a measure of linguistic demand, the number of words within 20-second epochs was correlated with BOLD responses.
Results: Participants developed S-ketamine-induced psychotic symptoms, particularly positive FTD. Ketamine vs. placebo was associated with enhanced neural responses in the right middle and inferior temporal gyri.
Discussion: Similar to a previous fMRI study in schizophrenia patients vs. healthy controls applying the same design, S-ketamine reversed functional lateralization during speech production in healthy subjects. Results demonstrate an association between glutamatergic imbalance, dysactivations in lateral temporal brain areas, and FTD symptom formation. Left superior temporal gyrus (STG) cortical volume is decreased in schizophrenia patients (SZ) with pFTD in structural magnetic resonance imaging (sMRI) studies and shows reversed activation in functional MRI (fMRI) experiments during speech production. pFTDs are related to synaptic rarefication in the glutamate system of the superior and middle lateral temporal cortices.
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F147. RESTING STATE NETWORKS ALTERATION IN PANTOTHENATE-KINASE ASSOCIATED NEURODEGENERATION (PKAN)

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Background: While functional MRI and PET studies have shown altered task-related brain activity in PKAN, we want to find such differences also in the resting state (RS).
Here we used ICA based analysis to investigate RS fMRI data to compare connectivity of 11 well known networks (Auditory, Cerebellum, Default Mode Network (DMN), Exectutive Control, Fronto-parietal 1, Fronto-parietal 2, Salience, Sensorimotor, Visual1, Visual2, Visual3 network) between patients with PKAN and healthy controls suggesting deficits in related neuropsychological functions.
Methods: We obtained RS fMRI series (3T, 3x3x3mm resolution, 45 slices, TR 2s, 300 volumes) in 17 PKAN patients but 3 were discarded because of excessive movement, (mean age 17.2a±7.1) on stable medication and 15 healthy controls (22.5a±8.3).
Subjects were asked to lie in the scanner keeping eyes closed with no further specific instructions. Data were pre-processed; we applied FSL MELODIC (pICA) yielding IC, we used FIX to auto-classify ICA components which represent artifacts and an automated routine to select for each subject the component matching the anatomical definition of resting state networks.
SPM12 was used for second level analysis, we used two sample t-test to compare networks functional connectivity between groups. In addition, we used multiple regression to correlate RS networks activity components with Dystonia score.
Results: Our method reliably identified all networks in every control and patients. We found significant differences in the anatomical pattern of areas. Patients showed decreased functional connectivity in comparison to healthy controls in portions of Fronto-parietal 1, Fronto-parietal 2 and Visual1 networks; in addition, patients showed increased functional connectivity in comparison to healthy controls in portions of Cerebellum, DMN, Executive Control, Salience and Visual1 networks. Finally, significant correlation was found between dystonia score and functional connectivity of Cerebellum, Fronto-parietal1, Fronto-parietal2, Salience, Sensorimotor and Visual2 networks.
Discussion: Well known resting state networks were reliable identified from RS fMRI in PKAN patients. The differences in anatomical distribution point to possible alterations in functional connectivity in PKAN, which suggests disruption in cerebellum, DMN, fronto-parietal, salience and visual activity. Correlations with dystonia suggest a direct relation to motor items, which would support a clinical significance of altered RS networks activity.

F148. A PILOT STUDY OF [11C] (R)-MEQAA PET BRAIN IMAGING ANALYSIS OF ALPHA 7 NICOTINIC ACETYLCHOLINE RECEPTORS AVAILABILITY IN SCHIZOPHRENIA

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Background: A growing body of evidence suggests that the aberrant cholinergic system may underlie the pathophysiology in schizophrenia. Nicotinic acetylcholine receptor (nAChR) subtype α7 (henceforth 'α7 nAChR') is located in presynaptic and postsynaptic constructs in the cerebral cortex and considered to play a key role in the regulation of learning and memory. Additionally, α7 nAChR is deemed to exert neuroprotective effects. Therefore, α7 nAChR is one of the potent therapeutic targets for negative symptoms and cognitive impairment in schizophrenia. In effect, several randomised trials to assess the efficacy and safety of α7 nAChR agonists are currently underway.
There is some evidence in support of aberrant α7 nAChR in schizophrenia. In postmortem studies, protein levels of α7 nAChR in the frontal cortex (Guan et al., 1999) have been reported to be decreased in patients with schizophrenia. However, the availability of α7 nAChR in individuals with schizophrenia has yet to be examined in vivo. In this pilot study, we aim to clarify availability of α7 nAChR in the brains of patients with schizophrenia using positron emission tomography (PET) with a ligand of [11C] (R)-2-methylamino-benzoic acid 1-aza-bicyclo[2.2.2]oct-3-yl ester ([11C] (R)-MeQAA).
Methods: All participants provided informed consent. Inclusion criteria included diagnosis of schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition (DSM-5, 2013). Patients were excluded if they had (1) full IQ under 69 measured with the Wechsler Adult Intelligent Scale-III; (2) current or past history of tobacco smoking; (3) history of neurological disorder or structural brain abnormality; (4) use of benzodiazepines, antidepressants, or anticholinergics in the past 6 months; and (5) substance abuse. Although scanning drug-free or drug-naïve patients for investigation is optimal, it is extremely difficult to attain this. Consequently, participants with schizophrenia comprised medicated cases.
We evaluated the availability of α7 nAChR by estimating non-displaceable binding potential (BPND) of the tracer using PET with [11C] (R)-MeQAA, a selective PET tracer for α7 nAChR. Four patients with schizophrenia (age: range 27–39; m/f: 2/2) and 5 age-matched healthy adults (age: range 22–32; m/f: 2/3) underwent the PET scan. The level of BPND in patients with schizophrenia was compared with that for control participants by applying regions of interest (ROIs) approach. In this pilot study, we opted for 4 cortical areas, the superior frontal, middle frontal, parietal, and temporal cortices, for ROIs. This study was approved by the Hamamatsu University School of Medicine Ethics Committee.

