Association between brain network stratification and cognition in schizophrenia spectrum disorders

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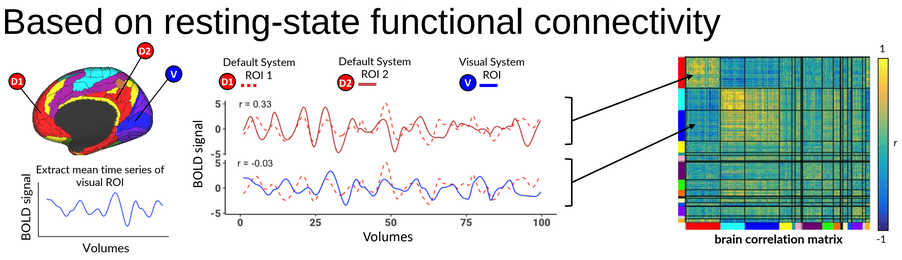
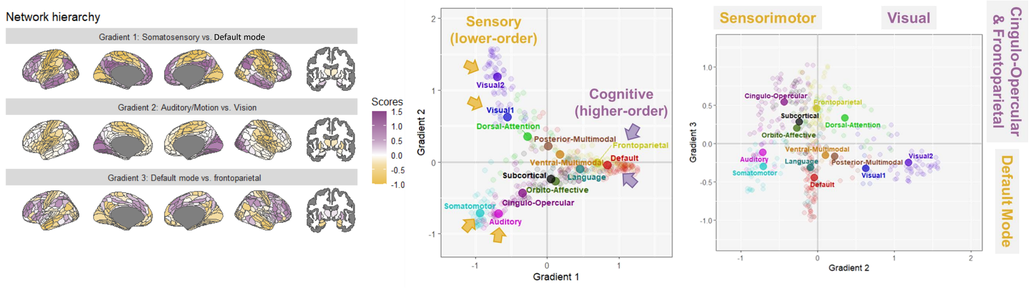
1. Introduction

Background

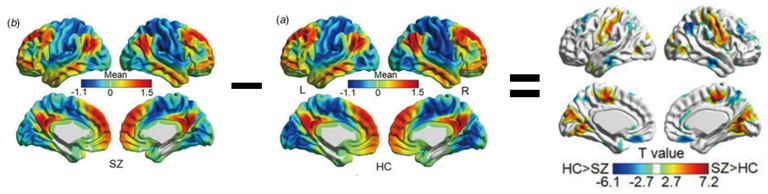
- Schizophrenia spectrum disorder (SSD) has been associated with dysconnectivity in cortical networks (Dong et al., 2018; Oliver et al., 2021)
  - Lower-order (e.g., visual, auditory) vs. higher-order (e.g., default mode, frontoparietal)
- **Principal gradients** (Margulies et al., 2016)
  - Diffusion map embedding
  - Characterizing network dysconnectivity
  - Based on resting-state functional connectivity



- Provides different levels of network stratification



- Dong et al. (2020) showed *compression* on Gradient 1 of SSD



(Dong et al., 2020)

Gradient compression: less distinct networks

Sensorimotor & Visual ⟵ ⟶ Default mode & Frontoparietal

- Such network dysconnectivity correlates with behaviours (Wang et al., 2020)
  - Negative and general, but not positive, symptoms
  - Processing speed

Aims

1. Does such **gradient compression in SSD** exist **beyond Gradient 1**?
2. Are there multivariate relationships between **gradient compressions** and **domains of *social*** and ***non-social*** **cognition** of SSD?

2. SPINS data

- Multi-site large sample study of social processes in SSD
  - 3 sites, 5 years
  - *N* = 466 (286 SSD, 180 matched controls)
  - Ages 18-59
  - Spectrum of social functions across SSDs and controls
- **Resting-state fMRI**
- **Cognitive measures:**

