Network connectivity correlates of variability in fluid intelligence performance

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ABSTRACT

Abstract reasoning requires a pattern of spatial and temporal coordination among regions across the entire brain. Recent evidence suggests a very high similarity between spontaneous and evoked brain activity in humans, implying that a fine characterization of brain dynamics recorded during resting-state might be informative for the understanding of evoked behavior. In a recent work, we listed and detailed the sets of regions showing robust co-activation during the solution of fluid intelligence (*gf*) tasks, decomposing such meta-analytic maps in stimulus- and reasoning stage-specific sub-maps. However, while anatomical overlap with well-known resting-state fMRI networks (RSNs) has been documented, we here propose a quantitative validation of such findings via functional connectivity analysis in a sample of healthy participants. Results highlight a striking degree of similarity between the connectivity profile of the *gf* network and that of the dorsal attention network, with additional overlap with the left and right fronto-parietal control networks. Interestingly, a strong negative correlation with structures of the default mode network (DMN) was also identified. Results of regression models built on two independent fMRI datasets confirmed the negative correlation between *gf* regions and medial prefrontal structures of the DMN as a significant predictor of individual *gf* scores. These might suggest a framework to interpret previously reported aging-related decline in both *gf* and the correlation between "task-positive" networks and DMN, possibly pointing to a common neurophysiological substrate.

1. Introduction

Fluid intelligence (*gf*) represents the ability to solve problems regardless of previously acquired knowledge (Cattell, 1963). This ability contributes to efficient encoding of new information and its manipulation, constituting a pivotal component of human cognition with strong predictive power over both educational and professional success (Deary, 2008). At the same time, *gf* also represents one of the most elusive cognitive constructs, where theoretical and psychometric definitions have challenged scientists for half a century. While its theoretical definition seems challenging, with theories suggesting both uni- and multi-factorial nature of *gf*, its neurobiological underpinnings are probably even less understood. Modern technologies in neuroscience allow researchers to investigate brain activity at different spatial and temporal scales, allowing for inference about what, where, when and how *gf* resides in the human brain. Studies have provided correlates at the structural level, showing *gf*-related variability in the shape and volume of gray and white matter structures (Colom et al., 2009, 2013). Hypotheses about metabolic correlates of *gf* have been proposed as well, with evidence of a counterintuitive decrease in brain activity in higher *gf* individuals; a concept now well-accepted in the framework of a brain efficiency theory of intelligence (Haier et al., 1988). Studies investigating electrical brain activity using electroencephalography (EEG) have shown correlations with activity in specific frequency bands (Thatcher, Palmero-Soler, North, & Biver, 2016), as well as the importance of the coupling between multiple brain oscillatory patterns (Anja Pahor & Jaušovec, 2014). Finally, works looking at both evoked and spontaneous brain activity using functional magnetic resonance

imaging (fMRI) (Cole, Yarkoni, Repovs, Anticevic, & Braver, 2012; Ebisch et al., 2012; Geake & Hansen, 2005, 2010; Preusse, Meer, Deshpande, Krueger, & Wartenburger, 2011), (Hearne, Mattingley, & Cocchi, 2016), have shown the relevance of a network of regions belonging to a so-called "parieto-frontal" network. This network, mostly involving brain regions of the prefrontal and parietal lobes bilaterally (Colom et al., 2013) (Vakhtin, Ryman, Flores, & Jung, 2014), resembles the map supporting the *parieto-frontal integration theory* (P-FIT) of general intelligence by Jung and Haier (2007), advancing the field a step closer to understanding the brain functional correlates of *gf*.

Recently, a fine characterization of such networks has been also proposed via a quantitative meta-analysis, including different anatomo-functional maps representing *gf*-related processing at the cortical and subcortical levels. The maps also include sub-maps specifically showing average brain activations for different types of reasoning (e.g. verbal vs visuospatial), those crucially recruited where more challenging trials are faced, as well as those engaged in different processing stages (i.e. Rule inference and Rule application) (Santarnecchi, Emmendorfer, & Pascual-Leone, 2017). This might help define within- and between-network dynamics subtending *gf* abilities, as well as targets for cognitive training (Anguera & Gazzaley, 2015) and brain stimulation interventions (Filmer, Dux, & Mattingley, 2014; Santarnecchi et al., 2015).