Results: We found the levels of [11C] (R)-MeQAA BPND significantly lower in the middle frontal cortex (p = 0.036) in patients with schizophrenia. Additionally, there was a trend towards a decreased level of BPND in the temporal cortex (p = 0.067) and parietal cortex (p = 0.087) in the brains of schizophrenia patients, although it failed to reach statistical significance. There was no difference in the superior frontal cortex.
Discussion: To our knowledge, this represents the first demonstration of anomalies in the acetylcholinergic system in the in vivo brains of schizophrenia patients. However, this is regarded as a pilot study, and further recruitment of schizophrenia patients with a recent onset and minimal use of antipsychotic medication, followed by scanning and data analyses, will be continued.

F149. NEUROBIOLOGY OF SELF-AGENCY DURING REALITY MONITORING AND SPEECH FEEDBACK MONITORING: IMPLICATIONS FOR TREATMENT DEVELOPMENT IN SCHIZOPHRENIA

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Background: Self-agency is the experience of being the agent of one's own thoughts and motor actions. The intact experience of self-agency is necessary for successful interactions with the outside world (i.e., reality monitoring). Reality monitoring is the ability to distinguish internally self-generated information from outside reality (externally-derived information). We found that healthy control (HC) participants recruit medial prefrontal cortex (mPFC) during encoding of self-generated information, which is also activated during accurate retrieval of self-generated information. By contrast, patients with schizophrenia (SZ) have specific self-agency impairments and do not show mPFC activation during encoding or retrieval of self-generated information. These findings indicate that SZ may rely more on environmental externally-derived information, rather than on internal self-generated information, to guide reality monitoring. Here, we relate the experience of self-agency during a lower-level speech feedback monitoring (i.e., monitoring what we hear ourselves say) to our higher-level cognitive reality monitoring task. We examine whether the sense of self-agency during speech feedback monitoring and reality monitoring are driven by the same fundamental mechanism that we hypothesize underlies the capacity to experience self-agency—the ability to make reliable predictions about the outcomes of self-generated actions.
Methods: During speech feedback monitoring we assess self-agency by altering environmental auditory feedback so that participants listen to a perturbed version of their own speech. When subjects hear minimal perturbations in their auditory feedback while speaking, they make corrective responses, indicating that they judge the perturbations as errors in their speech output. These corrective responses are modulated by subjects' reliance on internal predictions about the outcome of their speech output; the more subjects rely on their internal predictions, i.e. their sense of self-agency, the less they rely on external auditory feedback, resulting in smaller corrective responses. Thus, subjects who produced smaller corrective responses manifested an enhanced sense of self-agency in that they relied more on their internal predictions to generate their own actions (i.e., their speech output).
Results: We found that self-agency judgments in the reality-monitoring task were higher in people who had smaller corrective responses (p=.05) during minimal speech perturbations of their auditory feedback. These results provide support for a unitary process for the experience of self-agency resulting from the ability to reliably predict the outcomes of self-generated actions, that governs low-level speech control and higher level reality monitoring.
Discussion: These findings have important therapeutic implications in SZ, suggesting that the more participants rely on internal predictions to guide their actions, the smaller their corrective responses in their speech output, and the more likely they are to make correct judgments of self-agency during reality monitoring. In conclusion, these findings, therefore, indicate that reality monitoring and speech monitoring paradigms provide quick and robust markers of the experience of self-agency, indicating which subjects followed their internal predictions to guide their own actions. Together, these findings have important therapeutic implications for potentiating improvements in self-agency judgments not only in HC, but in patients with schizophrenia who suffer from critical self-agency impairments.

F150. OVERESTIMATING ENVIRONMENTAL VOLATILITY INCREASES SWITCHING BEHAVIOR AND IS LINKED TO ACTIVATION OF DORSOLATERAL PREFRONTAL CORTEX IN SCHIZOPHRENIA

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Background: Reward-based decision-making is impaired in schizophrenia, as reflected by increased switching between choices. The underlying cognitive mechanisms and associated neural signatures remain unknown. Reinforcement learning (RL) and hierarchical Bayesian learning account for this behavior in different ways. We hypothesized that enhanced switching during flexible reward-based decision-making in schizophrenia relates to higher-order beliefs about environmental volatility and examined the associated neural signatures.
Methods: 46 medicated schizophrenia patients and 43 controls underwent a reward-based decision-making task requiring flexible behavior to changing action-outcome contingencies during functional Magnetic Resonance Imaging (fMRI). Computational modeling of behavior was performed, including RL and the Hierarchical Gaussian Filter (HGF). The estimated learning trajectories informed the analysis of fMRI data.
Results: A three-level HGF accounted best for the observed choice data and revealed a heightened prior belief about environmental volatility and a stronger influence of volatility on lower-level learning of action-outcome contingencies in schizophrenia. This finding was replicated in an independent sample of unmedicated patients. Beliefs about environmental volatility were reflected by higher activity in dorsolateral prefrontal cortex (dlPFC) of patients compared to controls.
Discussion: This study suggests a mechanistic explanation for instable behavior in schizophrenia: patients inferred the environment as being too volatile and thus overestimated environmental changes, leading to maladaptive choice switching. Our data suggest enhanced dlPFC activity related to beliefs about environmental volatility as a neural learning signature of instable behavior. Such detailed 'computational phenotyping' may provide useful information to dissect clinical heterogeneity and could improve prediction of outcome.