Brain Research 1657 (2017) 288–296

Contents lists available at ScienceDirect

Brain Research

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

Research report

Increase of posterior connectivity in aging within the Ventral Attention Network: A functional connectivity analysis using independent component analysis

Johnathan Deslauriers [a,b,c], Jennyfer Ansado [c], Guillaume Marrelec [d], Jean-Sébastien Provost [e], Yves Joanette [a,b,*]

[a] Centre de Recherche, Institut Universitaire de Gériatrie de Montréal, Canada
[b] Université de Montréal, Montreal, Quebec, Canada
[c] Université du Québec en Outaouais, Gatineau, Quebec, Canada
[d] Sorbonne Universités, UPMC Univ Paris 06, CNRS, INSERM, Laboratoire d'imagerie biomédicale (LIB), F-75013 Paris, France
[e] Helen Wills Neuroscience Institute, University of California, Berkeley, United States

ARTICLE INFO

Article history:
Received 29 March 2016
Received in revised form 23 November 2016
Accepted 20 December 2016
Available online 21 December 2016

Keywords:
Aging
Ventral Attention Network
Functional connectivity
Visual selective attention

ABSTRACT

Multiple studies have found neurofunctional changes in normal aging in a context of selective attention. Furthermore, many articles report intrahemispheric alteration in functional networks. However, little is known about age-related changes within the Ventral Attention Network (VAN), which underlies selective attention. The aim of this study is to examine age-related changes within the VAN, focusing on connectivity between its regions. Here we report our findings on the analysis of 27 participants' (13 younger and 14 older healthy adults) BOLD signals as well as their performance on a letter-matching task. We identified the VAN independently for both groups using spatial independent component analysis. Three main findings emerged: First, younger adults were faster and more accurate on the task. Second, older adults had greater connectivity among posterior regions (right temporoparietal junction, right superior parietal lobule, right middle temporal gyrus and left cerebellum crus I) than younger adults but lower connectivity among anterior regions (right anterior insula, right medial superior frontal gyrus and right middle frontal gyrus). Older adults also had more connectivity between anterior and posterior regions than younger adults. Finally, correlations between connectivity and response time on the task showed a trend toward connectivity in posterior regions for the older group and in anterior regions for the younger group. Thus, this study shows that intrahemispheric neurofunctional changes in aging also affect the VAN. The results suggest that, in contexts of selective attention, posterior regions increased in importance for older adults, while anterior regions had reduced centrality.

1. Introduction

Because our environment contains hundreds of visual stimuli, it is impossible for the human brain to analyze them all at once. Instead, it relies on selective attention to focus only on stimuli that are relevant to the task at hand and ignore irrelevant or distracting stimuli. Tasks requiring selective attention activate numerous networks, including the Ventral Attention Network (VAN) (Corbetta et al., 2008; Scalf et al., 2014; Vossel et al., 2012). The VAN allows us to direct our attention toward a stimulus that shares similar characteristics with the anticipated target, especially when the searched-for object appears somewhere unexpected (Bays et al., 2010; Chica et al., 2013; Corbetta et al., 2008; Corbetta and Shulman, 2011; Fox et al., 2006; Indovina and Macaluso, 2007; Macaluso and Doricchi, 2013). The VAN can also act as a circuit-breaker either to interrupt the detection process when the target is located or when our expectations are no longer in line with our environment (Parks and Madden, 2013; Scalf et al., 2014; Shulman et al., 2003). It has further been proposed that this network analyzes the features of stimuli on a trial-by-trial basis to judge their relevance to the ongoing task (Macaluso and Doricchi,

---

Abbreviations: VAN, Ventral Attention Network; DAN, Dorsal Attention Network; DMN, Default Mode Network; ICA, Independent Component Analysis.

* Corresponding author at: Centre de Recherche de l'Institut Universitaire en Gériatrie de Montréal, 4565 Queen-Mary Road, Montreal, Quebec H3W 1W5, Canada.

E-mail address: yves.joanette@umontreal.ca (Y. Joanette).

http://dx.doi.org/10.1016/j.brainres.2016.12.017

2013), which allows one to focus on features that help detect a target and inhibit those that do not. Thus, the VAN both mediates sensory-driven (bottom-up) target discovery by allowing detection in unexpected locations and also contributes to controlled (top-down) search by adjusting our expectations to our environment (Macaluso and Doricchi, 2013). Not surprisingly, neurological lesions in regions of the VAN have a severe impact on everyday functioning (Corbetta and Shulman, 2011; Foldi et al., 2002; He et al., 2007; Ptak, 2012; Vecera and Rizzo, 2003). The VAN is a frontoparietal network that has been associated mainly with the right frontal and parietal regions of the human brain, including the temporoparietal junction and ventral prefrontal cortex (Corbetta et al., 2008; Fox et al., 2006; Hahn et al., 2006; Kucyi et al., 2012; Li et al., 2011; Shulman et al., 2010). Since frontal and parietal cortices are the two areas most affected by healthy aging (Raz et al., 1998), it is hardly surprising that selective attention processing declines with age.

It has been reported that healthy older adults perform slower and less accurately on selective attention tasks than young adults (Madden et al., 2014). However, not all attention processes are equally affected in aging. Older adults benefit as much as if not more than younger adults from guiding cues (Geerligs et al., 2014; Madden et al., 2014; Madden and Whiting, 2004; Müller-Oehring et al., 2013). On the other hand, older adults' attention is more easily captured by distracting stimuli (Geerligs et al., 2014; Porter et al., 2012; Whiting et al., 2007). These results have led many authors to believe that the top-down ability to direct attention based on prior information is preserved in aging, but the capacity to inhibit attention capture by distractors declines (Madden, 2007; Porter et al., 2012). This suggests that the VAN would become less efficient in aging as it would be less efficient in its ability to resist attentional capture towards distracters. Alternatively, it could be that the attentional processes of older adults could rely more heavily on the cognitive abilities supported by the VAN. In this case, a more active VAN could help to redirect the attention locus towards the target (Corbetta and Shulman, 2002) but would increase the vulnerability to distractors (Shulman et al., 2003). However, there is a lack of behavioral data to support either hypothesis (Madden, 2007). Similarly, Chica et al. (2013) reported that studies showing vulnerability to distractors in aging had hitherto used experimental designs that did not differentiate between task-relevant and irrelevant distractors. Because the VAN reacts only to task-relevant distractors (Corbetta et al., 2008; Corbetta and Shulman, 2011; Geng and Mangun, 2011) even when task-unrelated distractors are highly salient (Kincade et al., 2005), it is impossible to determine whether the obtained results are caused by a dysfunction in this network or an inability to inhibit salient but task-irrelevant distractors. As such, to our knowledge, there are no data available about possible age-related changes that could specifically implicate the cognitive abilities supported by the VAN.

