Neurobiology of Aging 34 (2013) 1925–1934

Contents lists available at SciVerse ScienceDirect

Neurobiology of Aging

journal homepage: www.elsevier.com/locate/neuaging

Functional brain connectivity and cognition: effects of adult age and task demands

Ying-hui Chou [a], Nan-kuei Chen [a,b], David J. Madden [a,c,d,*]

[a] Brain Imaging and Analysis Center, Duke University Medical Center, Durham, NC, USA
[b] Department of Radiology, Duke University Medical Center, Durham, NC, USA
[c] Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC, USA
[d] Center for Cognitive Neuroscience, Duke University, Durham, NC, USA

ARTICLE INFO

Article history:
Received 16 March 2012
Received in revised form 9 February 2013
Accepted 15 February 2013
Available online 21 March 2013

Keywords:
Brain connectivity
fMRI
Resting state
Default mode
Behavior-based connectivity analysis
Aging
Attention
Cognition
Visual search
Reaction time

ABSTRACT

Previous neuroimaging research has documented that patterns of intrinsic (resting state) functional connectivity (FC) among brain regions covary with individual measures of cognitive performance. Here, we examined the relation between intrinsic FC and a reaction time (RT) measure of performance, as a function of age group and task demands. We obtained filtered, event-related functional magnetic resonance imaging data, and RT measures of visual search performance, from 21 younger adults (19–29 years old) and 21 healthy, older adults (60–87 years old). Age-related decline occurred in the connectivity strength in multiple brain regions, consistent with previous findings. Among 8 pairs of regions, across somatomotor, orbitofrontal, and subcortical networks, increasing FC was associated with faster responding (lower RT). Relative to younger adults, older adults exhibited a lower strength of this RT-connectivity relation and greater disruption of this relation by a salient but irrelevant display item (color singleton distractor). Age-related differences in the covariation of intrinsic FC and cognitive performance vary as a function of task demands.

1. Introduction

Event-related functional magnetic resonance imaging (fMRI) studies measure the brain activation associated with a behavioral task by contrasting the blood oxygen level-dependent (BOLD) signal during on-task periods with the BOLD signal during a baseline or control condition. Over the past decade, researchers have directed increased attention to the baseline activity of the brain that can be measured without requiring participants to perform a perceptual or behavioral task. During an awake but resting state, spontaneous, low-frequency (less than 0.08 Hz) fluctuations in the BOLD signal occur that are temporally coherent among spatially distinct brain regions (Biswal et al., 1995). The interregional temporal correlations, referred to as intrinsic functional connectivity (FC) represent neuronal activity that is intrinsically generated by the brain (Shmuel and Leopold, 2008; Shmuel et al., 2002). Reliable measures of intrinsic FC can be obtained both from "pure" resting-state periods (i.e., those without a behavioral task) and from task-related BOLD data in which the higher frequency temporal components have been attenuated (Fair et al., 2007; Van Dijk et al., 2010).

Using either predefined regions of interest (Biswal et al., 1995; Greicius et al., 2003) or whole-brain methods such as independent component analysis (Esposito et al., 2008; Greicius et al., 2004; McKeown et al., 1998), researchers have identified a default mode network (DMN), which includes a set of brain regions (in particular, medial prefrontal, posterior cingulate, lateral parietal, and parahippocampal cortex) that consistently show highly correlated brain activity during resting state and a reduced level of task-related activation, with BOLD signal level often below baseline, across a wide range of tasks (Biswal et al., 2010; Buckner et al., 2008; Fox and Raichle, 2007; Greicius et al., 2003; Raichle and Snyder, 2007; van den Heuvel and Hulshoff Pol, 2010). Other networks of brain regions, however, outside of the DMN, also exhibit coherent intrinsic connectivity, and these networks appear to support specific domains of cognitive performance (Allen et al., 2011; Anderson et al., 2011; Dosenbach et al., 2007; Fox et al., 2007; Laird et al., 2011; Vincent et al., 2008). For example, Salvador et al. (2005) used hierarchical clustering to analyze resting state data and obtained 6 large clusters corresponding approximately to 4 neocortical systems, plus temporal lobe and subcortical systems. A recent,

* Corresponding author at: Brain Imaging and Analysis Center, Box 2737, Hock Plaza, Duke University Medical Center, Durham, NC 27710, USA. Tel.: +1 919 681 9345; fax: +1 919 681 7033.
E-mail address: madden@biac.duke.edu (D.J. Madden).

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http://dx.doi.org/10.1016/j.neurobiolaging.2013.02.012

seminal study by Yeo et al. (2011) characterized the organization of large-scale distributed networks, based on analyses of resting state data from 1000 healthy, young adults. These authors applied clustering algorithms to the resting state data that yielded either 7 or 17 networks of functionally connected regions, depending on the level of resolution. Resting state network structure is constrained by anatomical connectivity (Damoiseaux and Greicius, 2009; He et al., 2012; Ystad et al., 2011), and aspects of intrinsic FC might be predictive of specific forms of neurodegenerative disease (Bano et al., 2011; Greicius et al., 2004; Hafkemeijer et al., 2012; Hedden et al., 2009; Zhou et al., 2012).

