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Individual differences in functional connectivity during naturalistic viewing conditions

Tamara Vanderwal[a,*], Jeffrey Eilbott[a], Emily S. Finn[a], R. Cameron Craddock[b,c], Adam Turnbull[a], F. Xavier Castellanos[d]

[a] Yale University, 230 South Frontage Road, New Haven, CT 06520, USA
[b] Child Mind Institute, 445 Park Avenue, New York, NY 10022, USA
[c] Nathan Kline Institute for Psychiatric Research, 140 Old Orangeburg Road, Orangeburg, NY 10962, USA
[d] Child Study Center at New York University Langone Medical Center, 1 Park Avenue, New York, NY 10016, USA

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ABSTRACT

Naturalistic viewing paradigms such as movies have been shown to reduce participant head motion and improve arousal during fMRI scanning relative to task-free rest, and have been used to study both functional connectivity and stimulus-evoked BOLD-signal changes. These task-based hemodynamic changes are synchronized across subjects and involve large areas of the cortex, and it is unclear whether individual differences in functional connectivity are enhanced or diminished under such naturalistic conditions. This work first aims to characterize variability in BOLD-signal based functional connectivity (FC) across 2 distinct movie conditions and eyes-open rest (n=31 healthy adults, 2 scan sessions each). We found that movies have higher within- and between-subject correlations in cluster-wise FC relative to rest. The anatomical distribution of inter-individual variability was similar across conditions, with higher variability occurring at the lateral prefrontal lobes and temporoparietal junctions. Second, we used an unsupervised test-retest matching algorithm that identifies individual subjects from within a group based on FC patterns, quantifying the accuracy of the algorithm across the three conditions. The movies and resting state all enabled identification of individual subjects based on FC matrices, with accuracies between 61% and 100%. Overall, pairings involving movies outperformed rest, and the social, faster-paced movie attained 100% accuracy. When the parcellation resolution, scan duration, and number of edges used were increased, accuracies improved across conditions, and the pattern of movies > rest was preserved. These results suggest that using dynamic stimuli such as movies enhances the detection of FC patterns that are unique at the individual level.

1. Introduction

As psychiatric research has shifted towards a dimensional conceptualization of symptoms and behaviors (Insel et al., 2010), neuroimaging has expanded to include brain-based characterization at the individual level (Arbabshirani et al., 2013). Despite the reliability of BOLD-signal based functional connectivity (FC) patterns across individuals and testing sessions (Damoiseaux et al., 2006; O'Connor et al., 2016; Shehzad et al., 2009; Yeo and Krienen et al., 2011; Zuo et al., 2010), FC relationships have also been shown to capture significant inter-individual variability, generating optimism for their eventual use as biomarkers of mental illness (Finn and Shen et al., 2015; Gordon et al., 2017; Rosenberg et al., 2016; Shen et al., 2017). Recent work has begun to characterize the spatial and state-based aspects of individual differences in FC. The current study tests whether individually unique patterns of FC can be detected when the brain engages in the complex, dynamic processing that occurs when watching movies. We also examine multiple aspects of FC variability to better understand what factors might contribute to the detection of individually distinct FC patterns under naturalistic conditions.

1.1. Spatial distribution of FC variability

Functional neuroimaging data sets containing retest scans have been leveraged to investigate inter-individual variability in FC patterns, after regressing out intra-individual variability. Mueller et al. demonstrated that this residual variability in FC was greatest in association cortex including lateral prefrontal regions and the temporoparietal junction (Mueller et al., 2013). Unsurprisingly, unimodal sensory and motor regions were the least variable across subjects. At the network

* Corresponding author.
E-mail address: tamara.vanderwal@yale.edu (T. Vanderwal).

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level, frontoparietal and ventral attention networks exhibited the largest variability in FC, followed next by the default and dorsal attention networks. This pattern of results was subsequently confirmed independently (Chen et al., 2015).

A second wave of studies extended these findings by using unsupervised test-retest sorting algorithms to match pairs of FC matrices that belong to a single subject from a group of FC matrices. Just as the Mueller approach above relied on the relationship between inter- and intra-subject variability, these matching algorithms require that a subject's intra-subject FC correlation be greater than that same subject's inter-subject FC correlation with every other subject (Airan et al., 2016; Finn and Shen et al., 2015). Using large samples from different publicly available databases, both studies demonstrated the important finding that group-level variability contains differences that are unique and reliable at the individual subject level. Further, they showed that the majority of FC edges that contributed to the successful identification of individuals from within a group were located in heteromodal cortex including the frontoparietal, default, and attentional networks.

1.2. Collection states and FC variability

The effects of acquisition conditions on FC continue to be examined and debated (Arbabshirani et al., 2013; Cole et al., 2014; Mennes et al., 2013). The question in the current context is whether inter-individual differences in FC are more robust under less constrained states such as rest versus tasks. Shah and colleagues showed that individual patterns in FC were preserved across multiple task and rest conditions (Shah et al., 2016). Finn, Shen and colleagues showed that when using an FC-based identification (i.e., matching) algorithm, the maximal accuracy (94%) was attained when using rest-rest correlations; accuracy decreased to 54–87% when using rest-task or task-task correlations, suggesting that individual differences are more easily identified during less constrained states, but are still present in task-based FC data. These studies indicate that inter-individual differences in FC are not abolished when using tasks, at least when the tasks are conventional and discrete such as were used in these studies.

