# Spontaneous striatal activity reflects disease states and symptom dimensions in schizophrenia

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## 1. Introduction:

Striatal dysfunction is thought to be fundamental in schizophrenia[1] and is assumed to underlie a large variety of psychotic symptoms[2,3]. Striatal dopamine transmission is elevated in patients[4] especially during prodromal and psychotic states and correlates with positive disease symptoms, which respond to anti-dopaminergic drugs. These increased dopamine levels have also been observed in schizophrenic patients at rest. Thus, *spontaneous resting state neuronal activity* in the striatum might be altered in patients with schizophrenia during both *acute state of psychosis* and *state of remission* and be associated with *severity of symptoms*. However, in-vivo evidence for altered spontaneous striatal activity in patients has not been reported yet.

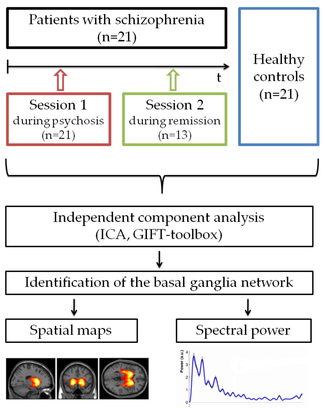
## 2. Questions:

(1) Is spontaneous striatal activity changed in schizophrenia?
(2) Are potential changes modulated by psychosis, i.e. are potential changes in spontaneous striatal activity different during acute state of psychosis and during psychotic remission?
(3) Are potential changes related to symptom dimensions?

## 3. Methods:

**Measurement:** BOLD-fMRI during a 10-minutes rest period (rs-fMRI).
**Participants:** Patients with schizophrenia (n=21) and healthy controls (HC, n=21). Patients were assessed during psychosis (SP, n=21) and during psychotic remission (SPR, remaining n=13) (see Tab. 1).
**Data analysis:** Independent component analysis (ICA, GIFT-toolbox) was performed to identify the basal ganglia network (BGN).
**Outcome measures:** (1) intensities of the BGNs spatial maps (connectivity / degree of coactivation), (2) power spectra of BGN´s time course (level of coherent activity).

**Approach to data analysis**




**Participants' demographic and clinical characteristics**

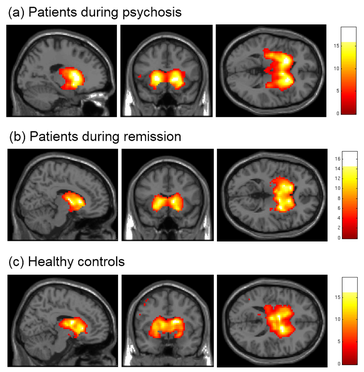
| | **HC** (n=21) | **SP** (n=21) | **SPR** (n=13) |
|---|---|---|---|
| Measure | **Mean (SD)** | **Mean (SD)** | **Mean (SD)** |
| Age | 33.57 (13.6) | 34.05 (12.27) | 33.69 (10.53) |
| Sex (m/f) | 10/11 | 10/11 | 9/4 |
| PANSS | | | |
| Total | 30.14 (0.65) | 80.76 (20.77) | 52.75 (13.93) |
| Positive | 7.05 (0.22) | 19.4 (6.09) | 11.92 (3.63) |
| Negative | 7.10 (0.44) | 21.14 (8.20) | 13.58 (5.63) |
| General | 16.05 (0.22) | 39.81 (11.06) | 27.25 (8.30) |
| GAF | 99.76 (1.09) | 39.62 (11.68) | 59.25 (14.44) |
| CPZ | | 388.61 (384.67) | 206,95 (189.67) |

HC, healthy control group; SP, group of patients with schizophrenia during psychosis; SPR, group of patients with schizophrenia during psychotic remission; PANSS, Positive and Negative Syndrome Scale; GAF, Global Assessment of Functioning Scale; CPZ, chlorpromazine equivalent dose.

**Analysis of coactivation:** group and session effects within the BGN: voxel-wise tests on participants´ spatial maps ($p<0.05$, FDR corrected). Tests were corrected for levels of medication, as measured by chlorpromazine equivalent dose (CPZ) and volumetric differences, as measured by voxel-based morphometry (VBM). Relationship between striatal co-activation and symptom dimensions: correlation of region-of-interest (ROI)-restricted z-scores derived from the BGN with selected scores from the Positive and Negative Syndrome Scale (PANSS) in patients (partial correlation, corrected for striatal volume (VBM) and medication (CPZ), $p<0.05$ Bonferroni-corrected). ROI coordinates for functional subdivisions of the striatum (ventral/limbic, dorsal/associative) were derived from a previous study[7].
**Analysis of power spectra:** spectral power of each time course was averaged across frequencies ranging from 0.01 to 0.1Hz. Differences across groups and sessions: two-sample t-tests and paired t-tests.

