Psychology. Journal of the Higher School of Economics.
2015. Vol. 12. N 4. P. 33–47.

AGE RELATED CHANGES IN FUNCTIONAL CONNECTIVITY OF THE RESTING STATE NETWORKS

O.V. MARTYNOVA, V.V. BALAEV

Martynova Olga V. — Head of the Laboratory of Human Higher Nervous Activity, Institute of Higher Nervous Activity and Neurophysiology of Russian Academy of Sciences*; Senior Researcher, Centre for Cognition and Decision Making, HSE**, Ph.D.
E-mail: olmart@mail.ru, omartynova@hse.ru

Address: * 5A Butlerova str., Moscow, 117485, Russian Federation
** 20 Myasnitskaya str., Moscow, 101000, Russian Federation

Balaev Vladislav V. — PhD student, Institute of Higher Nervous Activity and Neurophysiology of Russian Academy of Sciences
E-mail: vlad_balaev@mail.ru

Address: 5A Butlerova str., Moscow, 117485, Russian Federation

Abstract

Age-related brain changes are the main cause of cognitive decline. Active cognitive task performance as well as resting-state activity might be a sensitive index for studying differences in aging. We investigated age-related changes in the spontaneous neuronal activity with functional magnetic resonance imaging (fMRI) in a resting-state condition. To evaluate differences in aging, we analyzed functional connectivity between resting-state networks in two groups of older and younger healthy volunteers. Seven resting-state networks were isolated, and cross-correlation matrices were computed for the time courses. Older subjects showed decreased activity of the auditory, visual, sensory-motor networks, frontoparietal and salience networks accompanied by increased coupling of the salience network with the sensorimotor and default mode network

This study was supported by the Russian Foundation for Humanities (Grant N 14-06-00747) and within the framework of a subsidy granted to the National Research University Higher School of Economics by the Government of the Russian Federation for the implementation of the Global Competitiveness Program.

compared to younger subjects. The age-related differences in functional connectivity may be due to aging impairment of the prefrontal cortex leading to a loss of activation in the salience, sensorimotor and visual networks in older subjects compared to the younger subjects. However, the default mode network was more prominent in the left hemisphere and showed more coupling with the salience network in older subjects than in younger subjects, indicating possible compensatory engagement of cognitive control regions in resting-state cognition. The results show that independent of task design and performance the functional connectivity method reflects neural changes in the aging brain.

Keywords: aging, resting-state networks, fMRI, sensory networks, cognitive control.

Introduction

Modern non-invasive neuroimaging has increased our knowledge of neural correlates of the active cognitive process. At the same time, resting-state neuroimaging has become common method for studying the functional organization of the brain due to reproducibility in healthy populations and sensitivity to altered neural conditions including disease or aging. Numerous studies have reported structured neuronal activity reflected in spontaneous fluctuations in the blood oxygenation level-dependent (BOLD) signal, which was stably presented without active task performance or perceptive input (Fox & Raichle, 2007; Damoiseaux et al., 2006). This ongoing neural activity at rest has been typically localized with functional magnetic resonance imaging (MRI) into a set of neuronal networks or resting-state networks (RSNs). These RSNs include sensory networks consisting of auditory, visual or sensorimotor brain structures and more complex or cognitive networks such as the frontoparietal and salience networks (see review Lee, Smyser, & Shimony, 2013). The main resting-state network is the default mode network (DMN), which demonstrates a strong negative correlation with tasks. This feature of the DMN has initiated a number of assumptions about the DMN in resting-state cognition. Human consciousness is based not only on sensory input and active cognition. Non-sensory experience, self-reference and ongoing integration of cognitive and emotional states also has an essential part in consciousness highlighted as resting-state cognition.

Recently, the functional connectivity (FC) of resting-state networks has become an attractive method for studying the relationship between ongoing neural activity and resting-state cognition. FC analysis is used for the description of inter-regional neural interactions during cognitive or motor tasks as well as of spontaneous activity during rest. Different brain regions show strong coherence in temporal fluctuations or FC (Friston, Frith, Liddle, & Frackowiak, 1993) forming functional rather than structural networks. Abnormal patterns of resting-state FC have recently been investigated in a variety of neuropsychiatric disorders, and there is growing evidence that such abnormalities may potentially provide valid reliable biomarkers of diseases of the brain (Broyd et al., 2009; Greicius, 2008). Fundamental factors, such as age

and gender, also affect functional connectivity based on their strong associations with the underlying anatomy (Good et al., 2001; Balsters et al., 2013). Temporal fluctuations in resting-state brain activity are sensitive to age-related neural changes and are correlated with cognitive decline. In particular, robust aging differences have been observed in connectivity between nodes of the DMN (Buckner, Andrews-Hanna, & Schacter, 2008; Damoiseaux et al., 2008). However, in addition to repeated findings of decreased connectivity within the DMN, the results for other RSNs vary considerably. Many discrepancies in previously reported findings can be partially explained by uneven vascular changes, sample sizes, breathing and movement artifacts (Allen et al., 2011; Balsters et al., 2013). However, it is unclear why these discrepancies do not affect the DMN to the same extent.

In recent work, we focused on the effect of age on the intensity, lateralization and functional interconnection between robust sensory and cognitive RSNs. We evaluated age-related changes in large-scale RSNs in two groups of younger and older healthy volunteers. We employed independent component analysis (ICA) to identify additional robust RSNs. We used the intensity of RSN spatial maps to examine the size of the neural activity and possible lateral asymmetry. Finally, we applied FC analysis to each pair of the RSNs, described by Jafri, Pearlson, Stevens & Calhoun (2008). We hypothesized that differences due to age might appear not only within the DMN but also in the connectivity of sensory with cognitive networks. Data on altered resting-state FC can provide additional knowledge about the neuronal mechanisms of cognitive aging.