In this experiment, we investigated age-related differences in intrinsic FC for healthy, community-dwelling adults. Research on aging and the brain has focused primarily on atrophy and related tissue-integrity measures from structural imaging (Fjell and Walhovd, 2010; Madden et al., 2012; Raz, 2005; Salat, 2011) and task-related cortical activation from functional imaging (Dennis and Cabeza, 2008; Grady, 2008). Recent studies have also demonstrated that age-related differences in cognitive performance (typically, worse performance by older adults) are associated with the balance in the overall level of activity in the DMN relative to 1 or more task-related networks (Grady et al., 2010, 2012; Lustig et al., 2003; Park et al., 2010). The degree of intrinsic FC, both within the DMN and within other resting state networks, exhibits age-related differences, predominantly decreased connectivity strength for older adults relative to younger adults (Allen et al., 2011; Andrews-Hanna et al., 2007; Biswal et al., 2010; Damoiseaux et al., 2008; Ferreira and Busatto, 2013; Meier et al., 2012a; Tomasi and Volkow, 2012). For younger adults, an increasing degree of intrinsic FC, either within the DMN or within other, task-relevant networks, is generally associated with better cognitive performance (Baldassarre et al., 2012; Meier et al., 2012b; Seeley et al., 2007). This principle also holds true for older adults (Andrews-Hanna et al., 2007; Campbell et al., 2012; Chen et al., 2009; Dong et al., 2012), but few direct assessments of potential differences between younger and older adults in the relation between intrinsic FC and cognitive performance have been conducted.

This research extends previous work by Chen et al. (2009), who developed a whole-brain, behavior-based connectivity analysis (BBCA) to identify sets of regions whose level of intrinsic FC covaries with behavioral performance. The BBCA method integrates behavioral data at an early stage of processing and evaluates the covariation between performance and intrinsic FC between regions across the complete data set, without a priori selection. Thus, rather than relating a behavioral measure to FC from a predefined network or seed region (Andrews-Hanna et al., 2007; Campbell et al., 2012; Meier et al., 2012b), BBCA identifies all pairs of regions whose connectivity covaries with the behavioral measure, regardless of whether the regions are located within the same or different networks.

Chen et al. (2009) found that a widely distributed group of regions, comprised primarily of orbitofrontal regions, exhibited intrinsic FC that covaried with 1 measure of perceptual motor speed and choice reaction time (RT), but that the relation between RT and connectivity varied significantly across 2 adult age groups: the older adults, but not the younger adults, exhibited significantly increased FC in relation to faster responses (i.e., a negative correlation between RT and connectivity). Further, within the older adult group, individual differences in FC accounted for 87% of the variance in RT associated with age, suggesting that FC of these regions has an important role in age-related cognitive slowing.

The outcome measure in the BBCA analysis of Chen et al. (2009) was a single measure of elementary perceptual speed (choice RT). Other previous studies of age-related differences in the connectivity–performance relation have also relied on a univariate measure of cognitive performance (Andrews-Hanna et al., 2007; Dong et al., 2012; but see Campbell et al., 2012; Grady et al., 2010, 2012). In the present study, we sought to extend these previous findings using BBCA to investigate age-related differences in the connectivity–performance relation, in the context of task-dependent changes in RT. Specifically, we sought to identify age-related differences in the relation between intrinsic FC and RT, across different task conditions involving visual search for a target shape among nontarget (distractor) shapes. Behavioral studies of visual search and discrimination tasks have demonstrated that age-related decline occurs in some aspects of the information processing mechanisms underlying visual search, particularly those related to the efficiency of perceptual encoding and motor control (Hommel et al., 2004; Madden and Whiting, 2004; Madden et al., 1999; McAvinue et al., 2012). Other aspects of visual search performance, however, related to the ability to guide visual search based on task goals and context (i.e., top-down attention) demonstrate substantial preservation as a function of adult age (Madden, 2007; Madden et al., 2007). In this experiment, we sought to examine whether we could detect variations in the relation between intrinsic FC and RT, in relation to age group and the task demands of visual search.

We investigated a form of visual search in which target detection is typically highly efficient, a feature search task in which the target is always a shape that is different from all of the distractor shapes (e.g., search for a vertical bar among circles). Reaction time in feature search is usually constant as a function of the number of items in the display, indicating efficient target detection (Leber and Egeth, 2006; Wolfe et al., 2003), and this pattern holds for both younger and older adults (Plude and Doussard-Roosevelt, 1989; Whiting et al., 2005). The search task included elements of both top-down attention, in terms of the predictability of the target shape, and distraction, in terms of the presence of a visually salient nontarget display item. Our goal was to determine, for brain regions exhibiting covariation between intrinsic FC and search RT, whether this covariation changed as a function of the search task conditions.

The analyses proceeded from 3 general predictions. First, we hypothesized that older adults would show reduced strength in intrinsic FC, independently of behavior, relative to the younger adults (Allen et al., 2011; Andrews-Hanna et al., 2007; Biswal et al., 2010; Damoiseaux et al., 2008; Ferreira and Busatto, 2013; Meier et al., 2012a; Tomasi and Volkow, 2012). Second, we predicted that, overall, increased FC would be associated with improved behavioral performance (Baldassarre et al., 2012; Meier et al., 2012b; Seeley et al., 2007), in this case, lower RT. Our third hypothesis was that, for regions exhibiting a relation between FC and RT, the relation would vary in response to age group and task demands. In particular, in view of age-related decline in the efficiency of perceptual encoding and motor control (Hommel et al., 2004; Madden and Whiting, 2004; Madden et al., 1999; McAvinue et al., 2012), the demands of target detection and avoiding distraction from salient nontargets should influence the RT–connectivity relation more for older adults than for younger adults.

2. Methods

2.1. Participants

Forty-two right-handed participants included 21 younger adults between 19 and 29 years of age (mean [M] = 21.70, SD = 2.89 years; 12 women) and 21 older adults between 60 and 87 years of age (M = 69.24, SD = 5.62 years; 11 women). Participants scored a minimum of 27 points on the Mini Mental State Exam (Folstein