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Age effect on the default mode network, inner thoughts, and cognitive abilities

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ABSTRACT

Age-related effects on the default mode network (DMN) connectivity as measured at rest using functional magnetic resonance imaging (fMRI) are now well described. Little is known however about the relationships between these changes and age-related effects on cognition or on the unconstrained thoughts which occur during the resting-state scan, called inner experience. Brain resting-state activity, inner experience, and cognitive ability measurements were obtained in 70 participants aged 19–80 years. The anterior-posterior disruption of DMN activity with age reported in previous studies was recovered here. A significant effect of age was also found on cognitive abilities but not on inner experience. Finally, age-related changes in DMN connectivity were found to correlate with cognitive abilities, and more specifically with autobiographical memory performance. These findings provide new information to fuel the debate on the role of the brain default mode and more specifically on the effect of age-related changes in resting-state activity as measured with fMRI.

1. Introduction

Brain resting-state connectivity, as assessed with functional magnetic resonance imaging (fMRI), refers to interregional synchrony of low frequency fluctuations (Biswal et al., 1995; see Deco et al., 2011 for a review). Brain regions showing such synchronous activity constitute a network and multiple large-scale spatially distributed networks can be detected at rest (see Van den Heuvel and Hulshoff Pol, 2010 for a review). The development and changes of resting-state networks is an ongoing process across the human lifespan. Thus, anatomic segregation followed by functional integration processes allow the emergence of resting-state networks from early childhood to early adulthood. These networks are first organized by anatomic proximity, and progressively in a distributed manner across the brain (see Power et al., 2010 for a review). Then, normal aging induces resting-state activity changes so that older adults are characterized by connectivity modifications within these networks (Meunier et al., 2009). The default mode network (DMN) is the resting-state network that received the greatest attention, as it was the first described, and contains brain regions critical for several cognitive functions and/or particularly sensitive to neurodegenerative diseases such as Alzheimer's disease (see Buckner et al., 2008 for a review; Damoiseaux et al., 2012; Greicius et al., 2004). Indeed, the DMN includes the ventral medial prefrontal (vmPFC), anterior and posterior cingulate (PCC) cortices, as well as the precuneus, the inferior parietal cortices/angular gyri, and the hippocampi. It has been consistently shown that normal aging induces a connectivity disruption within the DMN, more specifically along the anterior-posterior axis of this network. According to this, decreases in coactivation between posterior regions, such as PCC, and anterior areas have been often reported in elderly (Andrews-Hanna et al., 2007; Biswal et al., 2010; Grady et al., 2010; Jones et al., 2011; Meunier et al., 2009; Wu et al., 2011). Note that none of these studies assessed linear versus nonlinear age effects across the entire adulthood, because they did not include middle-aged participants or only tested linear effects.

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Though changes with age in DMN connectivity have been described in several studies, the behavioral correlates of these changes remains largely unknown. There is a rich debate in the literature about the cognitive role of the DMN (see Buckner and Carroll, 2007; Mevel et al., 2011 for reviews; Spreng et al., 2009 for a meta-analysis), but it is still unclear whether the (co)activity of the DMN nodes either reflects the participant's mental content during the scan, called inner experience in what follows, or rather represents the brain base functioning of the individual, independent from the inner experience during the scan but potentially related to cognitive abilities. According to its specific topography, the DMN has been compared with several well-known networks. For instance, Buckner and Carroll (2007) underlined the remarkable similarity between the DMN and self-projection-related networks such as remembering, theory of mind, or prospection networks. Considering each region of the DMN separately, this network could be associated not only with the cognitive functions listed above but also to mental imagery or to the attention processes required for the monitoring of the external environment when focused attention is relaxed. Several studies have been conducted in young individuals, that reported a relationship between resting-state network activity and inner experience (Doucet et al., 2012), daydreaming (Mason et al., 2007), or cognitive performance including episodic memory (Wang et al., 2010b), and executive function (Seeley et al., 2007). As for the specific question of the links between age-related DMN changes and behavioral measures, previous studies reported a relationship in older subjects between connectivity of (1) the hippocampus in medial parietal areas; and (2) medial prefrontal in inferior parietal DMN areas, and episodic memory retrieval but not nonmemory performance (i.e., global functioning, processing speed, and executive function; He et al., 2012; Wang et al., 2010a). Conversely, decreased shifting performance in older adults has been shown to be associated with activity fluctuations in more anterior parts of the DMN (Damoiseaux et al., 2008), and in the whole executive-control network (Gour et al., 2011). However, there has been no study to date comparing the relationships between the functional connectivity within the main DMN nodes and both inner experience and cognitive abilities in normal aging. Consequently it is still unknown whether age-related changes in DMN activity rather reflect modifications in inner experience, decreases in cognitive performance, or both.