Materials and Methods

Participants

The study included 15 young (19–30 years old, mean age 24.3 ± 3.6, 8 males) and 15 older (61–82 years old, mean age 67.8 ± 5.1, 8 males) healthy right-handed participants recruited through the Center for Speech Pathology and Neurorehabilitation. All healthy participants had no history of psychiatric or neurological disorders and were not taking any psychiatric or neurological medications at the time of testing. Other exclusion criteria for the healthy volunteers were clinical or radiological evidence of a previous infarction and MRI contraindications.

Ethics statement

This study was approved by the Ethics Committee of the Institute of Higher Nervous System and Neurophysiology of the Russian Academy of Sciences and the Center for Speech Pathology and Neurorehabilitation (Moscow, Russia). All subjects provided written informed consent after they received a complete description of the study.

Data acquisition

Participants lay supine in an MRI scanner (1.5 T MAGNETOM AVANTO MRI Scanner, Siemens, Germany). They were instructed to remain calm, with their eyes closed, and awake and avoid thinking about something in particular. A high-resolution T1-weighted

anatomic rapid gradient-echo image was acquired first (T1 MPRAGE sequence: TR 1.9 s, TE 3.4 ms, FA 90°, 176 slices that were 1 mm thick with a 0.5 mm slice gap; field of view 256 mm with matrix size 256×256). Then each participant underwent a T2*-weighted echo planar imaging (EPI) session containing 180 volumes (9 min). The parameters of the EPI sequence were as follows: TR 3 s, TE 50 ms, FA 15°, 32 slices that were 3 mm thick with a 0.8 mm slice gap, the field of view was 192 mm and matrix size 64×64.

Data preprocessing

The functional images were processed with the statistical parametric mapping toolbox (SPM8; Wellcome Department of Imaging Neuroscience, London, England) for MATLAB 7.0.4 (MathWorks, Natick, MA, USA). The preprocessing procedure included realignment of the T2*-weighted images for motion correction; the mean functional image was used for co-registration with the anatomic image. Then all images were normalized into the standard MNI space (Friston et al., 1994) with the voxel size 1.5×1.0×1.5 mm3. Smoothing was applied to the fMRI images with a Gaussian kernel (FWHM = 6 mm). Since RSNs are observed at low frequencies (< 0.1 Hz) (Friston et al., 2000), we applied band-pass temporal filtering. A fifth-order Butterworth filter was used with the frequency window ranging from 0.01 Hz to 0.1 Hz.

ICA

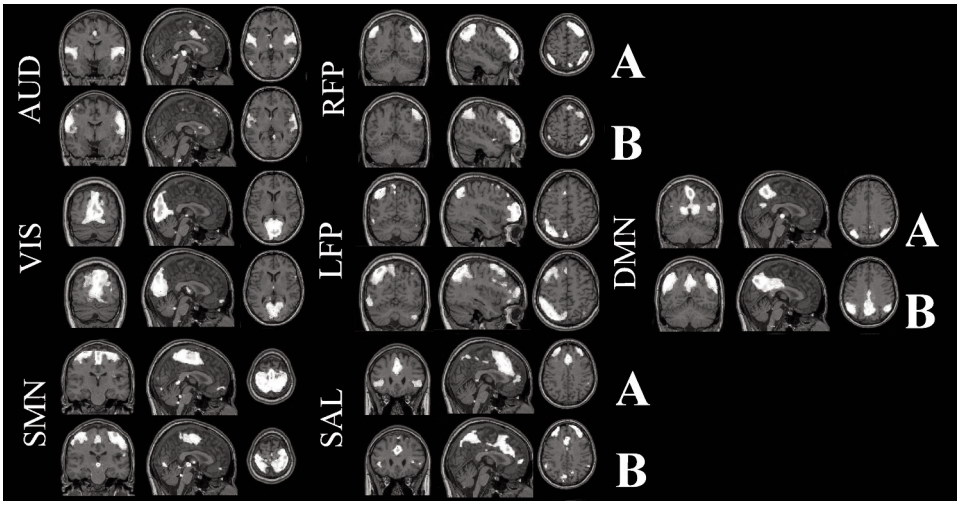
All fMRI data were decomposed into 30 independent components (ICs) using the Group ICA toolbox (GIFT, http://icatb.sourceforge.net/groupica.htm) with the Infomax ICA algorithm (Bell & Sejnowski, 1995). Additional preprocessing included removing the mean for each time point followed by principal component analysis with 45 principal components. Subject-specific spatial maps were estimated using the GICA3 back-reconstruction method (Calhoun, Adali, Pearlson, & Pekar, 2001) implemented in GIFT. Activation spatial maps were scaled to z-scores. Seven consistent networks (Figure 1) were chosen according to the following two criteria: the maximum overlap with the gray matter regions and the maximum correlation with known ICA spatial maps (Damoiseaux et al., 2006; Hacker et al., 2013) generated by WFU PickAtlas 3.0.4 (Maldjian, Laurienti, Kraft, & Burdette, 2003). The number of voxels (NoV) was estimated for symmetrical components in both hemispheres using activation maps thresholded at z = 2 (Damoiseaux et al., 2006). The laterality index (LI) was calculated by the subtraction of the NoV in the right hemisphere from the NoV in the left hemisphere divided by their sum. The NoV and LI scores are presented in Table 1.