Some information can, however, be obtained from a number of fMRI studies. Ansado and Monchi (2013), for example, have reported an age-related increase in BOLD signal in regions comprised within the VAN following a change in attention load. In this study, BOLD signals were compared between younger and older adults during a selective attention task with two attentional load levels (low-load vs. high-load condition). At a low attentional load condition, younger adults had higher metabolic activity in the occipital lobe when compared to older adults, while the latter had higher activity in prefrontal regions. When the task demand were high, then both groups showed an additional increase in activations of parietal regions, thus suggesting that these regions had an important contribution in mediating task difficulty. This study suggests that younger adults engage a parieto-occipital network during the task, whereas older adults would rather engage a frontoparietal network. While that study was a promising first step in examining functional variation of the frontoparietal network due to age, it remains unclear how the different regions of the VAN are affected since task-related paradigms do not quantify the relationship between the network's regions or how these relations differ in different age groups. Such a refinement in describing the changes in the involvement of the different regions of the VAN is part of the goals of the present study.

Unlike task-related paradigms, functional connectivity techniques can quantify relations between regions of functional networks by correlating their activity and then compare these connectivity ratios between groups. Functional connectivity has been used to study attention networks (Bastin et al., 2012; Betzel et al., 2014; Chou et al., 2013; Damoiseaux et al., 2008; Fox et al., 2006; Sun et al., 2012; Ystad et al., 2011), and age-related changes have been found. For instance, Geerligs et al. (2014) compared connectivity measures for different functional networks in young and older adults and found similar connectivity in an attention network, the Dorsal Attention Network (DAN), and higher connectivity between a cognitive-control network and a somatomotor network for older adults. Furthermore, elderly participants with the highest connectivity between the latter two networks achieved task performance levels similar to those of the younger adults. As such, these results suggest that there is an age-related neurofunctional modification in attention processes that are linked to cognitive performance. Attention networks were also found to be activated even when participants were not engaging in an attention task. Wu et al. (2011) selected brain regions known to be hypoactive during attention tasks, which form the Default Mode Network (DMN), and examined their negatively correlated areas. The resulting areas formed a network composed of multiple attention networks, including the VAN. Correlation coefficients were then compared between groups and showed an overall decrease in connectivity during aging in this super-network and the DMN. Thus, these results imply that aging is characterized by lessened deactivation between attention networks, possibly including the VAN, and the DMN. However, to our knowledge, functional connectivity has never been used to specifically investigate age-related changes in the VAN.

Instead, numerous studies have focused on the DMN. As mentioned above, the DMN is a large-scale system that is hypoactive during attention tasks and involves both anterior and posterior regions. This network has been linked to mental states such as remembering, planning and mental visualization (Andrews-Hanna, 2012; Buckner et al., 2008; Spreng, 2012). To assess changes in aging, Andrews Hanna et al. (2007) examined correlations between regions of the DMN in groups of younger and older adults and concluded that correlations within the network were decreased in the older group. Furthermore, the integrity of connectivity between anterior and posterior regions also decreased, suggesting that an anterior-posterior disconnection occurs in aging. Similar results were obtained by Tomasi and Volkow (2012), who found decreased connectivity in distant but functionally connected regions in both the DMN and the DAN for older participants. Also, Sun et al. (2012) found that older adults' frontal regions occupy a less central position in functional networks when compared to younger adults. Thus, it could expected that the VAN may undergo age-related intrahemispheric changes in connectivity, a change that could be different for the anterior and posterior regions of this network.

This study aims to investigate age-related alterations of interaction between regions of the VAN, both for the whole network and also for anterior and posterior regions only. To do this, the NetBrainWork toolbox was used (http://sites.google.com/site/netbrainwork/), a set of functional connectivity algorithms that apply Independent Component Analysis (ICA) to blood oxygenation level-dependent (BOLD) data sets to identify networks and quantify the BOLD signal correlation between regions. Previous studies have used ICA to identify multiple networks, including the DMN (Tomasi and Volkow, 2012) and the VAN (Bastin et al., 2012; Lee et al., 2012; Li et al., 2011, 2012; Perlbarg and Marrelec, 2008).

NetBrainWork's algorithms were applied to previously acquired data sets in which groups of healthy young adults and older adults were engaged in a selective attention task during fMRI acquisition (Ansado and Monchi et al., 2013). Thus, it compared the VAN's functional connectivity between groups. We also divided the VAN into anterior and posterior regions for both groups in order to assess possible anterior/posterior connectivity changes. In our experimental framework, we chose to acquire BOLD signals while participants were performing a selective attention task. This was done to solicit the attention networks more intensively and provide more homogeneity in the task, given that brain activity during the resting state is highly heterogeneous between participants (Allen et al., 2012). Furthermore, it allowed us to correlate performance on the task with connectivity in the chosen networks. Task performance is assessed by means of response time and accuracy. Another goal is to demonstrate that not all functional networks are affected equally by aging. To do so, we will compare our findings regarding the VAN to another network, the DMN.

In accordance with previous work that highlighted an task-related increase in activation in regions of the VAN, we expected that healthy older adults would show higher functional connectivity in the VAN (Ansado and Monchi et al., 2013). We also expected that the anterior regions of the VAN would show less functional connectivity in older adults. Regarding the DMN, it was expected that younger adults would have higher functional connectivity than older ones, which would be consistent with previous studies.

2. Results

2.1. Behavioral results

An independent-samples *t*-test examined the effects of group (younger vs. older) on task accuracy (% correct) and showed a significant mean difference (t(14.113) = 3.733, p = 0.002) with a large effect (effect size correlation r = 0.70). The older group performed less accurately. Another independent-samples *t*-test was conducted with response times for the two groups. The results showed significantly faster response times for young participants (t(25) = −5.048, p < 0.001), with a large effect (effect size correlation r = 0.71). See Table 1 for group means on the two variables.

2.2. Imaging results

During the first step of the analysis, NetBrainWork generates multiple brain maps of codependent activity for each group. Consequently, 18 maps were generated for the young group and 22 for the older group. By comparing the spatial distribution of activation on the maps with functional networks described in other studies, we were able to identify one map for each group that closely matched the VAN (Fig. 1A). Both have a representativity of 0.75 and a unicity of 1. We also picked two maps matching the DMN (Fig. 1B). The DMN map has a representativity of 1 and unicity of 0.94 for the young group and representativity of 0.69 and unicity of 1 for the older group.

Region selection on the VAN maps resulted in 24 ROIs for the younger group and 28 for the older one. By comparing the groups' components, we selected 8 common regions based on similar coordinates. These regions include the right medial superior frontal gyrus (mSFG), right middle frontal gyrus (MFG), right anterior insula (aI), right superior parietal lobule (SPL), right temporoparietal junction (TPJ), right middle temporal gyrus (MTG), right hippocampus and left cerebellum crus I (Table 2). These regions were then split into anterior (mSFG, MFG, aI) and posterior (SPL, TPJ, MTG, crus I, hippocampus) region groups.

The same procedure on the DMN maps yielded 30 regions for the young group and 22 regions for the older group with 7 common regions (Table 2). Those common regions consisted of the right precuneus, right medial prefrontal cortex, left posterior cingulum, left hippocampus, right middle temporal gyrus and right angular gyrus.

2.2.1. Hierarchical integration

Hierarchical integration of groups of regions was achieved by calculating total integration, integration for anterior/posterior regions and between-region group integration. Pairs of integration values were analyzed across groups. Mean integration values and their standard deviations for all integration values are shown in Fig. 2.