The main goal of this study was thus to determine whether age-related changes in DMN connectivity are paralleled by changes with age in inner experience and/or cognitive abilities within a sample of healthy volunteers covering the whole adult lifespan. We hypothesized that the age-related changes in DMN connectivity, assumed to involve a disruption between anterior and posterior brain DMN areas, would be associated with age-related changes in the inner experience during the scan and/or in cognitive performance.

2. Methods

2.1. Participants

Healthy subjects were enrolled in this study after detailed clinical and neuropsychological examinations. They were screened for the lack of abnormalities according to stringent inclusion/exclusion criteria including (1) normal somatic examination; (2) body mass index in the normal range; (3) no known vascular risk factor and smoking less than 10 cigarettes per day; (4) no alcohol or drug abuse; (5) blood pressure within normal limits; (6) no history or clinical evidence of neurological disease, dementia, or psychiatric disorder; (7) no current use of medication (except birth control pills, estrogen replacement therapy, and antihypertensive drugs); and (8) normal standard T1- and T2-weighted magnetic resonance imaging (MRI) scans as assessed by a medical doctor. The Mattis dementia rating scale was used for subjects older than 50 years to exclude those with scores below the normal range for age. They all had performance in the normal range (i.e., within 1.65 standard deviation of the normal mean for age) in all screening neuropsychological tests (assessing episodic memory, semantic memory, and executive function) and no subject complained about his or her memory. This protocol was approved by the regional ethics committee (CCP Nord Ouest III) and subjects gave written informed consent to the study before the investigation.

Seventy right-handed native French-speaking participants, ranging from 19 to 80 years (mean age: 44 ± 17.6 years; 49 females; mean years of education: 13.4 ± 3.5) and homogeneously distributed over the entire lifespan periods (Supplementary Table 1), were included in our study. There was a significant decrease in years of education with age (Pearson's correlation $r = -0.39$; $p = 0.001$) and a greater proportion of female subjects (21 males/49 females). Both variables were thus corrected for in all statistical analyses.

2.2. Resting state fMRI

2.2.1. Data acquisition

A Philips (Eindhoven, The Netherlands) Achieva 3.0 T scanner from the GIP Cyceron (Caen, France) was used for data acquisition. For each participant, a high-resolution T1-weighted anatomic volume was first acquired using a 3-dimensional fast field echo (FFE) sequence (3D-T1-FFE sagittal), followed by a high-resolution T2-weighted spin echo anatomical acquisition (2D-T2-SE sagittal) and a non-Echo-Planar Imaging (EPI) T2* volume (2D-T2*-FFE axial). Resting state functional acquisitions were obtained in the 70 subjects using an interleaved 2D T2* SENSitivity Encoding EPI sequence designed to reduce geometric distortions using parallel imaging, shorter echo time, and smaller voxels (2D-T2*-FFE-EPI axial, SENSitivity Encoding factor = 2; Time Repetition = 2382 ms; Time Echo = 30 ms; flip angle = 80°; 42 slices; slice thickness = 2.8 mm; no gap; in-plane resolution = 2.8×2.8 mm^2; 280 volumes). The first 6 volumes were discarded because of saturation effects. Subjects were equipped with earplugs and their heads were stabilized with foam pads to minimize head motion. During this acquisition, which was the last of the MRI scanning session, subjects were asked to relax, lie still in the scanner, and keep their eyes closed while not falling asleep. Immediately after the scanning, the participants were invited to complete a semidirected questionnaire especially designed for the evaluation of their inner experience during the resting state (see section 2.3. The postscan interview: Inner Experience Questionnaire (InExQ); See Supplementary Material, first section S1).

2.2.2. Data handling

Individual datasets were first checked for artifacts through the application of the TSDiffana routines (http://imaging.mrc-cbu.cam.ac.uk/imaging/DataDiagnostics), during which a variance volume was created for each subject to check that most signal variability was restricted to the cortex. Datasets showing evidence for significant movements (>3 mm translation or 1.5 degree rotation) associated with image artifacts and/or an abnormal variance distribution were excluded ($n = 2$). Only the 70 participants with usable data are referred to in the present article. The whole processing pipeline applied to each remaining subject dataset is detailed in Fig. 1. Briefly, the EPI volumes were corrected for slice timing and realigned to the first volume. Data were then spatially normalized using a technique designed to reduce geometric distortion effects (Villain et al., 2010). This procedure includes for each individual (1) a coregistration of the mean EPI volume, non-EPI T2*, T2, and T1 volumes; (2) a warping of the mean EPI volume to match the non-EPI T2* volume; (3) a segmentation of the T1 volume using the VBM 5.1 'Segment'