FC analysis

Time courses corresponding to the chosen ICs were processed with the Functional Network Connectivity toolbox (FNC; http://mialab.mrn.org/ software/fnc/index.html). Pearson's correlation coefficients (CC) between the time courses of the six chosen ICs were estimated within a ± 5 s window, and the maximum values for each pair of networks underwent Fisher's *r*-to-*z* transformation. The z-scores of the correlation

Figure 1

Spatial maps of the components revealed by ICA and corresponding to RSNs



Note. Auditory (AUD), default mode (DMN), right frontoparietal (RFP), left frontoparietal (LFP), salience (SAL), sensorimotor (SMN) and visual (VIS) networks are shown for z-scores thresholded at $z > 2$ at the equal slices for each neural network in younger (A) and older (B) subjects. Slices are presented in the neurological view.

coefficients, NoV in symmetrical components in both hemispheres and the LIs were subjected to factorial analysis of variance (ANOVA) with Group and Sex as the categorical predictors and Age and Lesion Volume as the nuisance variables. A post-hoc Tukey test was used to control Type I errors.

Results

Resting-state networks

Seven of the 30 components were selected for each group as they spatially overlapped with RSNs presented in previous studies (Damoiseaux et al., 2006; Hacker et al., 2013). These RSNs were classified as follows: The visual network (VIS) included the inferior, middle and superior occipital gyrus and the temporal-occipital regions along with the superior parietal gyrus; the auditory network (AUD) included the bilateral middle and superior temporal gyrus, Heschl gyrus, insular cortex and temporal pole; the sensory-motor network (SMN) included the pre- and postcentral gyrus; the default mode network (DMN) primarily involved the posterior cingulate cortex, bilateral inferior parietal gyrus, angular gyrus, middle temporal gyrus, superior frontal gyrus and medial frontal gyrus; the right frontoparietal network (RFP) and left frontoparietal network (LFP) included the dorsolateral prefrontal and inferior parietal cortices; and the salience network (SAL) encompassed dorsal anterior cingulate, insular and dorsolateral prefrontal cortices. All RSNs are shown in Figure 1. Activation of the frontal

Table 1

Number of voxels and laterality indices of RSNs for two groups of participants

	Younger group	Older group
The auditory network (AUD)		
Right hemisphere	$(7.6 \pm 1.0)*10^3$	$(7.1 \pm 1.1)*10^3$
Left hemisphere*	$(6.7 \pm 1.0)*10^3$	$(5.5 \pm 1.3)*10^3$
Laterality index	0.06 ± 0.10	0.12 ± 0.14
The visual network (VIS)		
Right hemisphere*	$(9.6 \pm 1.3)*10^3$	$(8.3 \pm 1.8)*10^3$
Left hemisphere	$(6.7 \pm 0.9)*10^3$	$(5.9 \pm 1.4)*10^3$
Laterality index	0.18 ± 0.05	0.17 ± 0.10
The sensory-motor network (SMN)		
Right hemisphere	$(6.8 \pm 1.7)*10^3$	$(6.4 \pm 1.3)*10^3$
Left hemisphere*	$(7.3 \pm 1.2)*10^3$	$(5.0 \pm 0.9)*10^3$
Laterality index*	-0.04 ± 0.15	0.13 ± 0.10
The frontoparietal network (FP)		
Right hemisphere*	$(6.2 \pm 1.3)*10^3$	$(1.9 \pm 0.8)*10^3$
Left hemisphere	$(5.9 \pm 1.3)*10^3$	$(3.6 \pm 2.0)*10^3$
Laterality index*	0.03 ± 0.12	-0.30 ± 0.20
The salience network (SAL)		
Right hemisphere*	$(7.5 \pm 1.4)*10^3$	$(6.2 \pm 0.9)*10^3$
Left hemisphere*	$(6.5 \pm 1.2)*10^3$	$(5.5 \pm 1.2)*10^3$
Laterality index	0.06 ± 0.11	0.06 ± 0.08
The default mode network (DMN)		
Right hemisphere	$(7.2 \pm 1.1)*10^3$	$(6.5 \pm 1.0)*10^3$
Left hemisphere*	$(5.5 \pm 1.0)*10^3$	$(7.4 \pm 0.9)*10^3$
Laterality index*	0.14 ± 0.10	-0.07 ± 0.07

* Significant differences between younger and older healthy participants.

lobe of the DMN was not observed in any of the groups under investigation.

Table 1 shows the differences in the NoV and LI scores for the RSNs in the two groups. The NoV of the AUD was significantly lower in the left hemisphere in older subjects compared to the younger subjects ($p < 0.001$). The VIS volume was significantly lower for older subjects in the right hemisphere compared to that for the younger subjects ($p < 0.001$). The NoV value of the VIS decreased in the left hemisphere, but this tendency was statistically insignificant. The LI scores did not differ for the VIS and the AUD in both

groups. The SMN was observed in less volume in the left hemisphere for older subjects in contrast with younger subjects ($p < 0.001$) with a significant difference in the LI score. The activation (the NoV and LI scores) in the frontoparietal networks was significantly larger in the right hemisphere for the younger subjects. The NoV value of the SAL varied in the hemispheres between the groups with a decrease from younger to older subjects ($p < 0.001$), but the SAL LI scores did not differ for the groups. The opposite tendency was observed only for the DMN volume, which was higher in the left hemisphere for the older subjects compared to the younger subjects ($p < 0.001$) with a significant difference in the LI scores (Table 1). However, the LI values of all networks for both groups were below the significant threshold of 0.2, which was previously used in laterality studies (Seghier, 2008).