Regarding the VAN, group comparison of network or anterior/-posterior region integration was calculated with independent-samples t-tests. Total integration was significantly different between the younger and older groups (t(15.868) = −3.016, p = 0.008). The older group showed more integration than the young group with a large difference in the means (effect size correlation r = 0.60). Both anterior and posterior regions also revealed significant differences between younger and older groups (respectively, t(25) = 2.453, p = 0.0.21 and t(25) = −2.88, p = 0.008). The older group had less integration in anterior regions than the young group, with a moderate difference in the means (effect size correlation r = 0.44), but more integration in posterior regions than the young group, with a large difference (effect size correlation r = 0.50). Between-region group integration was also significantly different (t(16.384) = −3.470, p = 0.003): the older group showed more integration than the young group, with a large difference (effect size correlation r = 0.65).

Group comparison of total DMN integration was calculated with an independent-samples *t*-test that revealed a significant difference between the young and older groups (t(25) = 2.663, p = 0.013). The older group showed less integration than the young group, with a moderate difference in means (effect size correlation r = 0.47). See Fig. 2 for more details.

2.2.2. Correlations between VAN and task performance

Correlations between task response time and VAN integration variables are presented in Table 3 for both groups.

Table 1
Behavioral performance on experimental task.

Variable	Group	N	Mean	Standard Deviation
Response Time (ms)***	Younger	13	1043.87	125.22
	Older	14	1356.94	188.14
Accuracy (%)**	Younger	13	0.97	0.03
	Older	14	0.83	0.14

Independent-samples *t*-tests between groups are shown as * = p < 0.05, ** = p < 0.01, *** = p < 0.001.

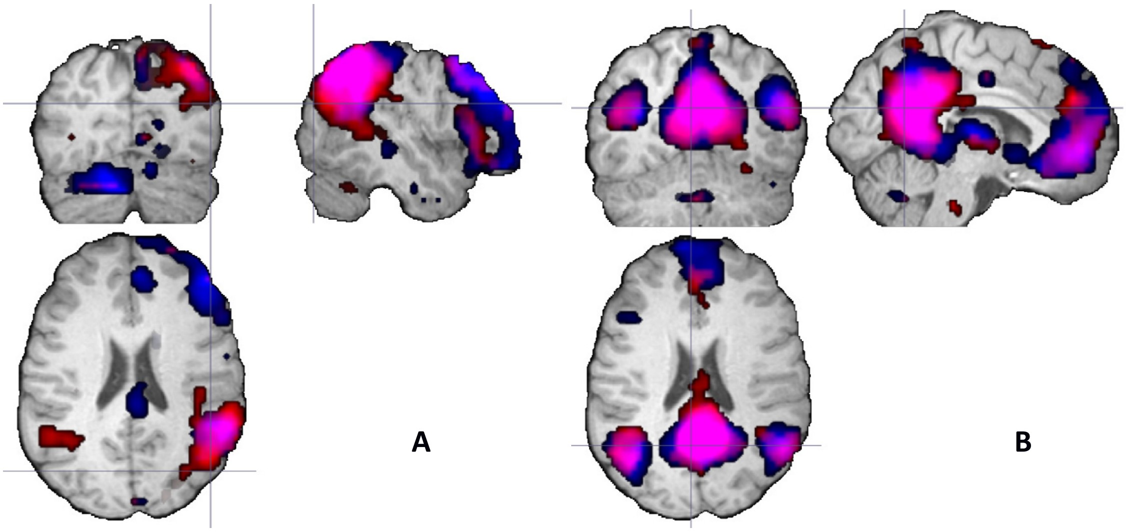

Fig. 1. Selected t-maps for (A) Ventral Attention Network and (B) Default Mode Network, with blue corresponding to young adult maps, red to older adult maps and purple to common areas.

Table 2
Groups' common regions coordinates.

ROI	Young X	Young Y	Young Z	Older X	Older Y	Older Z
Posterior Ventral Attention Regions						
Middle temporal gyrus (MTG)	58	−20	−15	65	−28	−11
Temporoparietal junction (TPJ)	55	−52	18	55	−51	11
Superior parietal lobule (SPL)	29	−74	53	30	−81	45
Cerebellum crus 1	−16	−80	−26	−22	−77	−27
Hippocampus	22	−35	3	23	−41	6
Anterior Ventral Attention Regions						
Middle frontal gyrus (MFG)	41	48	8	42	54	13
Medial superior frontal gyrus (mSFG)	3	34	39	3	28	44
Anterior insula (aI)	33	20	−7	32	23	−9
Default Mode Network						
Precuneus	−8	−57	23	−2	−58	23
Medial prefrontal cortex	−3	50	−1	−8	49	−2
Posterior cingular cortex	1	−11	39	4	−10	36
Hippocampus	−22	−46	−5	−29	−38	−13
Temporal middle gyrus	−59	−12	−19	−59	−10	−24
Angular gyrus	51	−62	26	52	−64	23

Abbreviations: VAN = Ventral Attention Network; DMN = Default Mode Network.

For the younger group, all integration variables correlated weakly with accuracy and none reached significance. Response time, however, correlated with $I_{BETWEEN}$, and a trend was observed with I_{ANT} ($r = 0.596$, $N = 13$, $p = 0.032$, and $r = 0.534$, $N = 13$, $p = 0.060$, respectively).

In the older group, all integration variables correlated weakly with accuracy and response time and none reached significance. Only I_{POST} and response time showed a moderate but not significant correlation ($r = 0.467$, $N = 14$, $p = 0.093$).

When correcting with Bonferroni for multiple comparison, the adjusted p value for an alpha level of 0.05 would be of 0.0127.

3. Discussion

The purpose of this study was to examine age-related changes in the VAN's connectivity using data-driven methods. Our framework yielded some interesting results regarding age-related changes in network connectivity and hinted at how they may interact with behavior.

The VAN and DMN identified in our analysis were composed of ROI located in brain regions frequently associated with these networks either in task-related activity protocols (Corbetta et al., 2008; Hahn et al., 2006; Kincade et al., 2005) or from ICA network detection (Betzel et al., 2014; Lee et al., 2012; Li et al., 2011, 2012; Perlbarg and Marrelec, 2008). While studies have reported a general decrease in functional networks' connectivity with aging (Betzel et al., 2014; Chou et al., 2013; Damoiseaux et al., 2008; Grady et al., 2010; Tomasi and Volkow, 2012; Wu et al., 2011), we found the opposite pattern for the VAN. Older adults showed higher BOLD signal dependency between all regions than younger subjects, which implied that VAN connectivity increases with age. The DMN, on the other hand, showed reduced connectivity in aging, consistently with previous reports (Andrews-Hanna et al., 2007; Damoiseaux et al., 2008). Higher connectivity in the VAN is an interesting result that is in line with behavioral measurement of attention abilities in aging. As mentioned above, the ability to use cues to guide the attention locus in the environment is preserved in aging while attention capture by distractors becomes more frequent. Since the VAN detects only target-related stimuli,

