# Functional connectivity gradients and thought-patterns in schizophrenia – negative symptoms

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## Introduction

Ongoing thought-patterns (TP) and their association with macroscale neural connectivity patterns known as "gradients" [1] have been investigated in healthy populations using rsfMRI[2]. In our study, we characterized the TPs and connectivity gradients in patients with schizophrenia (SZP) with predominantly negative symptoms and compared them to healthy controls (HC). Using these two measures, we examined the prediction of macroscale neuronal connectivity using the TPs.

## Methods

**Sample:** 143 participants (77 SZP and 66 HC), two research centers (Charité-Berlin and Geneva University Hospital), matched sample (Table 1), 9.8 min. rsfMRI.

**Analysis A: Comparing thought patterns between the groups:**

- Post scanning; completion of the Multi-Dimensional Experience Sampling (MDES; 25 items, Table 2, [3]).
- Extraction of six low-dimensional TPs using Principal Component Analysis (PCA), based on a scree plot.
- Group comparison via Multiple linear regression, controlling for center as a nuisance parameter (Fig. 3, Table 3).

**Creating macroscale connectivity gradients:** rsfMRI time-series were extracted using Schaefer parcellation (7 networks, 400 parcels, [5]). Connectivity matrices were calculated for each participant, and macroscale connectivity gradients were derived using PCA (Fig. 1 & 4).

**Analysis B: Group comparison at parcel /network level based on gradients score** (multiple linear regression)

- Dependent variable for the three gradients: parcel gradient score /network gradient score (median of the parcels within a network).
- Motion and gender were included as nuisance parameters (Fig.5, Table 3).

**Analysis C: Prediction of gradient-parcel-value based on group and TP** (multiple linear regression):

- Dependent variable: gradient scores of the significant parcels from analysis B.
- Independent variables: sig. TPs from analysis A, and group, motion, and center as nuisance parameters (Fig.6, Table 3).

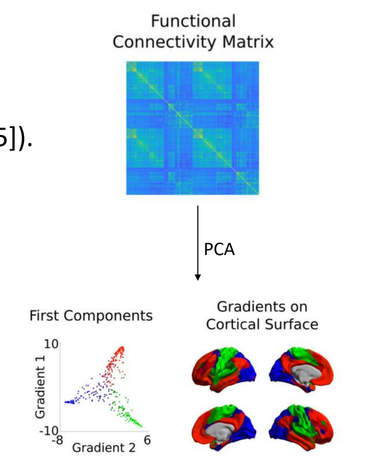
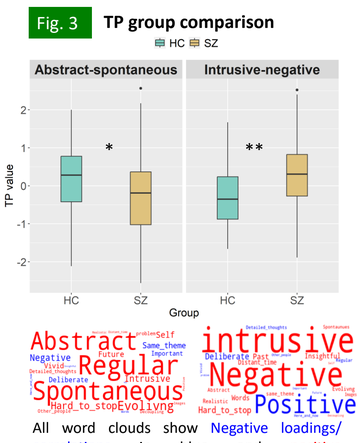



Fig.1 Creation of low dimensions cortical gradients [4]

## Results

### Analysis A

**Fig. 3 TP group comparison**




All word clouds show Negative loadings/ correlations in blue and positive loadings/correlations in red. Font size is scaled to the absolute value of the loading/ correlation. * p< 0.05, **p<0.005

**Table 2 Thought sampling post scanning ; MDES**

| Ongoing thought questionnaire of multidimensional experience sampling (MDES) | |
|---|---|
| **Item** | **Question** |
| | 1 2 3 4 (Not at all – completely) |
| *Vivid* | My thoughts were vivid as if I was there |
| *Regular* | My thoughts were similar to thoughts I often have |
| *Future* | My thoughts involved future events |
| *Negative* | My thoughts were about something negative |
| *Detailed thought* | My thoughts were detailed and specific |
| *Words* | My thoughts were in the form of words |
| *Evolving* | My thoughts tended to evolve in a series of steps |
| *Spontaneous* | My thoughts were spontaneous |
| *Positive* | My thoughts were about something positive |
| *Images* | My thoughts were in the form of images |
| *Other people* | My thoughts involved other people |
| *Past* | My thoughts involved past events |
| *Deliberate* | My thoughts were deliberate |
| *Self* | My thoughts involved myself |
| *Hard to Stop* | My thoughts were hard for me to stop |
| *Distant time* | My thoughts were related to a more distant time |
| *Abstract* | My thoughts were about ideas rather than events or objects |
| *Decoupling* | My thoughts dragged my attention away from the external world |
| *Important* | My thoughts were on topics that I care about |
| *Intrusive* | My thoughts were intrusive |
| *Problem solving* | My thoughts were about solutions to problems (or goals) |
| *Here and now* | My thoughts were related to the here and now |
| *Insightful* | My thoughts gave me a new insight into something I have thought about before |
| *Realistic* | My thoughts were about an event that has happened or could take place |
| *Same Theme* | My thoughts at different points in time were all on the same theme |