Differences in FC between each pair of RSNs

Figure 2 illustrates the correlation matrices between the seven networks for each group.

Significant differences in CCs were found between nine pairs of RSNs (Figure 3). Correlation of the AUD with the SMN and the SAL thus was higher for younger subjects than for older subjects ($p < 0.001$). Moreover, correlation of the VIS-LFP was more prominent for younger subjects than for older subjects ($p < 0.05$). The RFP correlated to a greater extent with the LFP network ($p < 0.001$); in addition, the CCs of the LF-DMN were significantly higher in the younger subjects than in the older subjects ($p < 0.05$). The opposite tendency with increased network coupling in older subjects was observed for the following pairs: SMN-RFP, SMN-SAL, RFP-SAL and SAL-DMN.

Figure 2

Functional connectivity between RSNs. Cross-correlation maps between the time courses of the RSNs for the two groups: younger (A) and older (B) subjects

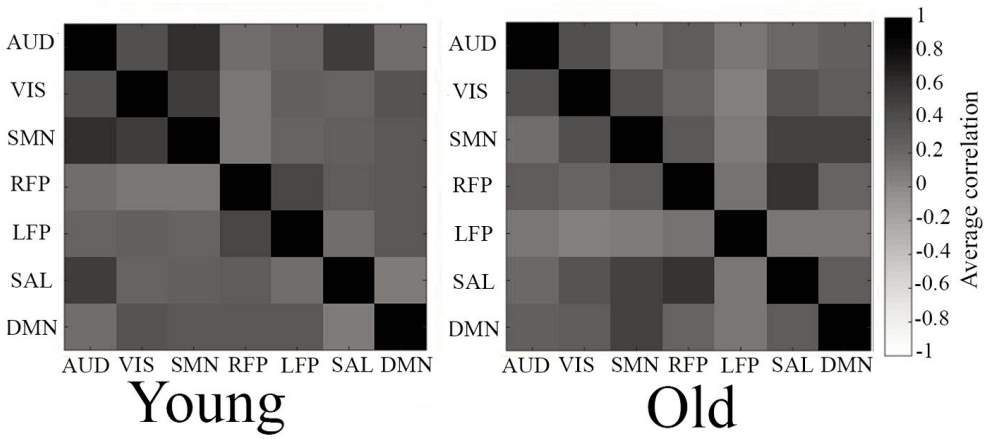
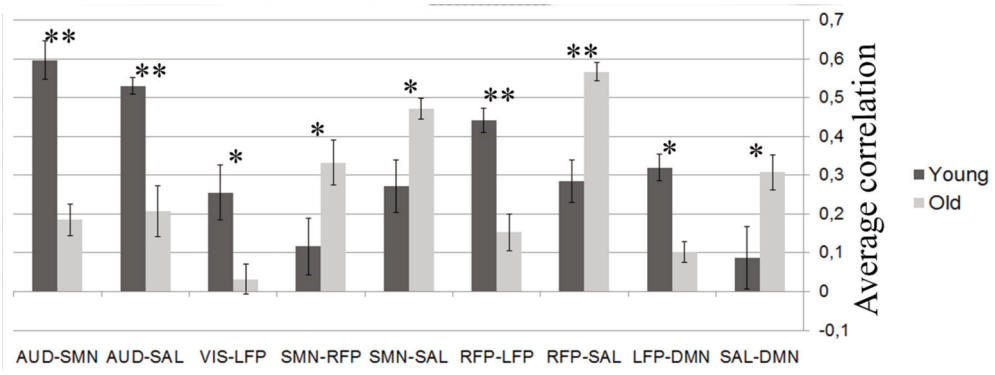


Figure 3

Mean correlation coefficients z-score comparison for two groups of subjects with dispersion



Note. Significant differences (according to factorial ANOVA) are indicated by * for $p < 0.05$ and ** for $p < 0.001$.

Thus, the SMN correlated with the SAL and the RFP significantly less in the younger subjects than in the older subjects ($p < 0.05$). The CCs of the RFP-SAL and the SAL-DMN were also higher in the older subjects than in the younger subjects. The CCs for the AUD and the other sensory networks (the VIS and the SMN) did not vary significantly across the two groups. In addition, there were no significant differences between the groups in the DMN-RFP-LFP interaction.

Discussion

In the current study, we used ICA and FC analysis in order to evaluate age-related differences in the interactions of well-known and widely described RSNs (Jafri et al., 2008). The ICA method of extracting neural activation avoids several issues. First, this method helps overcome the hemodynamic function shape changes followed by vascular changes in the aging brain and enhance the signal-to-noise ratio. Second, ICA successfully separates physiological noise from the BOLD signal changes related to neuronal activation (Beckmann, DeLuca, Devlin, & Smith, 2005).

We identified seven RSNs in the two groups: DMN, VIS, AUD, SMN, RFP, LFP and SAL networks. The AUD, the VIS and the SMN correspond to activity of sensory systems, while the DMN, the RFP, the LFP and the SAL are associated with higher cognitive functions. Age effects were found in the interhemispheric differences in RSN activation and FC between the networks. Analysis of the spatial maps of the RSNs showed more prominent activation in the left hemisphere for the AUD and the SMN in younger subjects compared to older subjects. The numbers of active voxels of the VIS and the frontoparietal network were higher for the right hemisphere in younger subjects than in older subjects. Activation of the SAL was significantly lower in both hemispheres in older subjects. However, activation of the DMN was more prominent in the

left hemisphere in older subjects compared to younger subjects.

