**8. Supplemental Files**

# 8.1 Analysis of the Jülich data

## fMRI data Analysis

fMRI data analysis was performed using a Matlab-based toolkit, DPABI [1]. DPABI contains libraries for processing fMRI data that depend on another Matlab-based software package, Statistical Parametric Mapping 12 (SPM12, Wellcome Trust Centre for Neuroimaging). The short range functional connectivity measure called regional homogeneity (ReHo) [2] and long range functional connectivity measure called degree centrality (DC) [3] were computed in fMRI data acquired during MMN task. Functional connectivity measures were computed after pre-processing steps which includes corrections for slice timing, motion and nuisance signal. A temporal filtering was performed between 0.01 to 0.08 Hz. ReHo (voxel cluster size 27) and DC values (correlation cutoff - Pearson r > 0.25, p <0.0001) were calculated in subject’s native space and were linearly standardized to Z values. Z standardized connectivity measures were then normalized to standard MNI space (2 mm3).

In-order to quantify the changes in connectivity values between the healthy and schizophrenic subjects, voxel values were extracted from whole brain grey matter (GM) mask and functional masks such as the auditory and salience networks for comparison. Whole brain GM mask was made by segmenting MNI152 brain template using FSL FEAT [4] software package. Finally, GM mask was created from segmented GM image voxels which have a higher than 50% probability. Functional masks were obtained from 90 fROI atlas [5]. The functional masks (auditory network (AN) and salience network (SN) masks) were corrected for GM using the GM mask created this was done in order to consider only the voxels in the GM region for further analyses.

A two-sample t-test was performed in Matlab (Version 8.5, Matworks) to compare functional connectivity measures between GM region and AN and SN within subjects. Similarly, a two-sample t-test was performed compare functional connectivity measures in GM, AN and SN between healthy subject and schizophrenic patient.

## PET data Analysis

PET images were smoothed with an isotropic Gaussian filter (3 mm), motion corrected and registered to MRI, the activity concentration was extracted from the precuneus, cingulum posterior part, hippocampus and parahippocampus, nucleus accumbens (volume-of-interest sphere of 8 mm radius), middle and inferior frontal and cerebellum cortices (PMOD software package, version 3.5).

The binding potential was calculated during MMN task period (at equilibrium). The non-displaceable binding potential was calculated as BPND = (Ct – Ccer)/ Ccer, where Ct represents the activity concentration in the brain tissue regions and Ccer is the reference tissue, in this case cerebellum.

A two-sample t-test between BPND values of healthy volunteer and schizophrenic subject in different target regions was done using Matlab software package (version 8.5).

## EEG data Analysis

EEG data were processed using EEGlab [6], a Matlab-based toolbox. The pre-processing steps included gradient artefact (GA) correction [7], down-sampling to 250 Hz, additional filtering using a Butterworth zero-phase filter with lower cut-off frequency of 1 Hz and higher cut-off frequency of 8 Hz for the ECG channel and 20 Hz for other the EEG channels and ballistocardiogram (BCG) artefact correction [7]. An ICA-based decomposition was performed using the Infomax extended algorithm [8] to all 63 EEG channels. Further, artefact components were identified and removed using MARA toolbox [9]. EEG signals were re-referenced to an average reference and segmented between -400 and +600 ms based on standard and frequent auditory stimuli marker position. The segmented EEG data were averaged over trials. The amplitude between the N1 and the P2 peaks was calculated for standard tone and amplitude of MMN was calculated for deviant tone from the averaged trials in Cz channel.

**8.2 Recruitment and inclusion criteria**

Recruitment of subjects with schizophrenia diagnosis according to ICD-10 and age- and education-matched healthy controls is described in the supplemental files. The recruitment took place at the two sites Jülich (between 16.03.2017-31.06.2017) and Munich (22.02.2017-31.07.2017), each one with a planned number of 20 patients and 20 controls. Inclusion criteria were identical for both study sites and are listed in the table below.

|  |
| --- |
| Inclusion criteria for all participants:   * age between 18 and 55 years * no persons unable to give informed consent will be involved * no mental retardation (IQ < 80) estimated with the WST (Wortschatztest) or MWT-B (tests for the premorbid intellectual performance level) * no drug dependency (except of nicotine) * no depressive or maniac episode, no bipolar disorder, no schizoaffective disorder, no PTSD * no neurologic or other severe somatic disorder * no contraindication for MRI or PET   Additional inclusion criteria for each group:   * for healthy controls: * no current (or history of) mental disorder, checked with the operationalized Mini International Neuropsychiatric Interview (MINI) * for subjects with manifest schizophrenia: * diagnostic criteria according to ICD-10 are met. * Patients in acute states of psychosis are excluded according to PANSS ratings ≤ 3 in the subscales 'Delusions (P1)', 'Conceptual disorganisation (P2)', 'Hallucinatory behaviour (P3)', 'Mannerisms and posturing (G5)' and 'Unusual thought content (G9)'. (According to van Os et al., 2006[10]) * stable antipsychotic medication for at least 15 days |

Table -: Inclusion criteria for both Munich and Julich sites.

# 8.3 References for the supplemental files

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