**Table 1 Demography and psychopathology**

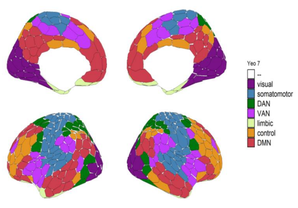
| | Mean ± SD | | | |
|---|---|---|---|---|
| T1 | HC | SZ | *p-value* | T/ $\chi^2$-value |
| n | 66 | 77 | | |
| Age | 38.2 ± 7.3 | 37.9 ± 9.8 | 0.80 | 0.24 |
| Center (B/G) | 35/31 | 35/42 | 0.36 | 0.81 |
| Gender (M/F) | 51/15 | 59/18 | 0.92 | 0.08 |
| Education years | 14.76 ± 2.15 | 12.97 ± 2.87 | <.001 | 4.14 |
| Education years_mother | 12.48 ± 2.87 | 11.39 ± 4.44 | 0.09 | 1.70 |
| Education years_father | 12.86 ± 2.98 | 11.8 ± 4.56 | 0.13 | 1.52 |
| BNSS_apathy | 1.51 ± 3 | 13.88 ± 8.76 | <.001 | -11.61 |
| BNSS_dimexp | 0.71 ± 1.7 | 7.25 ± 6.65 | <.001 | -8.31 |
| BNSS_total | 2.22 ± 3.86 | 21.13 ± 13.8 | <.001 | -15.63 |
| PANSS_positive | 7.5 ± 1.32 | 11.35 ± 4.47 | <.001 | -7.18 |
| PANSS_negative | 7.88 ± 1.76 | 16.16 ± 6.39 | <.001 | -10.18 |
| PANSS_total | 32.47 ± 4.37 | 51.9 ± 15.85 | <.001 | -10.31 |
| BACS_total | 0.52 ± 1.16 | -1.29 ± 1.17 | <.001 | 9.24 |

BNSS = Brief Negative Symptom Scale, PANSS = the Positive and Negative Syndrome Scale, BACS = the Brief Assessment of Cognition in Schizophrenia