The increased correlation of the AUD-SMN, the VIS-LFP and the AUD-SAL in the younger subjects in contrast with the older subjects could be associated with age-related vascular and neuronal changes resulting in decreasing power of sensory-cognitive coupling. Previously, Allen et al. (2011) showed a decrease in the majority of between-network correlations with the most prominent reduction in motor and attention networks. The decrease in the VIS volume in older subjects could also be associated with a loss of vision with age (Dagnelie, 2013). Additionally, the SMN also exhibited a decrease in the NoV in both hemispheres (with only the value for the left hemisphere significant) in the younger and older subjects in the current study.

The reduction in the VIS and SMN volumes was accompanied by a significant decrease in the activation of the SAL in both hemispheres in older subjects. Andres, Guerrini, Phillips & Perfect (2008) reported that the prefrontal cortex, which is the part of the SAL, mediates motor inhibition and sensory suppression. Consistent with this hypothesis, the decrease in the VIS and the SMN could also be associated with less activation of the SAL in older individuals. In addition, the SAL responds to behaviorally salient events (Seeley et al., 2007). In another study (McArdle, Ferrer-Caja, Hamagami, & Woodcock, 2002), older healthy participants showed poorer ability to inhibit irrelevant or distracting stimuli and greater difficulty with task-switching and rule-learning cognitive abilities, which are typically considered part of executive function. This reduced ability to prevent a prepotent response implies that top-down modulation to inhibit irrelevant information is less effective in older participants (Verhaeghen & Cerella, 2002). The decrease in the activation volume of the SAL with age might indicate an impairment of attention related to the inhibition deficit during task switching.

In the present study, the DMN lacked the activation of the frontal lobe described in resting-state research (Beckmann et al., 2005; Damoiseaux et al., 2006). Previously, several studies have indicated that the core region of the network is the precuneus (Utevsky, Smith, & Huettel, 2014) and the frontal lobe might be not identified statistically. In the current study, the analysis of the spatial maps revealed that the DMN was more prominent in the left hemisphere in older subjects than in younger subjects. This fact might be associated with increased functional connectivity within this network. Although most resting-state fMRI studies reported decreased functional connectivity in normal aging, some studies showed increased functional connectivity (Celone et al., 2006; Hafkemeijer, van der Grond, & Rombouts, 2012). For example, Celone et al. (2006) observed an increase in task-induced deactivation in patients with early stage mild cognitive impairment compared to those with advanced stage. However, the functions of the DMN are too vast. It engages in self-referential activity (D'Argembeau et al., 2005; Gusnard, Raichle, & Raichle, 2001) and autobiographical thoughts about the past and the future (Spreng, Stevens, Chamberlain, Gilmore, & Schacter, 2010; Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010). The DMN

has been suggested to reflect daydreaming or mind wandering (Gusnard et al., 2001). Activity in the DMN disappears when the brain is involved in attention-demanding cognitive tasks (Raichle et al., 2001) and is present when no such task is performed. Alterations in the DMN have been previously found in patients with various neurophysiological and psychiatric disorders (Broyd et al., 2009; Greicius, 2008), reflecting a possible role of the DMN in memory, integration of information, attention and theory of mind construction. The interaction of the DMN regions and brain areas involved in cognitive control has been considered to provide balance between internally and externally directed thoughts and thus might be implicated in the regulation of the focus of attention (Leech, Kamourieh, Beckmann, & Sharp, 2011). Moreover, an atypical pattern in the DMN can be associated with attention impairments (Bonnelle et al., 2011). Our findings on the increasing volume of activation of the DMN in the left hemisphere and increased FC between the DMN and the SAL in older subjects support the compensatory-recruitment hypothesis in which additional neural resources are used to compensate for sensory decline and to maintain task performance in older age.

The frontoparietal network has shown different time courses in the left and right hemispheres in most studies (Beckmann et al., 2005; Damoiseaux et al., 2006). In the present study, the frontoparietal networks encompassed regions identified previously as supporting cognitive control and decision-making processes, including the lateral prefrontal cortex and the inferior parietal lobule (Vincent, Kahn, Snyder, Raichle, & Buckner, 2008; Kroger et al., 2002). Previously, Allen et al. (2011) reported significant aging decreases within the LFP and the RFP, while Biswal et al. (2010) showed a significant reduction in activity only for the LFP. In the current study, RFP-LFP coupling decreased in older subjects, which was also related to significant reduction in the RFP intensity with age. In contrast, the functional connectivity of the RFP-SAL and the RFP-SMN increased in the older subjects, which is also consistent with the hypothesis of compensatory enlarged interaction within cognitive networks.

Limitations and relationship to previous work

An important limitation of this study that we did not acquired behavioral scores of participants. Thus, we cannot be sure whether individual data of FC actually reflect age-related changes in cognitive control or memory for each subject. The other critical issue relates to the question whether RSN activity reflects ongoing consciousness and resting-state cognition or nonconscious and physiological processes in the brain. Evidence for the latter possibility comes from sleep studies. For example, cognitive RSNs have been detected in subjects in the early stages of sleep (Fukunaga et al., 2006). Both sensory and association networks have been observed during light sleep and even FC within the dorsal attention network significantly increased during light sleep compared to wakefulness (Larson-Prior et al., 2009). These findings rather support the hypothesis that spontaneous BOLD fluctuations also reflect unconscious processes that

maintain the integrity of functional systems in the brain. However, there is no doubt that RSNs reflect functional communication pathways related to the underlying structural connections (Deco, Jirsa, & McIntosh, 2011; Hutchison et al., 2013). Moreover, a reliable correlation between FC of RSNs and behavioral scoring repeatedly demonstrates a relation between the dynamic variation in neural networks and psychological measures of experience and cognitive functions (Bonnelle et al., 2011; Leech et al., 2011; Damoiseaux et al., 2006). In addition, the data about altered FC within and between RSNs in various psychiatric disorders further support the possible relevance of RSNs to mental states and cognition (Fox & Greicius, 2010).