However, while such an anatomo-functional atlas of evoked activity provides useful information for understanding the brain correlates of *gf*, recent studies have also shown links between individual variability in *gf* abilities and the spontaneous organization of brain activity, as the one measured within the framework of functional connectivity functional magnetic resonance imaging (fMRI) analysis (van den Heuvel & Hulshoff Pol, 2010). Looking at the brain's spontaneous patterns of metabolic activity might be informative about - and even predict - individual evoked activity during sensorimotor and cognitive tasks (Fox et al., 2005), (Allen et al., 2014; Finn et al., 2015; Shirer, Ryali, Rykhlevskaia, Menon, & Greicius, 2012). Such intrinsic activity is thought to reflect not only the past experiences of each individual brain as a complex system, but it also forms the functional foundation from those evoked patterns which the brain will generate for future goal-oriented behavior (Tavor et al., 2016). Differently from canonical task-fMRI paradigms, where the signal is derived by contrasting brain activity during active and passive states, this approach relies on endogenous brain oscillations recorded during spontaneous brain activity, giving rise to a complex pattern of temporally and spatially independent resting-state networks (RSN) (Biswal et al., 2010). Such intrinsic organization of spontaneous brain activity is captured within the framework of brain connectivity analysis (Achard & Bullmore, 2007). Individual functional connectivity profiles have been proven reliable over multiple sessions (Braun et al., 2012), (Choe et al., 2015), holding enough information to identify pathological conditions (e.g. multiple sclerosis (Bonavita et al., 2016), schizophrenia (Bassett et al., 2008) and Alzheimer (Agosta et al., 2012)) as well as brain correlates of several cognitive (Santarnecchi, Polizzotto, Rossi, & Rossi, 2014), (Santarnecchi, Rossi, & Rossi, 2015; Yuan et al., 2012) and psychological traits (Adelstein et al., 2011).

An overview of the role played by regions activated during different *gf* tasks with respect to existing RSNs is not available to date, with recent meta-analytic data suggesting a major contribution by regions of the attention, salience and fronto-parietal control networks (Santarnecchi et al., 2017). However, thiss evidence, based on anatomical overlay between group-level RSNs maps and meta-analytic *gf* maps (using the activation likelihood estimate – ALE method), does not provide a comparison of actual functional connectivity patterns in humans and must be validated using real fMRI data. These, among other questions, should be answered: (i) Does the network of brain regions activated during *gf* problem-solving also constitute a functional network of positively correlated nodes at rest? (ii) Does the functional

profile of *gf* activation maps resemble those of specific RSNs? (iii) If yes, which RSNs show higher similarity? Finally, (iv) are the different meta-analysis maps generated for *gf* also different in terms of their respective functional connectivity patterns? To address these questions, we analyzed resting-state fMRI data from a dataset of healthy participants. We quantitatively compared the functional connectivity profile of the meta-analytic *gf* (ALE) networks and well-known RSNs using a similarity index, also looking at intra- and inter-network dynamics by means of canonical functional connectivity metrics and topographical measures related to modularity and centrality. We predicted *gf* regions to be positively correlated at rest, to show similarity with cognitive networks such as the fronto-parietal control network (FPCN) and the dorsal attention network (DAN), as well as a negative correlation with the default mode network (DMN).

Moreover, given the link between evoked and spontaneous fMRI activity (Tavor et al., 2016), we hypothesized that the spontaneous activity of regions belonging to the ALE task-fMRI *gf* network would explain variability in behavioral *gf* scores. Therefore, separate regression models based on two independent fMRI datasets collected at Harvard Medical School (Boston, MA, USA) and University of Siena School of Medicine (Siena, Italy) were built, predicting individual *gf* abilities on the basis of seed-based connectivity patterns of the *gf* network.

2. Methods

2.1. Connectivity profile of the gf-network

The characterization of the functional connectivity profile of regions of the *gf* network (as described in (Santarnecchi et al., 2017), was based on data from the freely available dataset INDI-NKI Rockland, including structural and functional MRI data of 207 healthy participants (age 8 to 82). From the NKI-Rockland database, a selection of subjects was made to ensure *(i)* an age range between 18 and 55 years old (to focus on healthy adult individuals), *(ii)* an equal number of males and females, given the evidence of interactions between biological sex and intellectual abilities (Haier, Jung, Yeo, Head, & Alkire, 2005), *(iii)* an equal distribution of age groups (i.e. participants per decade) and *(iv)* that all subjects were right-handed. The selection resulted in a final sample of 130 right-handed subjects (69 males), with mean age of 36 years (range 18–55, SD = 13). Each contributor's respective ethics committee approved submission of de-identified data to be implemented into the ICBM dataset in the 1000 Functional Connectomes Project. The institutional review boards of NYU Langone Medical Center and New Jersey Medical School approved the receipt and dissemination of the data (Song et al., 2012). Details about the MRI protocols and preprocessing procedures are included in the supplementary materials.

2.2. Meta-analytic gf maps and regions of interests

We included meta-analytic maps based on activation likelihood estimate (ALE) technique as published in (Santarnecchi et al., 2017) and available at (http://www.tmslab.org/SantaLab.php/). Information about anatomical localization of each cluster and their meaning is provided in the original report. Each map is available as a nifti (nii) volumetric file in MNI space; both network and single node level maps are provided. Specifically, the following maps were used: main fluid intelligence (*gf*); *gf* activation for verbal (v*gf*) and visuospatial (vs*gf*) stimuli; activation during more challenging trials (higher complexity, HC); fMRI activation while participants infer the organizational principle of a given trial (Rule inference phase, RI) as well as when the newly inferred rule is applied to novel stimuli (Rule application phase, RA).

For RSNs, binary spatial maps were used following the scheme by Shirer et al. (2012), thus defining 14 non-overlapping maps