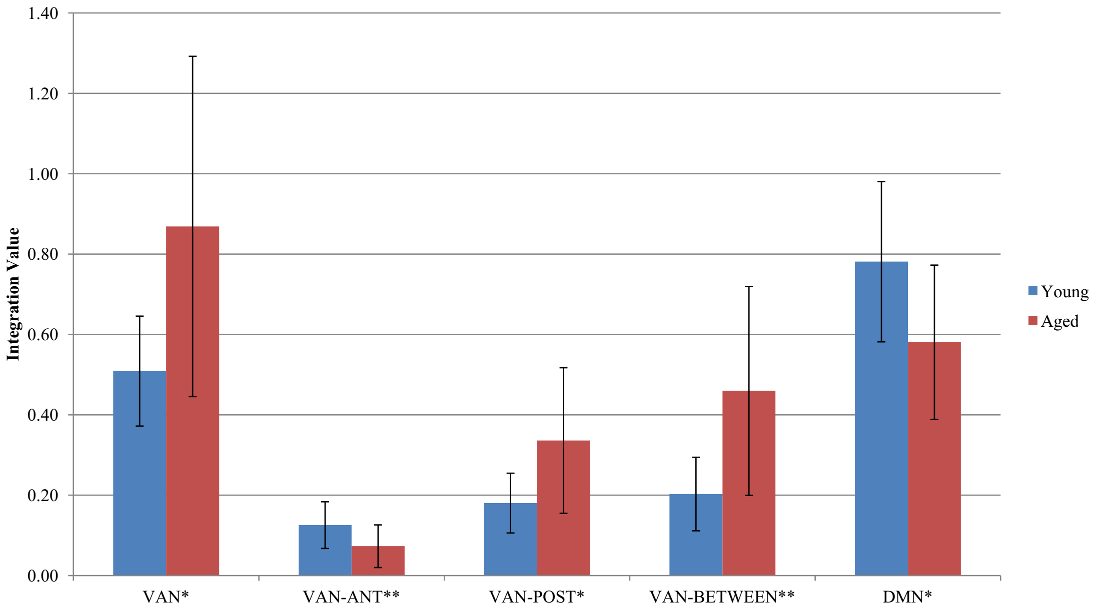

Fig. 2. Integration values and standard deviation at ±1. Independent-samples t-tests between group are shown as * = $p < 0.05$, ** = $p < 0.01$. Abbreviations: VAN = Ventral Attention Network; VAN-ANT = Integration for anterior VAN regions; VAN-POST = Integration for posterior VAN regions; VAN-BETWEEN = Integration between anterior and posterior VAN regions; DMN = Default Mode Network.

Table 3
Correlations between task performance and integration values.

			I-VAN	I-ANT	I-POST	I-BETWEEN
Younger	Response Time	Pearson Correlation	0.46	0.534	−0.305	0.596
		Sig. (2-tailed)	0.114	0.06	0.311	0.032
		N	13	13	13	13
Older	Response Time	Pearson Correlation	0.212	−0.222	0.467	0.065
		Sig. (2-tailed)	0.467	0.446	0.093	0.825
		N	14	14	14	14

Abbreviations: I-VAN = Integration of whole VAN; I-ANT = Integration of anterior VAN regions; I-POST = Integration of posterior VAN regions; I-BETWEEN = Integration between anterior and posterior VAN regions.

our hypothesis is that a hyperconnected VAN would be more efficient at directing the attention locus toward target-related stimuli based on cues but would also make any low-saliency task-related distractors more capable of directing the attention locus erroneously. This hypothesis is coherent with other studies that have shown higher activity in the VAN when the target frequently appeared in unexpected locations, which was associated with faster response times to locate the target but also made it more difficult to resist distractions by task-related stimuli (Macaluso and Doricchi, 2013; Shulman et al., 2003). Thus, while it was hypothesized that age-related changes in attention processes are related to the VAN, this study provides imaging evidence that in fact the VAN's connectivity increases with age. This phenomenon may be responsible for the behavioral changes in attention abilities as well.

To our knowledge, only one previous study had investigated VAN functional connectivity changes in aging (Betzel et al., 2014). However, they examined a bilateral network that overlapped the VAN, which they referred to as the VAN/Salience network. Contrary to our results, they found an overall age-related decrease in connectivity between regions of this network. It is important to point out that some ICA studies do find a similar bilateral network that overlaps the VAN, challenging the accepted idea that the VAN is right-lateralized (see Vossel et al., 2014, for a review). Other ICA studies, including our own, have found the VAN to be right-lateralized, which fits with the anatomical (Kucyi et al., 2012; Lee et al., 2012; Li et al., 2011), task-related functional (Kincade et al., 2005; Shulman et al., 2010) and clinical (Corbetta and Shulman, 2011) results. For instance, anatomical tracks are thicker in the right hemisphere (Kucyi et al., 2012) and right-hemisphere lesions impair attention capacities more severely than lesions in the left hemisphere (Corbetta and Shulman, 2011; Kleinman et al., 2007; Swan, 2001). Nonetheless, whether the right-lateralized VAN and the bilateral VAN (sometimes referred as the Salience network) are the same network or are distinct and have different behavioral functions is still a matter for debate. If the two networks are indeed distinct, then they could be affected differently in aging. Further, Betzel et al. (2014) found that the VAN/Salience network experienced an increase of connectivity in middle age followed by a decrease in older age, which could suggest that they analyzed two networks as one. A similar result would have been obtained if one network increased in connectivity with age while a second one decreased in later years. Thus, their results could be compatible with our own.

Because other studies had found a connectivity decrease between the anterior and posterior regions of the DMN (Andrews-Hanna et al., 2007; Damoiseaux et al., 2008; Wu et al., 2011), we further analyzed the VAN by dividing it into anterior and posterior regions. This revealed an interesting connectivity change in aging: older adults have less connectivity between anterior regions than younger adults but more between posterior regions, as well as increased interaction between anterior and posterior regions. The reduction in connectivity in anterior regions might be associated with the age-related reduction in anterior lobe mass. Furthermore, the posterior regions' increase in connectivity might represent a compensation strategy to moderate the effects of decreased connectivity in the anterior regions. Increased connectivity along the anterior/posterior axis might also signify the reduced independence of anterior regions when processing information, resulting in greater reliance on posterior regions. Similarly, Sun et al. (2012) found that older adults had reduced regional centrality in anterior regions than younger adults. However, this functional modification is not associated with maintained performance on our selective attention task, since the older adults were slower to answer and less accurate than the young adults. Nonetheless, we argue that this difference in the activation of the VAN's functional dynamic could represent the expression of a putative compensation mechanism similar to a "compensation to maintain performance" (Stern, 2009, p. 2021). Indeed, older participants still maintain a good performance on the task as accuracy was over 80% and response time was only 300 ms slower than the younger group. Alternatively, the difference in functional connectivity could be a characteristic of the elderly brain's processing style. The older participants could be engaging the VAN's connectivity differently, a pattern of activation that does not appear to generate the same performance as in younger adults, thus making what Stern's model (2009) predicts to be a less efficient response to the task.