In light of the above-mentioned findings, we can conclude that the connectivity strength between sensory and cognitive RSNs' FC correlates, in some extent, with human cognitive process. Due to RSNs' correspondence to underlying neural architecture, data on altered resting-state FC can provide additional knowledge about the neuronal mechanisms of cognitive aging. However, additional studies are needed to evaluate resting-state FC as a reliable index to study age-related neural and cognitive changes, using validated measures of inter- and intra-subject variability in large populations.

Conclusion

In summary, our results support the efficiency of the FC method for studying aging differences since it may potentially indicate the preservation or reduction of functional networks with age. The resting-state ICA spatial maps and their pairwise coupling demonstrated age-related changes in functional connections between sensory and cognitive networks. The present findings contribute to the hypothesis that normal aging results not only in local reductions in neural networks but also in alterations of their functional connectivity. Our findings show a lack of functional connectivity in the AUD-SMN, AUD-SAL, VIS-LFP, LFP-DMN and RFP-LFP in older healthy subjects implying possible reduced coupling between sensory and cognitive networks as an effect of age. The decreased volumes of the AUD, VIS, SMN, SAL and frontoparietal network in older healthy participants also suggest that the power of sensory and cognitive networks decreases as a result of aging. In contrast, the increased interaction of the SAL-SMN, SAL-RFP and SAL-DMN as well as the enlargement of the DMN in the left hemisphere possibly highlights the compensatory engagement of cognitive network interactions.

Acknowledgments

We would like to express our deep appreciation to the radiologists of the Center for Speech Pathology and Neurorehabilitation, Alexey Petrushevsky, MD, and Oxana Fedina, MD, for their help collecting the MRI data. We also thank the volunteers for participating in the study.

References

Allen, E. A., Erhardt, E. B., Damaraju, E., Gruner, W., Segall, J. M., Silva, R. F., ... Calhoun, V. D. (2011). A baseline for the multivariate comparison of resting-state networks. *Frontiers in System Neuroscience, 5*(2). doi:10.3389/fnsys.2011.00002

Andres, P., Guerrini, C., Phillips, L. H., & Perfect, T. J. (2008). Differential effects of aging on executive and automatic inhibition. *Developmental Neuropsychology, 33*(2), 101–123. doi:10.1080/87565640701884212

Andrews-Hanna, J. R., Reidler, J. S., Sepulcre, J., Poulin, R., & Buckner, R. L. (2010). Functional-anatomic fractionation of the brain's default network. *Neuron, 65*, 550–562. doi:10.1016/j.neuron.2010.02.005

Balsters, J. H., O'Connell, R. G., Galli, A., Nolan, H., Greco, E., Kilcullen, S. M., ... Robertson, I. H. (2013). Changes in resting connectivity with age: a simultaneous electroencephalogram and functional magnetic resonance imaging investigation. *Neurobiology of Aging, 34*(9), 2194–2207. doi:10.1016/j.neurobiolaging.2013.03.004

Beckmann, C. F., DeLuca, M., Devlin, J. T., & Smith, S. M. (2005). Investigations into resting-state connectivity using independent component analysis. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences, 360*, 1001–1013. doi:10.1098/rstb.2005.1634

Bell, A. J., & Sejnowski, T. J. (1995). An information-maximization approach to blind separation and blind deconvolution. *Neural Computation, 7*(6), 1129–1159. doi:10.1162/neco.1995.7.6.1129

Biswal, B. B., Mennes, M., Zuo, X. N., Gohel, S., Kelly, C., Smith, S. M., ... Milham, M. P. (2010). Toward discovery science of human brain function. *Proceedings of the National Academy of Sciences of the United States of America, 107*(10), 4734–4739. doi:10.1073/pnas.0911855107

Bonnelle, V., Leech, R., Kinnunen, K. M., Ham, T. E., Beckmann, C.F., De Boissezon, X., ... Sharp, D. J. (2011). Default mode network connectivity predicts sustained attention deficits after traumatic brain injury. *Journal of Neuroscience, 31*, 13442–13451. doi:10.1523/JNEUROSCI.1163-11.2011

Broyd, S. J., Demanuele, C., Debener, S., Helps, S. K., James, C. J., & Sonuga-Barke, E. J. (2009). Default-mode brain dysfunction in mental disorders: a systematic review. Neuroscience and *Biobehavioral Review, 33*, 279–296. doi:10.1016/j.neubiorev.2008.09.002

Buckner, R. L., Andrews-Hanna, J. R., & Schacter, D. L. (2008). The brain's default network: anatomy, function, and relevance to disease. *Annals of the New York Academy of Sciences, 1124*, 1–38. doi:10.1196/annals.1440.011

Calhoun, V. D., Adali, T., Pearlson, G. D., & Pekar, J. J. (2001). A method for making group inferences from functional MRI data using independent component analysis. *Human Brain Mapping, 14*, 140–151. doi:10.1002/hbm.1048

Celone, K. A., Calhoun, V. D., Dickerson, B. C., Atri, A., Chua, E. F., Miller, S. L., ... Sperling, R. A. (2006). Alterations in memory networks in mild cognitive impairment and Alzheimer's disease: an independent component analysis. *Journal of Neuroscience, 26*(40), 10222–10231.

