons (current depression versus no current diagnosis) and dimensional analyses (BDI-II [3], neuropsychological performance).

The LCGM resulted in two distinct classes: one with a stepwise increasing pupil size with increasing working memory load (n = 161), and the other one with a constant pupil size across conditions and only a higher value in the 2-back condition (n = 36). We used the latter class for further group comparison, as they showed a divergent pupillometric response profile. The groups differed in reaction time ($t(54) = 1.7$, $p = 0.008$, $d = -0.7$), and accuracy ($t(54) = 2.2$, $p = 0.03$, $d = 0.6$) in the 2-back condition, as well as in the subjective symptomatology of depression ($t(63) = -4.1$, $p < 0.001$, $d = -1.0$), and trait anxiety ($t(63) = -5.3$, $p < 0.001$, $d = -1.3$), with the divergent group showing higher symptom levels and lower performance. The statistical maps of the (group) mean pupil value per block were largely the same (FPN); the differential contrast indicated that the pupil response profile of the divergent group revealed more activity in bilateral fronto-parietal clusters. Classical group comparisons based on diagnosis and dimensional analyses did not yield significant clusters of activity. Only neuropsychological performance showed correlations with a few small clusters in the area of the occipital cortex, and the supramarginal gyrus.

The coupling between pupil size and the FPN during working memory seems to be largely unaffected by general neuropsychological functioning, diagnosis or subjective depressive symptomatology. However, with a data-driven approach to classify distinct individual pupil size response profiles, we could extract a potentially meaningful cross-diagnostic subgroup with cognitive difficulties and increased depression and anxiety symptoms.

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P.310
Effects of intranasal administration of the neuromodulator oxytocin on autonomic cardiac function

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