**Table 3 Statistical results of the analyses**

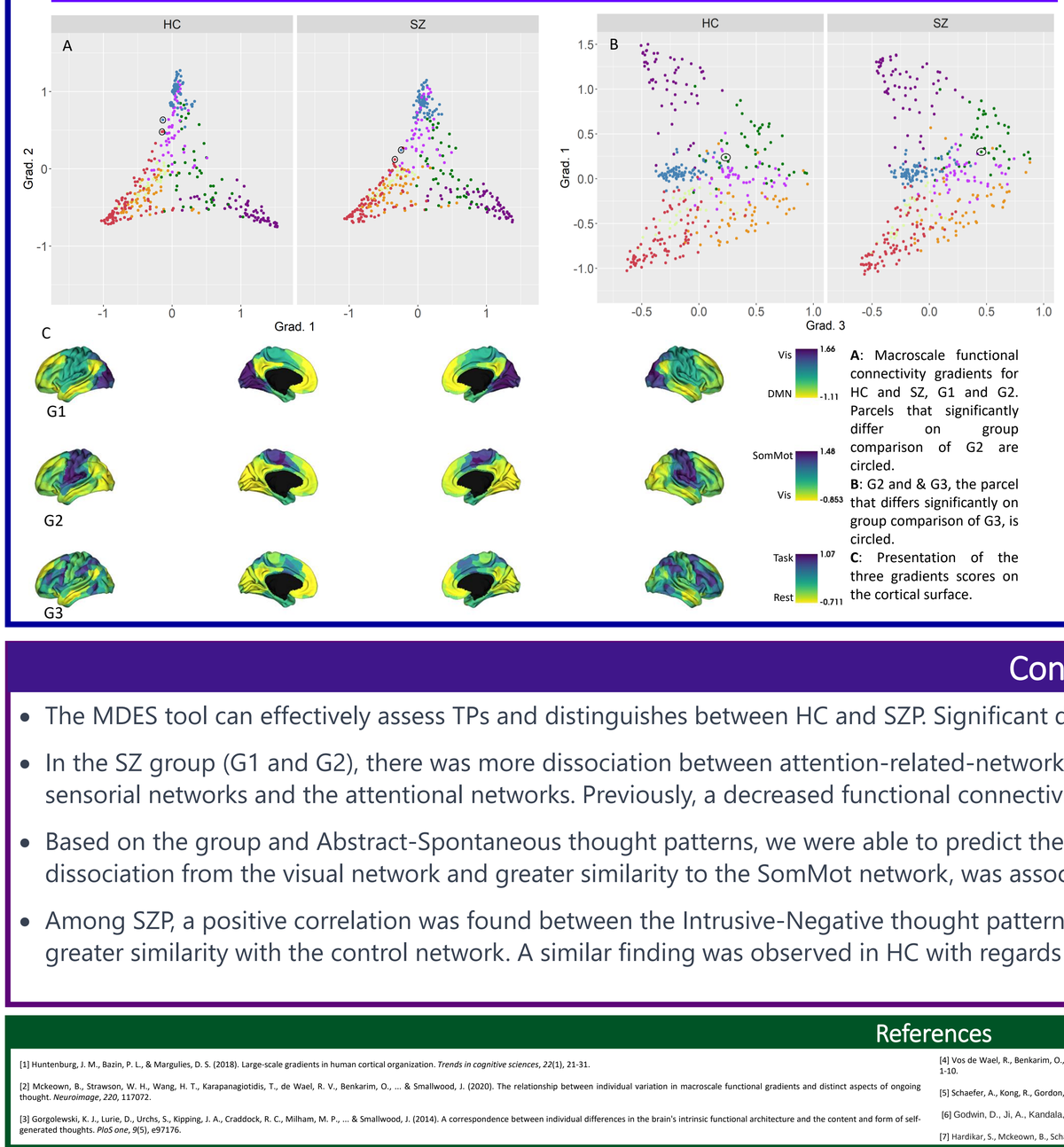
| | IV | DV | t(140) | Puncorr | Pbonf$_6$ < 0.05 |
|---|---|---|---|---|---|
| Analysis A | group | Intrusive-negative | 3.49 | <0.001 | 0.003 |
| | group | Abstract-spontaneous | -2.68 | 0.008 | 0.048 |
| | IV | DV (Yeo Network) | t(139) | Puncorr | Pbonf$_{21}$ < 0.025 |
| Analysis B (networks) | group | G1-DAN | 3.42 | <0.001 | 0.01 |
| | group | G2- Control | 3.33 | 0.001 | 0.021 |
| | group | G2 -Visual | 3.34 | 0.001 | 0.021 |
| | IV | DV (parcel/Yeo Network's belonging) | t(139) | Puncorr | Pfdr$_{1200}$ < 0.025 |
| Anslysis B (parcel) | group | G2-LH_Temporal_Parietal (156)/DMN | -4.59 | <0.001 | 0.003 |
| | group | G2-RH_Temporal_parietal_4 (232)/SomMot | -5.05 | <0.001 | 0.001 |
| | group | G3-RH_PostC_5 (283)/DAN | 4.63 | <0.001 | 0.003 |
| | IV | DV (parcel/Yeo Network's belonging) | t(136) | Puncorr | Pbonf$_3$ < 0.025 |
| Analysis C | TP Abstract-spontaneous | G2-RH_Temporal_parietal_4 (232)/SomMot | 2.63 | 0.01 | 0.02 |
| | group | G2-RH_Temporal_parietal_4 (232)/SomMot | -4.36 | <0.001 | <0.001 |

IV = Independent Variable, DV = Dependent Variable, G = Gradient, LH /RH = Left / Right Hemisphere, DAN = Dorsal Attention Network, DMN = Default Mode Network, SomMot = Somatomotor Network, PostC = Postcentral gyrus