Trends regarding the relations between response time and anterior/posterior region connectivity differed for the two groups. For young adults, longer response time nearly correlated with increased connectivity in anterior regions, but for older adults this relationship was neither high nor significant. Conversely, older adults showed a higher correlation with connectivity in parietal regions. While these results failed to reach the significance level and even more so after adjusting for multiple comparisons, we believe they are relevant to the discussion since the observed pattern is similar to the one described through functional connectivity analyses. Indeed, the posterior regions of the VAN in older adults share a higher degree of neurofunctional signal dependency than those in younger adults, but the latter exhibit a higher degree of integration between anterior regions. Together, these results suggest that attention abilities are mediated in different regions at different ages. Moreover, these data are coherent with previous studies that reported an age-related increase in the metabolic activity of posterior regions (Ansado and Marsolais, 2013), a result which differs from some suggestions according to which the frontal regions would be more active in aging in order to compensate for decreasing neuronal mass and thus maintain performance (Davis et al., 2008). Instead, we found that the anterior regions were less connected and less likely to mediate attention processes, whereas the posterior regions increased in connectivity and were more likely to do so. However, we had expected that higher connectivity would result in faster response times. We therefore present a few hypotheses as to why a more connected VAN should be associated with slower response times. First, it is possible that participants who had more difficulty performing the attention task required more active attention networks. Alternatively, more connected regions might represent a network that shares more information, which does not necessarily equate with a more efficient network. Indeed, it is possible that they process more irrelevant information, perhaps because lower-level processes are unable to inhibit stimuli that are unrelated to the task. It is also possible that strategies differed among individuals in the two groups, and one less efficient strategy relied more on the VAN, so that connectivity there was higher, as were response times. Again, the results of the correlations did not reach the significance level even when not adjusted for multiple comparisons, so it is also possible that relations between performance on task and functional connectivity in older and younger adults did not differ.

While this study helped us gain a better understanding of age-related changes in an important attention functional network, it has a few limitations. First, our experimental protocol does not allow to measure situations in which more complex attention processes interact, such as when distractors or cues to the location of a target exist. In such environments, it is possible that a hyperconnected VAN might allow comparable performance in young and older adults. For instance, if additional low-saliency task-related distractors had been part of our task, such as letters in less contrasting colors, we predict that older adults would have been more likely to choose those distractors as possible targets and thus produce longer response times, whereas younger adults would not. However, when the target is a low-saliency letter, older adults should be quicker at locating it than younger adults. A second limitation of this study was our choice of experimental task. The experimental task was developed to solicit the cognitive abilities supported by the frontoparietal network as a whole, but did not allow to isolate the specific cognitive functions of the VAN. While it would have been interesting to correlate performance between the VAN integration and performance variables that are specific to this network, functional connectivity analysis requires a block design protocol and so far no task has been shown to solicit and maintain metabolic activity in the VAN for prolonged periods of time. Another limitation in our method was to select only regions that were common to both groups' VAN. While it would have been interesting to investigate whether older and younger adults had different brain regions forming the VAN, the goal of our experiment was to compare the interaction among regions composing the VAN. As such, our methodology is more in line with the analysis of what Stern (2009) described as neural reserve, that is, the flexibility in a network dynamic that allows a person to maintain performance as task difficulty increases or, in the case of aging, to maintain performance when brain capacities are reduced. As well, choosing only common regions made it less likely that the selected regions were artifacts caused by either the data acquisition or analysis procedures.

In conclusion, this study reports on age-related changes in connectivity in the VAN and behavioral differences in performance on a visual selective attention task. First, we found that the VAN is more integrated in older adults than in young adults, which would mean that it is one of the few functional networks to show an increase in connectivity in aging. Nevertheless, older adults responded more slowly and were less accurate. Thus, this alteration in brain functionality is not sufficient to maintain similar attention abilities compared to the younger adults in our study. Even though the elderly group's performance was poorer than the younger group's, this neurofunctional change could still be compensatory because performance differences were marginal and would have likely little impact on daily life functioning. We propose that the hyperconnected VAN is helpful at directing attention based on prior information on the stimulus, an ability that is preserved in aging (Madden and Whiting, 2004). We believe that without the hyperconnected VAN, the older adults' performance on our task would have been worse.

4. Experimental procedure

4.1. Participants

Twenty-seven healthy adults – 13 younger adults (6 males; age range: 18–30 years; average 22.92) and 14 older adults (8 males; age range: 60–75 years; average 70) – participated in the study. All participants were healthy, right-handed, native French speakers, with no history of neurological or psychiatric episodes and had normal or corrected-to-normal vision. They were recruited from a pool of volunteers at the Centre de Recherche de l'Institut Universitaire de Gériatrie de Montréal (CRIUGM) and gave written informed consent. The study was reviewed and approved by the Scientific and Ethics Committees of the Regroupement Neuroimagerie Québec (RNQ). All participants had normal range scores (>27) on the Mini-Mental State Examination (MMSE; Folstein et al., 1975).

4.2. fMRI task

The items in the experimental task were 13 letters, namely 10 consonants and 3 vowels: B, C, D, H, J, N, P, R, S, T and A, E, U. In 50% of trials, a total of three letters (one target, two distracters) were used and five letters (one target, four distracters) in the other trials. Trials were randomly distributed. The letters appeared in white on a black background in Courier New Bold 40 and were presented simultaneously along the vertical mid-line of the screen. One of the letters was presented 0.5 degrees below the fixation point and the other letters were presented 0.5 degrees above the fixation point and then one above another at 0.5-degree intervals. Exposure times for the exploration of the letter display were selected to avoid ceiling and floor effects in the experimental task. They were validated with a pre-test conducted on 32 other participants (16 younger and 16 older ones) who went through the same protocol in the fMRI simulator at the Unité de Neuroimagerie Fonctionnelle (UNF) of the CRIUGM.

For each run, the target letter was presented below the fixation point; in 50% of the trials, it matched one of the probes above the fixation point. The experimental task blocks had the participants respond with "yes" when the target letter presented below the fixation point matched one of the letter probes above the fixation point (e.g., a/A) and "no" when there was no match (e.g., U/A). Participants had to respond as quickly as possible without compromising their accuracy by giving a binary response with a bimanual joystick. Following the presentation of the letter display, a black screen with a central fixation point was presented until the subject responded.

4.3. Procedure

During the scanning session, participants were given the experimental task. Each run included three blocks of 90 trials, and scan duration was four runs. For both tasks, the trials began with the presentation of a central fixation point for 1000 ms, which was followed by the presentation of the letter display for 600 ms. A black screen was presented with jittered interstimulus interval of either 800, 1000 or 1200 ms to minimize confounds due to a subject's habituation and expectations (Liu et al., 2001). Before the acquisition, the participants took part in a training session inside the fMRI simulator.

Participants were scanned using a Trio TIM 3.0T Siemens MRI scanner at the UNF. Each scanning session began with a T1-weighted 3D volume acquisition for anatomical localization, followed by acquisitions of echo planar T2*-weighted images with BOLD contrast. Functional images were acquired in four runs containing 144 volumes each acquired every 2.5 s, TE: 30 ms. Volumes contained 40 slices, with voxel size of $4.0 \times 4.0 \times 4.0\ \mathrm{mm}^3$.

4.4. Data analysis

4.4.1. Preprocessing

The first three volumes of each run were discarded. Preprocessing was done with SPM8 and included spatial realignment, slice timing and smoothing through a 6-mm full-width half-maximum isotropic Gaussian filter. Maximum translation values did not exceed 3 mm in any direction. To reduce physiological noise, a retrospective estimation and correction of breathing and heartbeat was applied (Hu et al., 1995). A temporal cut-off (cut-off frequency 4.16×10^{-3} Hz was applied to the functional data to filter out subject-specific low-frequency signal drifts.