Social cognitive measures

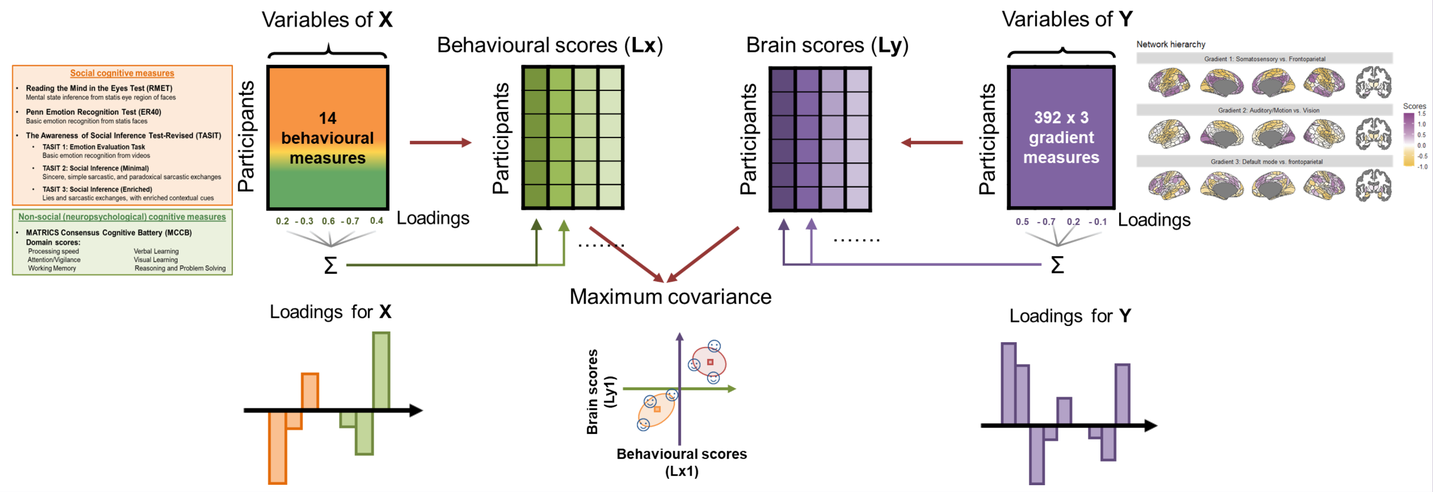
- **Reading the Mind in the Eyes Test (RMET)**
  Mental state inference from statis eye region of faces
- **Penn Emotion Recognition Test (ER40)**
  Basic emotion recognition from statis faces
- **The Awareness of Social Inference Test-Revised (TASIT)**
  - **TASIT 1: Emotion Evaluation Task**
    Basic emotion recognition from videos
  - **TASIT 2: Social Inference (Minimal)**
    Sincere, simple sarcastic, and paradoxical sarcastic exchanges
  - **TASIT 3: Social Inference (Enriched)**
    Lies and sarcastic exchanges, with enriched contextual cues

Non-social (neuropsychological) cognitive measures

- **MATRICS Consensus Cognitive Battery (MCCB)**
  Domain scores:
  Processing speed — Verbal Learning
  Attention/Vigilance — Visual Learning
  Working Memory — Reasoning and Problem Solving

- **Functioning and symptoms measures:**
  - Birchwood Social Functioning Scales (BSFS)
  - Quality of Life Scale (QLS)
  - Brief Psychiatric Rating Scale (BPRS)
  - SANS Negative Symptoms Scale (SANS)

3. Partial least square correlation (PLSC)



4. Results

- SSD group showed significant lower scores across *all* behaviour measures except for TASIT2 sincere.
- **Group differences in Gradients**: Control ⟶ SSD

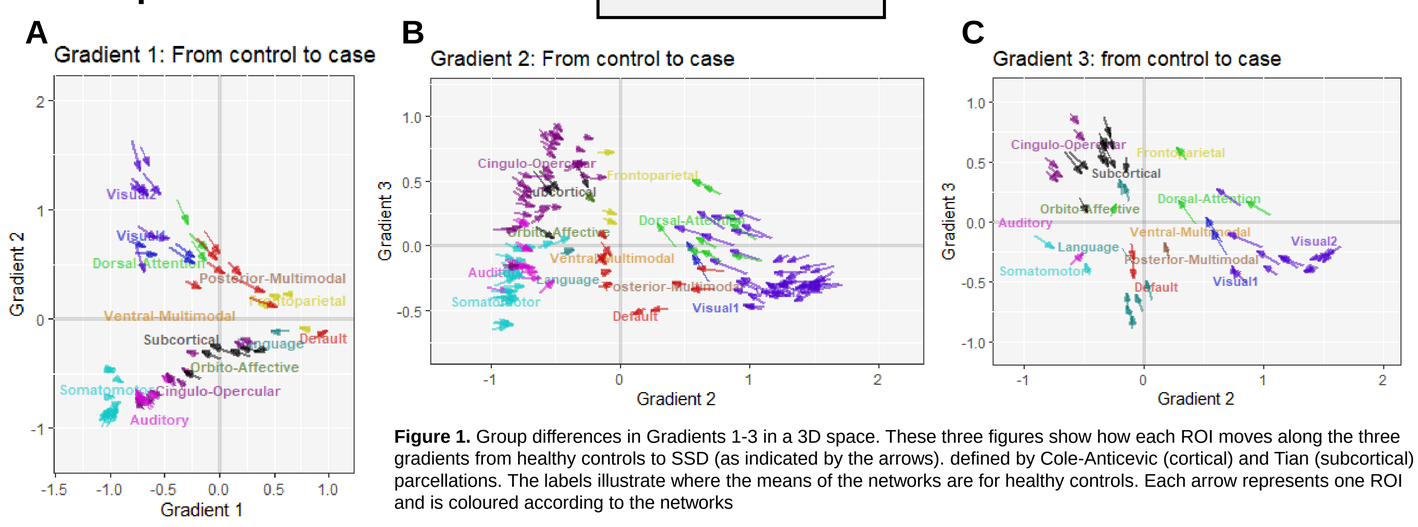
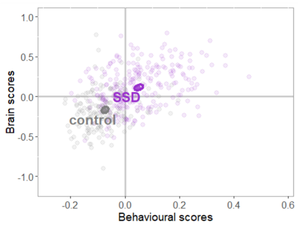