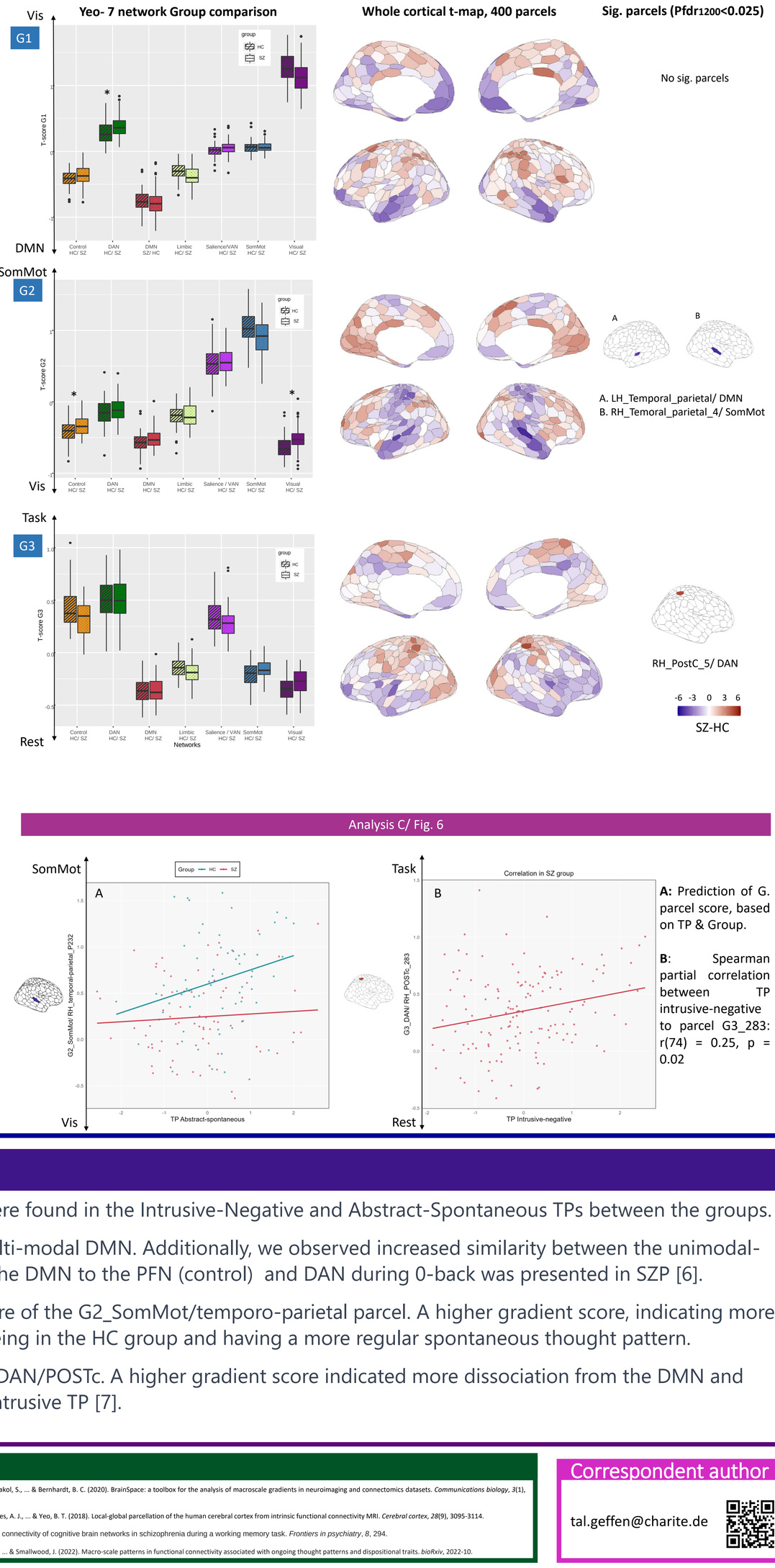

**Yeo – 7 networks parcellation**

### Macroscale functional connectivity Gradients/ Fig. 4




**A**: Macroscale functional connectivity gradients for HC and SZ, G1 and G2. Parcels that significantly differ on group comparison of G2 are circled.
**B**: G2 and & G3, the parcel that differs significantly on group comparison of G3, is circled.
**C**: Presentation of the three gradients scores on the cortical surface.

### Analysis B /Fig. 5




### Analysis C/ Fig. 6




**A:** Prediction of G. parcel score, based on TP & Group.

**B**: Spearman partial correlation between TP intrusive-negative to parcel G3_283: r(74) = 0.25, p = 0.02

## Conclusions

- The MDES tool can effectively assess TPs and distinguishes between HC and SZP. Significant differences were found in the Intrusive-Negative and Abstract-Spontaneous TPs between the groups.
- In the SZ group (G1 and G2), there was more dissociation between attention-related-networks and the multi-modal DMN. Additionally, we observed increased similarity between the unimodal-sensorial networks and the attentional networks. Previously, a decreased functional connectivity between the DMN to the PFN (control) and DAN during 0-back was presented in SZP [6].
- Based on the group and Abstract-Spontaneous thought patterns, we were able to predict the gradient score of the G2_SomMot/temporo-parietal parcel. A higher gradient score, indicating more dissociation from the visual network and greater similarity to the SomMot network, was associated with being in the HC group and having a more regular spontaneous thought pattern.
- Among SZP, a positive correlation was found between the Intrusive-Negative thought pattern and the G3_DAN/POSTc. A higher gradient score indicated more dissociation from the DMN and greater similarity with the control network. A similar finding was observed in HC with regards to Specific-Intrusive TP [7].

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