4.4.2. Data-driven network detection and identification

In order to maximize statistical power, volumes from all four runs were pooled together in a single run. We then applied an exploratory method based on spatial ICA (McKiernan et al., 2003) of a single time series, followed by hierarchical clustering to gather spatially similar components across subjects, leading to group-representative classes. Group representative large-scale networks were extracted for each fMRI session and for both young adults and healthy older adults using spatial ICA (Perlbarg and Marrelec, 2008) as implemented in NetBrainWork. First, the 40 spatial components explaining most of the variance in each young subject were extracted. In the older group, we choose to retain the first 80 spatial components to account for the greater heterogeneity (Marcotte et al., 2013). These components were scaled to z-scores and registered to the Montreal Neurological Institute (MNI) standard space using nonlinear spatial transformations implemented in SPM5. Then, based on their spatial similarity (Esposito et al., 2005), the components were clustered across the subjects in each group. The higher number of components in the older group helped to ensure that the clustered components maps would be more coherent with the functional networks of the younger adults, which were more homogenous. The definition of the group-representative classes was automatically processed. From these classes, fixed-effect group t-maps were computed and we used a threshold of $p < 0.05$ (uncorrected for multiple comparisons, to keep enough voxels to design the regions of interest). From the resulting large-scale networks, we reviewed the resulting set of maps from each group and identified the functional networks using the results from other ICA studies as visual templates (Fornito et al., 2012; Yeo et al., 2013). For each group, one map that showed temporal neurofunctional signal dependency in regions typically associated with the VAN (right hemispheric temporoparietal junction and right ventral prefrontal cortex) and another map matching the DMN (bilateral medial temporal lobe and medial prefrontal) were used in the following analysis.

4.4.3. Region selection

On the network identified as the VAN and DMN for both groups, we used a procedure that consists of selecting the peaks of the group t-map as seed voxels. Then, the regions were determined from these peaks using a region-growing algorithm that recursively added to the region the adjacent voxel with the highest t-score and stopped when there were no more significant surrounding voxels. Regions are used to compose networks to be analyzed using hierarchical integration. To maintain a data-driven approach, any similar regions between groups for the VAN or DMN were included in the hierarchical integration measures, regardless of our *a priori* hypothesis regarding which regions should be included in the networks.

4.4.4. Hierarchical integration

We examined the functional interactions within the anterior and posterior parts of the VAN as well as the integration between these regions. To do so, we computed the inter-regional temporal correlations using hierarchical integration (Marrelec et al., 2008). Hierarchical integration establishes the degree of connectivity within a system itself and between systems. Integration does not assess pairwise interactions between its various components. Instead, it captures the overall level of statistical dependence within a brain system. Briefly, hierarchical integration provides an overall measure of functional information exchanges between time courses of BOLD signals recorded in the selected regions of interest (ROIs). In other words, hierarchical integration is a decomposition of the integration measure of the whole network. The method was introduced by (Tononi, 1994) in subnetworks and between these subnetworks.

4.4.5. Integration measures

The functional connectivity between two regions is defined as the correlation between the time courses of these two regions. For instance, working with 8 regions within a network yields $[8] * ([8] - 1)/2 = 28$ correlation coefficients, which form the correlation matrix **R**. To summarize this information in one overall measure of connectivity within the network, we used a measure originating from information theory (Watanabe, 1960) and known in neurocomputing and neuroimaging as integration (Marrelec et al., 2008; Tononi, 1994). If $\mathbf{R}_{\mathbf{VAN}}$ is the correlation matrix corresponding to the regions within the VAN, then the corresponding integration reads

$$\mathrm{I}_{\mathrm{VAN}} = -1/2 \ln |\mathrm{R}_{\mathrm{VAN}}|,$$

where ln is the natural log function and | | the determinant function. Integration is equal to zero if and only if all correlation coefficients are equal to zero; otherwise, it is positive. The more correlated the regions, the higher the integration; a correlation of 1 corresponds to an infinite integration. We also examined the levels of integration within the anterior and posterior parts of the VAN separately ($\mathrm{I}_{\mathrm{ANT}}$ and $\mathrm{I}_{\mathrm{POST}}$, respectively), as well as the interactions between the two groups of regions ($\mathrm{I}_{\mathrm{BETWEEN}}$). $\mathrm{I}_{\mathrm{ANT}}$ and $\mathrm{I}_{\mathrm{POST}}$ are easily computed as

$$\mathrm{I}_{\mathrm{ANT}} = -1/2 \ln |\mathrm{R}_{\mathrm{ANT}}|$$

and

$$\mathrm{I}_{\mathrm{POST}} = -1/2 \ln |\mathrm{R}_{\mathrm{POST}}|,$$

while $\mathrm{I}_{\mathrm{BETWEEN}}$ can be calculated as

$$\mathrm{I}_{\mathrm{BETWEEN}} = \frac{1/2 \ln |\mathrm{R}_{\mathrm{ANT}}| * |\mathrm{R}_{\mathrm{POST}}]}{|\mathrm{R}_{\mathrm{VAN}}|.}$$

A key property of integration is that it is hierarchically additive, that is,

$$\mathrm{I}_{\mathrm{VAN}} = \mathrm{I}_{\mathrm{ANT}} + \mathrm{I}_{\mathrm{POST}} + \mathrm{I}_{\mathrm{BETWEEN}}.$$

In other words, integration within the VAN can be decomposed into the sum of the integration within the ANT and POST regions, and the integration between the ANT and POST regions. For each participant, these four integration values were calculated on the VAN; only whole network integration was assessed on the DMN ($\mathrm{I}_{\mathrm{DMN}}$).

4.5. Statistical analysis

Independent-samples t-tests were used with the VAN integration values ($\mathrm{I}_{\mathrm{VAN}}$, $\mathrm{I}_{\mathrm{ANT}}$, $\mathrm{I}_{\mathrm{POST}}$ and $\mathrm{I}_{\mathrm{BETWEEN}}$) as dependent variables to assess group effects. Independent-samples t-tests were also used to compare DMN integration across groups. Finally, task performance as measured by accuracy and response times was compared for both groups using two independent-samples t-tests (accuracy vs. group, response time vs. group). Note that response time was calculated using only items for which the participants answered correctly.

Correlations between VAN integration values ($\mathrm{I}_{\mathrm{VAN}}$, $\mathrm{I}_{\mathrm{ANT}}$, $\mathrm{I}_{\mathrm{POST}}$ and $\mathrm{I}_{\mathrm{BETWEEN}}$) and task performance (accuracy and response time) were calculated independently for each group.

Contributions

JA and YJ designed the study and JA performed the experiment. JD, JA, YJ and GM analyzed and interpreted the data. JD, JA and YJ wrote the manuscript. All authors have approved the present article.

Disclosure

The authors have declared no conflict of interest related to this study.

Acknowledgements

This work was supported by Canadian Institutes of Health Research - Canada Grant (200809MOP-191272-BCA-CFCL-18141 to Yves Joanette). The funding source had no contribution to the study design, collection, analysis, interpretation of the data or writing of the report for publication.