Dagnelie, G. (2013). Age-related psychophysical changes and low vision. *Investigative Ophthalmology and Visual Science, 54*, 88–93. doi:10.1167/iovs.13-12934

Damoiseaux, J. S., Beckmann, C. F., Arigita, E. J., Barkhof, F., Scheltens, P., Stam, C. J., ... Rombouts, S. A. (2008). Reduced resting-state brain activity in the "default network" in normal aging. *Cerebral Cortex, 18*(8), 1856–1864. doi:10.1093/cercor/bhm207

Damoiseaux, J. S., Rombouts, S. A. R. B., Barkhof, F., Scheltens, P., Stam, C. J., Smith, S. M., & Beckmann, C. F. (2006). Consistent resting-state networks across healthy subjects. *Proceedings of the National Academy of Sciences of the United States of America, 103*, 13848–13853.

D'Argembeau, A., Collette, F., Van der Linden, M., Laureys, S., Del Fiore, G., Degueldre, C., ... Salmon, E. (2005). Self-referential reflective activity and its relationship with rest: a PET study. *Neuroimage, 25*(2), 616–624. doi:10.1016/j.neuroimage.2004.11.048

Deco, G., Jirsa, V. K., & McIntosh, A. R. (2011). Emerging concepts for the dynamical organization of resting-state activity in the brain. *Nature Review Neuroscience, 12*(1), 43–56. doi:10.1038/nrn2961

Fox, M. D., & Greicius, M. (2010). Clinical applications of resting state functional connectivity. *Frontiers System Neuroscience, 4*, 19. doi:10.3389/ fnsys.2010.00019

Fox, M. D., & Raichle, M. E. (2007). Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. *Nature Reviews Neuroscience, 8*, 700–711. doi:10.1038/nrn2201

Friston, K. J., Frith, C. D., Liddle, P. F., & Frackowiak, R. S. (1993). Functional connectivity: the principal-component analysis of large (PET) data sets. *Journal of Cerebral Blood Flow and Metabolism, 13*, 5–14.

Friston, K. J., Holmes, A. P., Worsley, K. J., Poline, J. P., Frith, C. D., & Frackowiak, R. S. J. (1994). Statistical parametric maps in functional imaging: A general linear approach. *Human Brain Mapping, 2*, 189–210.

Friston, K. J., Josephs, O., Zarahn, E., Holmes, A. P., Rouquette, S., & Poline, J. B. (2000). To smooth or not to smooth?: Bias and efficiency in fMRI time-series analysis. *NeuroImage, 12*, 196–208. doi:10.1006/nimg.2000.0609

Fukunaga, M., Horovitz, S. G., van Gelderen, P., de Zwart, J. A., Jansma, J. M., Ikonomidou, V. N., ... Duyn, J. H. (2006). Large-amplitude, spatially correlated fluctuations in BOLD fMRI signals during extended rest and early sleep stages. *Magnetic Resonance Imagining, 24*, 979–992. doi:/10.1016/j.mri.2006.04.018

Good, C. D., Johnsrude, I., Ashburner, J., Henson, R. N., Friston, K. J., & Frackowiak, R. S. (2001). Cerebral asymmetry and the effects of sex and handedness on brain structure: a voxel-based morphometric analysis of 465 normal adult human brains. *NeuroImage, 14*, 685–700. doi:10.1006/nimg.2001.0786

Greicius, M. D. (2008). Resting-state functional connectivity in neuropsychiatric disorders. *Current Opinion in Neurology, 21*, 424–430. doi:10.1097/WCO.0b013e328306f2c5

Gusnard, D. A., Raichle, M. E., & Raichle, M. E. (2001). Searching for a baseline: functional imaging and the resting human brain. *Nature Reviews Neuroscience, 2*, 685–694. doi:10.1038/35094500

Hacker, C. D., Laumann, T. O., Szrama, N. P., Baldassarre, A., Snyder, A. Z., Leuthardt, E. C., Corbetta, M. (2013). Resting state network estimation in individual subjects. *NeuroImage, 82*, 616–633. doi:10.1016/j.neuroimage.2013.05.108

Hafkemeijer, A., van der Grond, J., & Rombouts, S. A. R. B. (2012). Imaging the default mode network in aging and dementia. *Biochimica et Biophysica Acta (BBA) – Molecular Basis of Disease, 1822*, 431–441. doi:10.1016/j.bbadis.2011.07.008

Hutchison, R. M., Womelsdorf, T., Allen, E. A., Bandettini, P. A., Calhoun, V. D., Corbetta, M., ... Chang, C. (2013). Dynamic functional connectivity: promise, issues, and interpretations. *Neuroimage, 80*, 360–378. doi:10.1016/j.neuro image.2013.05.079

Jafri, M. J., Pearlson, G. D., Stevens, M., & Calhoun, V. D. (2008). A method for functional network connectivity among spatially independent resting-state components in schizophrenia. *NeuroImage, 39*, 1666–1681.

Kroger, J. K., Sabb, F. W., Fales, C. L., Bookheimer, S. Y., Cohen, M. S., & Holyoak, K. J. (2002). Recruitment of anterior dorsolateral prefrontal cortex in human reasoning: a parametric study of relational complexity. Cerebral Cortex, 12, 477–485.