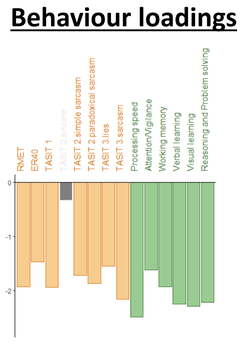
Figure 1. Group differences in Gradients 1-3 in a 3D space. These three figures show how each ROI moves along the three gradients from healthy controls to SSD (as indicated by the arrows). defined by Cole-Anticevic (cortical) and Tian (subcortical) parcellations. The labels illustrate where the means of the networks are for healthy controls. Each arrow represents one ROI and is coloured according to the networks

- **PLSC results** (Dimension 1; 67%)

A Latent variables

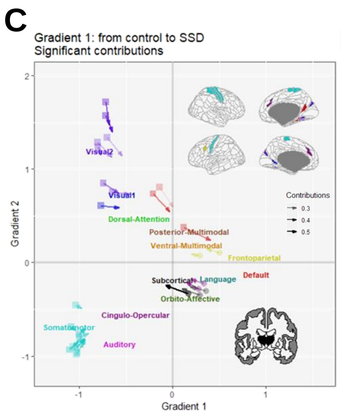


B Behaviour loadings



Gradients (shown in group effects) with significant contributions

C



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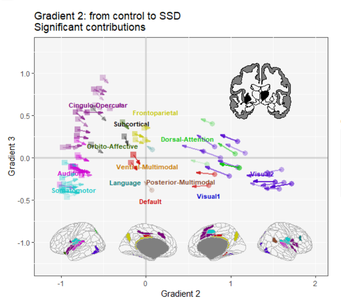

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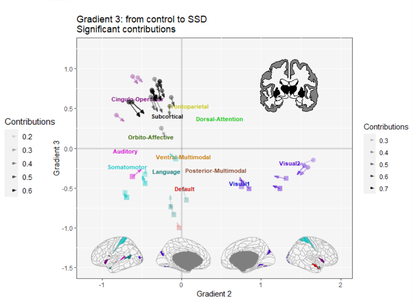
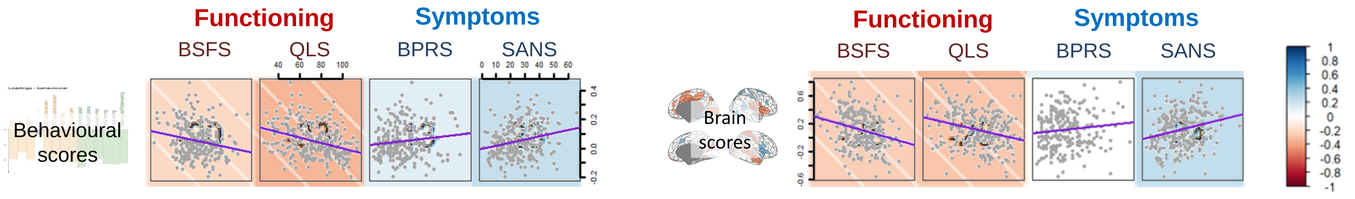


Figure 2. The latent variables of Dimension 1 are shown in **A** where SSD and health controls are significantly different according to bootstrap tests both according to the network hierarchy and to their cognitive measures. The loadings for the cognitive measures are shown in **B**. Because this dimension is characterised by the group difference, in **C**-**E**, we highlighted such group differences (indicated by the arrows) of the identified regions of interest (ROIs) on Gradients 1, **C**; 2, **D**; and 3, **E**). On these figures, each arrow indicates the change from controls to SSD. The shade of the arrows illustrates the amount of contribution, and the shape of the starting point illustrates the direction of how these ROIs load on the Dimension 1 of PLSC (i.e., positive as square and negative as circle). The labels illustrate where the means of the networks are for healthy controls.

- **Correlation tests between latent variables and clinical assessment** (FDR corrected)



5. Conclusion

- Compressions are found in all three gradients.
- The strongest network compressions related to social and non-social cognition are between networks of different perception modalities.
- Such network compression is related to negative symptoms, quality of life, and functioning in SSD.

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