References

Allen, E.A., Damaraju, E., Plis, S.M., Erhardt, E.B., Eichele, T., Calhoun, V.D., 2012. Tracking whole-brain connectivity dynamics in the resting state. Cerebral Cortex. bhs352.

Andrews-Hanna, J.R., 2012. The brain's default network and its adaptive role in internal mentation. Neuroscientist 18 (3), 251–270.

Andrews-Hanna, J.R., Snyder, A.Z., Vincent, J.L., Lustig, C., Head, D., Raichle, M.E., Buckner, R.L., 2007. Disruption of large-scale brain systems in advanced aging. Neuron 56 (5), 924–935.

Ansado, J., Marsolais, Y., Methqal, I., Alary, F., Joanette, Y., 2013. The adaptive aging brain: evidence from the preservation of communication abilities with age. Eur J Neurosci 37, 1887–1895.

Ansado, J., Monchi, O., Deslauriers, J., Ennabil, N., Jubault, T., Faure, S., Joanette, Y., 2013. Coping with task demand in aging using neural compensation and neural reserve triggers primarily intra-hemispheric-based neurofunctional reorganization. Neurosci. Res. 75, 295–304.

Bastin, C., Yakushev, I., Bahri, M.A., Fellgiebel, A., Eustache, F., Landeau, B., Ellipsis Salmon, E., 2012. Cognitive reserve impacts on inter-individual variability in resting-state cerebral metabolism in normal aging. NeuroImage.

Bays, P.M., Singh-Curry, V., Gorgoraptis, N., Driver, J., Husain, M., 2010. Integration of goal- and stimulus-related visual signals revealed by damage to human parietal cortex. J. Neurosci. 30 (17), 5968–5978.

Betzel, R.F., Byrge, L., He, Y., Goñi, J., Zuo, X.-N., Sporns, O., 2014. Changes in structural and functional connectivity among resting-state networks across the human lifespan. NeuroImage.

Buckner, R.L., Andrews-Hanna, J.R., Schacter, D.L., 2008. The brain's default network. Ann. N. Y. Acad. Sci. 1124 (1), 1–38.

Chica, A.B., Bartolomeo, P., Lupiáñez, J., 2013. Two cognitive and neural systems for endogenous and exogenous spatial attention. Behav. Brain Res. 237, 107–123.

Chou, Y.-H., Chen, N.-K., Madden, D.J., 2013. Functional brain connectivity and cognition: effects of adult age and task demands. Neurobiol. Aging 34 (8), 1925–1934.

Corbetta, M., Patel, G., Shulman, G.L., 2008. The reorienting system of the human brain: from environment to theory of mind. Neuron 58 (3), 306–324.

Corbetta, M., Shulman, G.L., 2002. Control of goal-directed and stimulus-driven attention in the brain. Nat. Rev. Neurosci. 3 (3), 201–215.

Corbetta, M., Shulman, G.L., 2011. Spatial neglect and attention networks. Annu. Rev. Neurosci. 34, 569–599.

Damoiseaux, J.S., Beckmann, C.F., Arigita, E.J.S., Barkhof, F., Scheltens, P., Stam, C.J., Ellipsis Rombouts, S.A.R.B., 2008. Reduced resting-state brain activity in the 'default network' in normal aging. Cerebral Cortex (New York, N.Y.: 1991) 18 (8), 1856–1864.

Davis, S.W., Dennis, N.A., Daselaar, S.M., Fleck, M.S., Cabeza, R., 2008. Que PASA? The posterior-anterior shift in aging. Cerebral Cortex (New York, N.Y.: 1991) 18 (5), 1201–1209.

Esposito, F., Scarabino, T., Hyvarinen, A., Himberg, J., Formisano, E., Comani, S., Ellipsis Di Salle, F., 2005. Independent component analysis of fMRI group studies by self-organizing clustering. NeuroImage 25 (1), 193–205.

Foldi, N.S., Lobosco, J.J., Schaefer, L.A., 2002. The effect of attentional dysfunction in Alzheimer's disease: theoretical and practical implications. Semin. Speech Lang. 23 (2), 139–150.

Folstein, M.F., Folstein, S.E., McHugh, P.R., 1975. 'Mini-mental state'. A practical method for grading the cognitive state of patients for the clinician. J. Psychiat. Res. 12, 189–198.

Fornito, A., Harrison, B.J., Zalesky, A., Simons, J.S., 2012. Competitive and cooperative dynamics of large-scale brain functional networks supporting recollection. Proc. Natl. Acad. Sci. 109 (31), 12788–12793.

Fox, M.D., Corbetta, M., Snyder, A.Z., Vincent, J.L., Raichle, M.E., 2006. Spontaneous neuronal activity distinguishes human dorsal and ventral attention systems. Proc. Natl. Acad. Sci. U.S.A. 103 (26), 10046–10051.

Geerligs, L., Saliasi, E., Maurits, N.M., Renken, R.J., Lorist, M.M., 2014. Brain mechanisms underlying the effects of aging on different aspects of selective attention. NeuroImage 91, 52–62.

Geng, J.J., Mangun, G.R., 2011. Right temporoparietal junction activation by a salient contextual cue facilitates target discrimination. NeuroImage 54 (1), 594–601.

Grady, C.L., Protzner, A.B., Kovacevic, N., Strother, S.C., Afshin-Pour, B., Wojtowicz, M., Ellipsis McIntosh, A.R., 2010. A multivariate analysis of age-related differences in default mode and task-positive networks across multiple cognitive domains. Cerebral Cortex (New York, N.Y.: 1991) 20 (6), 1432–1447.

Hahn, B., Ross, T.J., Stein, E.A., 2006. Neuroanatomical dissociation between bottom-up and top-down processes of visuospatial selective attention. NeuroImage 32 (2), 842–853.

He, B.J., Snyder, A.Z., Vincent, J.L., Epstein, A., Shulman, G.L., Corbetta, M., 2007. Breakdown of functional connectivity in frontoparietal networks underlies behavioral deficits in spatial neglect. Neuron 53 (6), 905–918.

Hu, X., Le, T.H., Parrish, T., Erhard, P., 1995. Retrospective estimation and correction of physiological fluctuation in functional MRI. Magn. Reson. Med. 34 (2), 201–212.

Indovina, I., Macaluso, E., 2007. Dissociation of stimulus relevance and saliency factors during shifts of visuospatial attention. Cerebral Cortex (New York, N.Y.: 1991) 17 (7), 1701–1711.

Kincade, J.M., Abrams, R.A., Astafiev, S.V., Shulman, G.L., Corbetta, M., 2005. An event-related functional magnetic resonance imaging study of voluntary and stimulus-driven orienting of attention. J. Neurosci. 25 (18), 4593–4604.

Kleinman, J.T., Newhart, M., Davis, C., Heidler-Gary, J., Gottesman, R.F., Hillis, A.E., 2007. Right hemispatial neglect: frequency and characterization following acute left hemisphere stroke. Brain Cogn. 64 (1), 50–59.