## 4. Results:

### 4.1. ICA revealed a basal ganglia network (BGN), which comprised the dorsal/ associative and the ventral/limbic striatum.

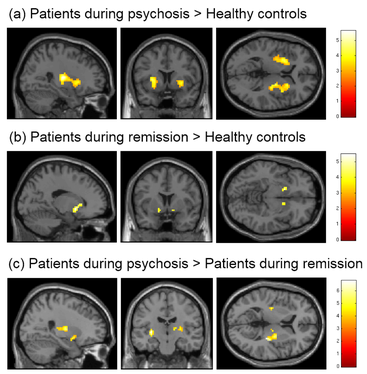



Spatial maps of the BGN:
(a) shows the BGN in patients during psychosis
(b) shows the BGN in patients during remission
(c) shows the BGN in healthy controls

The striatum is integrated into multiple cortico - basal ganglia - cortical loops. The ventral part projects into limbic, the associative part into associative and the sensorimotor part into sensorimotor cortices.[5]

The BGN was spatially consistent across groups and sessions, matched previous results[6] and included the ventral/limbic, the dorsal/associative, and the sensorimotor striatum.

### 4.2. Spatial maps of co-activation reflect psychosis and psychotic remission in distinct parts of the striatum



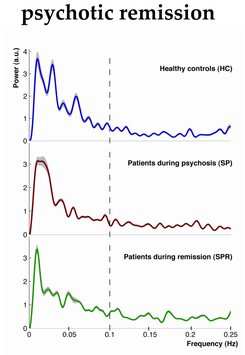

Spatial maps of the BGN with significantly increased co-activation in distinct locations:

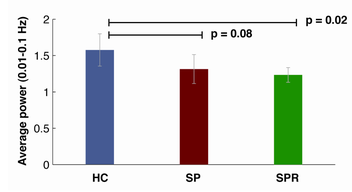
(a) During psychosis, patients showed localized increased co-activation in the dorsal/associative and the sensorimotor striatum of the BGN compared to healthy controls.

(b) During psychotic remission, the same patients showed stronger co-activation in the ventral/limbic striatum compared to healthy controls.

(c) Contrasting both disorder states directly, patients in state of psychosis showed increased co-activation in the dorsal/associative and the sensorimotor striatum compared to patients in state of psychotic remission.

### 4.3. Spectral power of time courses of synchronous activity was changed during psychotic remission

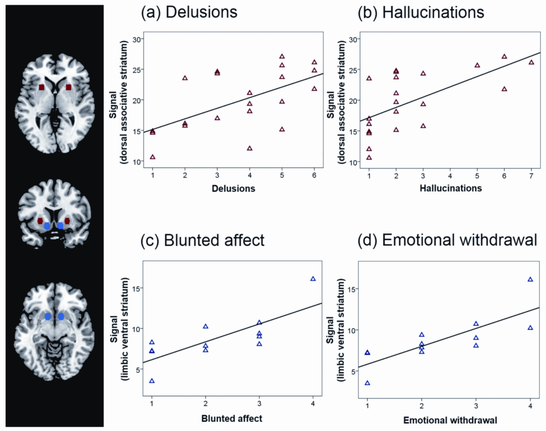



Patients in psychotic remission had significantly reduced power compared to controls ($p=0.02$).

Patients during psychosis had a trend for reduced power compared to controls ($p=0.08$).

### 4.4. Co-activation in the associative striatum correlated with delusions and hallucinations, co-activation in the limbic striatum with blunted affect and emotional withdrawal




Dorsal/associative striatum: The co-activation correlated significantly with total positive symptoms during psychosis and psychotic remission. Furthermore, a significant positive correlation with the severity of (a) delusions and (b) hallucinations could be demonstrated.

Ventral/limbic striatum: The correlation between the co-activation and the total negative symptoms during psychotic remission demonstrated a trend to significance ($p=0.09$, corrected). Furthermore, a significant positive correlation with the severity of (c) blunted affect and (d) emotional withdrawal could be demonstrated.

## 5. Conclusion:

These data reveal spontaneous activity in the striatum as a neuronal mechanism reflecting disease states and symptom dimensions in schizophrenia. We suggest that the regional shift of increased spontaneous co-activity from ventral to dorsal striatum reflects both an elevated striatal dopamine function and the corresponding shift from non-psychotic flexible to psychotic habit-like behaviour.

## 6. References:

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## 7. Acknowledgements:

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