Though the number of studies is currently limited, different results have been demonstrated using more complex, naturalistic tasks. For example, Geerligs and colleagues investigated inter-individual variance during movie watching using a Hitchcock film (*Bang! You're Dead*) (2013). This study showed that the least amount of overlap and the highest amount of FC variance occurred within the movie-task comparison relative to both the movie-rest and task-rest comparisons, suggesting that perhaps movies have a unique effect on FC patterns. To date, it remains unclear which collection states might be most advantageous for the study of FC patterns that are distinct at the individual level.

1.3. Movies and FC variability

Due to the significant improvement in compliance regarding head movement and arousal levels conferred by movie watching in the scanner (Vanderwal et al., 2015), we wanted to evaluate the effects of movie watching on BOLD-signal based FC variability. The present study used two distinct movie-watching conditions (one complex social movie and our low-processing abstract movie) and eyes-open rest. Sequence parameters were kept constant across conditions, and rigorous motion thresholds and correction procedures were used. The study is divided into two parts. First, we characterize multiple aspects of FC variability, including analyses of variance across collection states, measures of within- and between-subject correlations of FC, and the spatial distribution of inter-individual variability of FC. Based on these cross-condition comparisons of variability, we predicted that movies would enhance the ability to detect individual differences in FC that are unique at the individual level. The second part of the study tested this hypothesis. We ran an unsupervised test-retest matching algorithm that used FC matrices to identify individual subjects from among a group. We also ran the algorithm using different parcellation resolutions, acquisition durations, and percentages of edges used to test whether these factors differentially affected the two types of movies and rest. The primary outcome was the accuracy of the identification algorithm across the three conditions. As such, this study is the first to show the spatial distribution of inter-individual variability under naturalistic viewing conditions and to report accuracies of an FC-based identification algorithm using movies.

2. Materials and methods

2.1. Data collection

Participants. Healthy right-handed adults were recruited from the community. Exclusion criteria included neurological or psychiatric diagnoses, use of centrally acting medications, heavy alcohol use, illicit drug use in the past 6 months, cardiovascular disease, significant visual or hearing impairment, and self-reporting less than six hours of sleep per night. Forty-six participants completed two testing sessions with a one-week interval, and 12 participants self-reported falling asleep during one or both sessions and were excluded from further analysis. Three additional subjects were excluded for having fewer than 50% volumes remaining after scrubbing procedures (see below), leaving our final cohort at n = 31 (17 females, mean age 24.5 +/− 5.3 years). Data from a subset (n = 22) were published previously (Vanderwal et al., 2015). All participants gave written consent and were compensated for their participation. The study was approved by the Human Investigations Committee at Yale University School of Medicine.

2.1.1. Procedure

Imaging was performed on a Siemens Trio 3-Tesla scanner with a 32-channel head coil. Standard structural images used an MP-RAGE sequence (TR=1900 ms, TE=2.52 ms, TI=900 ms, flip angle=9°) yielding 1 mm^3 voxel size. Functional data were collected using a single shot echo planar imaging sequence (TR=2500 ms, TE=30 ms, flip angle=80°, voxel size=3 mm isotropic) across 38 slices. All participants completed 3 functional scans during which stimuli were presented via E-Prime software, version 2.0 (Psychology Software Tools, Pittsburgh, PA). Images were back-projected onto a screen that participants viewed via a mirror mounted on the head coil. Sound-reducing headphones over protective earplugs enabled participants to hear the soundtracks. Three 7 min and 20 s conditions included *Inscapes*, a nonverbal, nonsocial series of slowly evolving abstract shapes with a piano score (detailed description of this movie is provided in Vanderwal et al., 2015), a clip from the movie *Ocean's Eleven* (Warner Brothers, 2001, directed by Steven Soderbergh) referred to here as Oceans, and Rest (see Fig. 1). Condition order was counter-balanced across participants. Each condition started and ended with 10 s of fixation; the first 10 s were dropped for all analyses. Participants were asked to watch the screen and to stay as still as possible during each condition. Foam wedges were fitted around the participant's head for comfort and to decrease movement. Retest sessions occurred 1 week later at the same time slot whenever possible. Six participants had different time slots for scan 1 and scan 2, but the 1-week interval was maintained.

2.1.2. Data preprocessing

Standard data preprocessing was performed using the Configurable Pipeline for the Analysis of Connectomes (C-PAC) including motion realignment and transformation into Montreal Neurological Institute (MNI) space using Advanced Normalization Tools (ANTS) (Avants et al., 2008). ANTS employs a series of sequential transformations to optimize image registration, beginning with a rigid and affine linear transformation and ending with a nonlinear diffeomorphic transform (Symmetrical Normalization or SyN) that maximizes the cross-correla-