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# Highlights

Inter-subject functional correlation (ISFC) isolates stimulus-induced brain network dynamics. "Intrinsic" networks, such as the default mode network, can be tightly locked to external drive. ISFC dramatically improves signal-to-noise ratio and is more robust to physiological confounds.

### How to Construct a Brain Network from MRI Data

### TARGET AUDIENCE

Clinicians and scientists with an interest in mapping brain networks in settings beyond pure resting state condition; clinicians and scientists who aim to gather brain network data that is robust to physiological confounds.

### **OBJECTIVES**

This lecture will demonstrate new approach to isolated stimulus-induced neural responses that are shared across individuals, allowing us to map large-scale brain networks and their dynamics in a precise and reliable manner.

# PURPOSE

Using present recording methods, it is difficult to separate the different factors that give rise to functional connectivity (FC): these factors include (i) physiological and instrumental noise, (ii) stimulus-induced neural processes and (iii) stimulus-independent neural processes. We introduce a method called *inter-subject functional correlation* (ISFC) which can isolate the networks arising from stimulus-induced neural processes.

# **METHODS**

Thirty-six subjects listened to a full 7-minute auditory narrative. Additionally, they listened to versions of the story in which different levels of coherence were preserved by reordering of words or of paragraphs.

During stimulus presentation, we recorded BOLD signal using at 3T full-body MRI scanner (Skyra; Siemens) with a sixteen-channel head coil. Functional images were acquired using a T2\* weighted echo planer imaging (EPI) pulse sequence [repetition time (TR), 1500 ms; echo time (TE), 28 ms; flip angle, 64°], each volume comprising 27 slices of 4 mm thickness with 0 mm gap; slice acquisition order was interleaved. In-plane resolution was 3×3 mm2 [field of view (FOV), 192×192 mm2].

ISFC was computed by correlating the response timecourse in one brain area in one individual against the response timecourses in all brain areas of all other individuals. ISFC was computed for all areas in all stimulus conditions. All analyses were replicated in a second set of subjects. Seeded ISFC analyses were performed both at a whole-brain voxelwise level, as well as in a set of regions-of-interest (ROIs) outlining the default mode network (DMN).

<u>**RESULTS</u>**: Using the ISFC approach, we find that:</u>

- (i) stimulus-induced brain networks resemble those observed during the resting state, but are much more precisely quantifiable and more sensitive to changes in external stimulus features;
- (ii) we can precisely and reliably track stimulus-induced network states over time, even in networks such as the DMN whose dynamics are considered to be stimulusindependent;
- (iii) the overall reliability of network dynamics in higher-order regions, including the DMN, increases monotonically with the semantic coherence of the stimulus.

The three results above are replicable across independent groups of subjects, and are preserved when correcting for confounding physiological factors such as breathing and heart rate. For a typical group of 18 subjects, we observe an increase in signal-to-noise ratio of more than 20 decibels, when decoding the stimulus-induced covariance pattern using ISFC rather than standard FC approaches.

<u>DISCUSSION</u>: The original view of DMN function was that it is involved with intrinsic processes such as mind wandering, stimulus-independent thought and self-referential mentation. More recent studies, however, have begun to implicate the DMN in high-level cognitive functions such as prospective and episodic memory, decision making and social reasoning, and self-generated thoughts. Using ISFC, one can demonstrate that the large-scale dynamics of the DMN can be precisely and reliably locked to the processing of an externally presented narrative.

More generally, the ISFC approach provides a tool for isolating brain networks, and network dynamics, that are locked to an external stimulus. This allows networks to be estimated with greater precision, in smaller time windows, and in a manner that is amenable to direct experimental manipulation by modifying the external stimulus.

<u>CONCLUSION</u>: Stimulus-induced network dynamics, mapped using ISFC, are highly sensitive to the semantic content of real-world stimuli. The ISFC method is a promising avenue for collecting functionally grounded brain network data in which specific network states are precise and replicable, with dramatically improved signal-to-noise.

There are two clinical implications of the ISFC approach. First, it provides a method for estimating brain network states in clinical populations that is more robust against population-level changes in breathing, heart rate, and arousal (see Tagliazucchi et al, 2012, for an example of how such confounds can affect clinical conclusions). Second, the ISFC provides a method for detecting abnormalities in wide-ranging brain networks (including higher order executive, attentional and mnemonic systems), by directly comparing the network responses in clinical groups against functional benchmarks obtained from healthy controls (see, for example, Hasson et al., 2009; Naci et al., 2014).

#### **REFERENCES**

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