Kucyi, A., Moayedi, M., Weissman-Fogel, I., Hodaie, M., Davis, K.D., 2012. Hemispheric asymmetry in white matter connectivity of the temporoparietal junction with the insula and prefrontal cortex. PLoS ONE 7 (4), e35589.

Lee, M.H., Hacker, C.D., Snyder, A.Z., Corbetta, M., Zhang, D., Leuthardt, E.C., Shimony, J.S., 2012. Clustering of resting state networks. PLoS ONE 7 (7), e40370.

Li, R., Chen, K., Fleisher, A.S., Reiman, E.M., Yao, L., Wu, X., 2011. Large-scale directional connections among multi resting-state neural networks in human brain: a functional MRI and Bayesian network modeling study. NeuroImage 56 (3), 1035–1042.

Li, R., Wu, X., Fleisher, A.S., Reiman, E.M., Chen, K., Yao, L., 2012. Attention-related networks in Alzheimer's disease: a resting functional MRI study. Hum. Brain Mapp. 33 (5), 1076–1088.

Liu, T.T., Frank, L.R., Wong, E.C., Buxton, R.B., 2001. Detection power, estimation efficiency, and predictability in event-related fMRI. NeuroImage 13, 759–773.

Macaluso, E., Doricchi, F., 2013. Attention and predictions: control of spatial attention beyond the endogenous-exogenous dichotomy. Front. Human Neurosci. 7, 685.

Madden, D.J., 2007. Aging and visual attention. Curr. Direct. Psychol. Sci. 16 (2), 70–74.

Madden, D.J., Parks, E.L., Davis, S.W., Diaz, M.T., Potter, G.G., Chou, Y., Ellipsis Cabeza, R., 2014. Age mediation of frontoparietal activation during visual feature search. NeuroImage 102, 262–274.

Madden, D., Whiting, W., 2004. Age-related changes in visual attention. In: Costa, P., Siegler, I. (Eds.), Recent Advances in Psychology and Aging. Elsevier, Amsterdam, pp. 41–88.

Marcotte, K., Perlbarg, V., Marrelec, G., Benali, H., Ansaldo, A.I., 2013. Default-mode network functional connectivity in aphasia: therapy-induced neuroplasticity. Brain Lang. 124 (1), 45–55.

Marrelec, G., Bellec, P., Krainik, A., Duffau, H., Pélégrini-Issac, M., Lehéricy, S., Ellipsis Doyon, J., 2008. Regions, systems, and the brain: hierarchical measures of functional integration in fMRI. Med. Image Anal. 12 (4), 484–496.

McKiernan, K.A., Kaufman, J.N., Kucera-Thompson, J., Binder, J.R., 2003. A parametric manipulation of factors affecting task-induced deactivation in functional neuroimaging. J. Cognitive. Neurosci. 15, 394–408.

Müller-Oehring, E.M., Schulte, T., Rohlfing, T., Pfefferbaum, A., Sullivan, E.V., 2013. Visual search and the aging brain: discerning the effects of age-related brain volume shrinkage on alertness, feature binding, and attentional control. Neuropsychology 27 (1), 48–59.

Parks, E.L., Madden, D.J., 2013. Brain connectivity and visual attention. Brain Connectivity 3 (4), 317–338.

Perlbarg, V., Marrelec, G., 2008. Contribution of exploratory methods to the investigation of extended large-scale brain networks in functional MRI: methodologies, results, and challenges. Int. J. Biomed. Imaging 2008, 218519.

Porter, G., Wright, A., Tales, A., Gilchrist, I.D., 2012. Stimulus onsets and distraction in younger and older adults. Psychol. Aging 27 (4), 1111–1119. http://dx.doi.org/10.1037/a0028486.

Ptak, R., 2012. The frontoparietal attention network of the human brain action, saliency, and a priority map of the environment. Neuroscientist 18 (5), 502–515.

Raz, N., Gunning-Dixon, F.M., Head, D., Dupuis, J.H., Acker, J.D., 1998. Neuroanatomical correlates of cognitive aging: evidence from structural magnetic resonance imaging. Neuropsychology 12 (1), 95–114.

Scalf, P.E., Ahn, J., Beck, D.M., Lleras, A., 2014. Trial history effects in the ventral attentional network. J. Cogn. Neurosci., 1–10

Shulman, G.L., McAvoy, M.P., Cowan, M.C., Astafiev, S.V., Tansy, A.P., d'Avossa, G., Corbetta, M., 2003. Quantitative analysis of attention and detection signals during visual search. J. Neurophysiol. 90 (5), 3384–3397.

Shulman, G.L., Pope, D.L.W., Astafiev, S.V., McAvoy, M.P., Snyder, A.Z., Corbetta, M., 2010. Right hemisphere dominance during spatial selective attention and target detection occurs outside the dorsal frontoparietal network. J. Neurosci. 30 (10), 3640–3651.

Spreng, R.N., 2012. The fallacy of a 'task-negative' network. Cognition, 145.

Stern, Y., 2009. Cognitive reserve. Neuropsychologia 47 (10), 2015–2028.

Sun, J., Tong, S., Yang, G.-Y., 2012. Reorganization of brain networks in aging and age-related diseases. Aging Dis. 3 (2), 181–193.

Swan, L., 2001. Unilateral spatial neglect. Phys. Ther. 81 (9), 1572–1580.

Tomasi, D., Volkow, N.D., 2012. Aging and functional brain networks. Mol. Psychiatry 17 (5). 471, 549–558.

Tononi, G., 1994. Reentry and the problem of cortical integration. Int. Rev. Neurobiol. 37 (127–52), 203–207 (discussion).

Vecera, S.P., Rizzo, M., 2003. Spatial attention: normal processes and their breakdown. Neurol. Clin. 21 (3), 575–607.

Vossel, S., Geng, J.J., Fink, G.R., 2014. Dorsal and ventral attention systems: distinct neural circuits but collaborative roles. Neuroscientist 20 (2), 150–159.

Vossel, S., Weidner, R., Driver, J., Friston, K.J., Fink, G.R., 2012. Deconstructing the Architecture of Dorsal and Ventral Attention Systems with Dynamic Causal Modeling. J. Neurosci. 32 (31), 10637–10648.

Watanabe, S., 1960. Information Theoretical Analysis of Multivariate Correlation. IBM. J. Res. Dev. 4, 66–82.

Whiting, W.L., Madden, D.J., Babcock, K.J., 2007. Overriding age differences in attentional capture with top-down processing. Psychol. Aging 22 (2), 223–232.

Wu, J.-T., Wu, H.-Z., Yan, C.-G., Chen, W.-X., Zhang, H.-Y., He, Y., Yang, H.-S., 2011. Aging-related changes in the default mode network and its anti-correlated networks: a resting-state fMRI study. Neurosci. Lett. 504 (1), 62–67.

Yeo, B.T.T., Krienen, F.M., Chee, M.W.L., Buckner, R.L., 2013. Estimates of segregation and overlap of functional connectivity networks in the human cerebral cortex. NeuroImage 88C, 212–227.

Ystad, M., Hodneland, E., Adolfsdottir, S., Haász, J., Lundervold, A.J., Eichele, T., Lundervold, A., 2011. Cortico-striatal connectivity and cognition in normal aging: a combined DTI and resting state fMRI study. NeuroImage 55 (1), 24–31.