Larson-Prior, L. J., Zempel, J. M., Nolan, T. S., Prior, F. W., Snyder, A. Z., & Raichle, M. E. (2009). Cortical network functional connectivity in the descent to sleep. *Proceedings of the National Academy of Sciences of the United States of America, 106*, 4489–4494. doi:10.1073/pnas.0900924106

Lee, M., Smyser, C., & Shimony, J. (2013). Resting-state fMRI: a review of methods and clinical applications. *American Journal of Neuroradiology, 34*(10), 1866–1872. doi:10.3174/ajnr.A3263

Leech, R., Kamourieh, S., Beckmann, C. F., & Sharp, D. J. (2011). Fractionating the default mode network: distinct contributions of the ventral and dorsal posterior cingulate cortex to cognitive control. *Journal of Neuroscience, 31*, 3217–3224. doi:10.1523/JNEUROSCI.5626-10.2011

Maldjian, J. A, Laurienti, P. J., Kraft, R. A., & Burdette, J. H. (2003). An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *Neuroimage, 19*, 1233-1239. doi:10.1016/S1053-8119(03)00169-1

McArdle, J. J., Ferrer-Caja, E., Hamagami, F., & Woodcock, R. W. (2002). Comparative longitudinal structural analyses of the growth and decline of multiple intellectual abilities over the life span. *Developmental Psychology, 38*(1), 115–142. doi:10.1037/0012-1649.38.1.115

Raichle, M. E., MacLeod, A. M., Snyder, A. Z., Powers, W. J., Gusnard, D. A., & Shulman, G. L. (2001). A default mode of brain function. *Proceedings of the National Academy of Sciences of the United States of America, 98*(2), 676–682. doi:10.1073/pnas.98.2.676

Seeley, W. W., Menon, V., Schatzberg, A. F., Keller, J., Glover, G. H., Kenna, H., ... Greicius M. D. (2007). Dissociable intrinsic connectivity networks for salience processing and executive control. *Journal of Neuroscience, 27*(9), 2349–2356. doi:10.1523/JNEUROSCI.5587-06.2007

Seghier, M. L. (2008). Laterality index in functional MRI: methodological issues. *Magnetic Resonance Imaging, 26*(5), 594–601. doi:10.1016/j.mri.2007.10.010

Spreng, R. N., Stevens, W. D., Chamberlain, J. P., Gilmore, A. W., & Schacter, D. L. (2010). Default network activity, coupled with the frontoparietal control network, supports goal-directed cognition. *Neuroimage, 53*(1), 303–317. doi:10.1016/j.neuroimage.2010.06.016

Utevsky, A. V., Smith, D. V., & Huettel, S. A. (2014). Precuneus is a functional core of the default-mode network. *Journal of Neuroscience, 34*(3), 932–940. doi:10.1523/JNEUROSCI.4227-13.2014.

Verhaeghen, P., & Cerella, J. (2002). Aging, executive control, and attention: a review of meta-analyses. *Neuroscience & Biobehavioral Reviews, 26*(7), 849–857. doi:10.1016/S0149-7634(02)00071-4

Vincent, J. L., Kahn, I., Snyder, A. Z., Raichle, M. E., & Buckner, R. L. (2008). Evidence for a frontoparietal control system revealed by intrinsic functional connectivity. *Journal of Neurophysiology, 100*(6), 3328–3342. doi:10.1152/jn.90355.2008

Возрастные изменения в функциональной связанности сетей состояния покоя

Ольга Владимировна Мартынова
Заведующая лабораторией высшей нервной деятельности человека, Институт высшей нервной деятельности и нейрофизиологии РАН; старший научный сотрудник Центра нейроэкономики и когнитивных исследований НИУ ВШЭ, Ph.D.
Контакты: olmart@mail.ru, omartynova@hse.ru

Владислав Викторович Балаев
Аспирант, Институт высшей нервной деятельности и нейрофизиологии РАН
Контакты: vlad_balaev@mail.ru

Резюме

Нейронные возрастные изменения являются основной причиной снижения когнитивных функций у человека. Не только активное выполнение когнитивных задач, но и деятельность мозга в состоянии покоя может быть чувствительным индексом последствий старения в мозге. Мы исследовали возрастные изменения в спонтанной активности мозга с помощью функциональной магнитно-резонансной томографии (МРТ) в состоянии покоя. Для оценки возрастных различий мы проанализировали функциональные связи между сетями состояний покоя мозга у двух групп здоровых добровольцев молодого и пожилого возраста. В результате были выделены семь сетей покоя, и для их временно́й динамики были вычислены кросс-корреляционные матрицы. У пожилых испытуемых наблюдалось снижение активности слуховой, зрительной, сенсорно-моторной сетей, лобно-теменной и сети салиентности, которое сопровождалось увеличением связанности сети салиентности с сенсомоторной сетью и с базовой сетью покоя по сравнению с молодыми участниками исследования. Полученные возрастные различия в функциональной связанности сетей покоя могут быть результатом снижения активности префронтальной коры, ведущего к потере активации в сети салиентности, а также в сенсомоторной и зрительной сетях в группе пожилых в отличие от молодых участников. Тем не менее базовая сеть покоя была лучше выражена в левом полушарии и показала бо́льшую связь с сетью салиентности у пожилых, чем у молодых испытуемых, что указывает на возможное компенсаторное участие областей когнитивного контроля в состоянии спокойного бодрствования. Представленные результаты показывают, что вне зависимости от дизайна и выполнения задач психологических тестов метод функциональной связанности сетей покоя отражает возрастные нейронные изменения в мозге человека.

Ключевые слова: старение, сети состояния покоя, МРТ, сенсорные сети, когнитивный контроль.