



HAL
open science

Increased functional connectivity supports language performance in healthy aging despite gray matter loss

Aurélie Pistono, Laura Guerrier, Patrice Péran, Marie Rafiq, Mélanie Giméno, Catherine Bézy, Jérémie Pariente, Mélanie Jucla

► To cite this version:

Aurélie Pistono, Laura Guerrier, Patrice Péran, Marie Rafiq, Mélanie Giméno, et al.. Increased functional connectivity supports language performance in healthy aging despite gray matter loss. *Neurobiology of Aging*, 2021, 98, pp.52 - 62. 10.1016/j.neurobiolaging.2020.09.015 . hal-03492876

HAL Id: hal-03492876

<https://hal.science/hal-03492876>

Submitted on 15 Dec 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

Increased functional connectivity supports language performance in healthy aging despite grey matter loss

Pistono, A.^{a,d}, Guerrier, L.^b, Péran, P.^b, Rafiq, M.^c, Gimeno, M.^a, Bézy, C.^c, Pariente, J.^{b,c} and
Jucla, M.^a

^aOctogone-Lordat interdisciplinary research unit (EA 4156), University of Toulouse II-Jean
Jaurès, Toulouse, France

^bToulouse NeuroImaging Center, Toulouse University, Inserm, UPS, France.

^cNeurology Department, Neuroscience Centre, Toulouse University Hospital, Toulouse,
France

^dGhent University, department of experimental psychology

Corresponding and first author:

Pistono Aurélie

Ghent University, Department of experimental psychology

aurelie.pistono@ugent.be

Henri Dunantlaan, 2

9000 Gent

Belgium

+32 9 264 64 07

Abstract

Although language is quite preserved from aging, it remains unclear whether age-related differences lead to a deterioration or reorganization in language functional networks, or to different dynamics with other domains (e.g. the Multiple-Demand system). The current study is aimed at examining language networks, [using resting-state fMRI](#) in typical aging in relation to language performance. Twenty-three (23) [younger adults](#) and 24 healthy older adults were recruited. Volumetric grey matter differences between the two groups were assessed using voxel-based morphometry (VBM). Then, seed-based analyses, integrated local correlations in core regions of the language network, and within- and between-network connectivity were performed. We expected less extended connectivity maps, local coherence diminution, and higher connectivity with the Multiple-Demand system in older adults. On the contrary, analyses showed language network differences in healthy aging (i.e. increased connectivity with areas inside and outside language network), but no deterioration, despite widespread atrophy in older adults. Integrated local correlation revealed alterations that were unnoticeable with other analyses. While grey matter loss was not correlated with language performance, connectivity differences were positively correlated with fluency performance in the older group. These results differ from the literature concerning other cognitive networks in aging in that they show extra inter-network connections without a decrease in intra-network language connections. This reorganization could explain older adults' good language performance, and could be interpreted according to the scaffolding theory of aging and cognition.

Keywords: Resting-state; functional connectivity; aging; language

1. Introduction

Language is usually characterized as the most preserved cognitive function during typical aging (Park et al., 2002). However, while language comprehension is marginally affected in the aging [process](#) (Burke et al., 2018), several studies have shown that older participants have lower capacities than [younger](#) participants during production tasks (e.g. naming: Connor et al., 2004; verbal fluency: Meinzer et al. 2009). Additionally, task-related fMRI studies have found more activations in older participants during these tasks (i.e. an increase in neural activity in prefrontal regions and/or contralateral regions: Meinzer et al., 2009), suggesting the use of compensatory mechanisms. A number of theories examined these age-related functional compensations. For example, according to the hemispheric asymmetry reduction in older adults (HAROLD) model, increased bilateral frontal activation in older adults may serve a compensatory function when associated with improved or maintained behavioral performance (Cabeza, 2002). On the contrary, when increased brain activation is associated with a decline in behavioral performance, it is interpreted as evidence of neural “dedifferentiation” (Li et al., 2001; Park et al., 2004). A hybrid model, the compensation-related utilization of neural circuits hypothesis (CRUNCH, Reuter-Lorenz & Cappell, 2008) proposes an interaction between task difficulty and brain activation. Increased brain activation in older adults can help maintain behavioral performance during low difficulty tasks. However, if the task is too demanding, it will exceed neural resources available to older adults. Finally, the STAC model ([Scaffolding Theory of Aging and Cognition](#), Reuter-Lorenz & Park, 2014) provides an integrative account of the different theories mentioned so far. It posits that the aging brain is subject to a range of neural challenges to which it must adapt (i.e. atrophy, amyloid deposition, white matter deterioration, etc.), leading to continuous functional reorganization. Importantly, the model states that both lifespan (aging) and life experience variables affect the development of compensatory scaffolding.

Most studies that explored the activation pattern of the aging brain have used fMRI in the context of task-induced activation paradigms. Analyzing functional networks rather than discrete brain regions may provide interesting insights into the core (re)organization of language networks during aging. Resting-state functional connectivity is one of the current methods that describe the relationship between neural activation patterns of anatomically separated brain regions, which is consistent with the notion of networks used to perform a

specific cognitive task. To reveal these relevant resting-state networks, several studies used a seed-based approach focusing on the left inferior frontal gyrus (LIFG, including Broca's area) as a seed. They showed that in [younger adults](#), the average BOLD-signal dynamics of the LIFG are positively correlated with bilateral frontotemporal as well as subcortical regions (e.g. Muller & Meyer, 2014; Tomasi et al., 2012). However, these networks are disrupted in neurodegenerative diseases (e.g. Alzheimer's disease: Mascali et al., 2018; primary progressive aphasia: Bonakdarpour et al. 2019). Studies concerning typical aging are limited. Some authors found highly overlapping patterns of connectivity in older and [younger adults](#) (Antonenko et al., 2013). Others suggest that aging disrupts the organization of language networks by reducing within-network integration and increasing between-network connectivity (Shafto & Tyler, 2014).

The functional integration of brain networks during aging could also be evaluated through local functional correlation analyses. Local connectivity (Deshpande et al., 2009) is characterized by the strength and sign of connectivity between a given voxel and the neighboring areas in the brain that capture synchronous activity from adjacent sub-regions within an ROI (Region of interest). Local connectivity changes have proven to be a marker of various disorders. For example, Liu et al., (2008) stated that increased local coherence in specific areas in Alzheimer's patients could compensate for decreased distributed connectivity. Although language networks have never been examined using this method, the hypothesis can be posited that aging is characterized by local differences within brain regions involved in language, which would participate in the reorganization of the language system (Ansado et al., 2013).

Beyond the effects of aging, language is always partially reliant on domain-general abilities. Recent models of the neural architecture of language maintain that the language network is more extensive than was assumed in classical models (Geschwind, 1970). The Memory-Unification-Control (MUC) model, for example, (Hagoort, 2005, 2017) distinguishes three hubs that dynamically interact to guarantee processing of multiword utterances. Areas in the temporal cortex/angular gyrus store information such as phonological word forms, word meanings, etc. The left inferior frontal cortex (including Broca's area) is crucial for unification operations, which concern the assembly of pieces stored in memory into larger structures.

Control regions involve parts of the dorsolateral prefrontal, anterior cingulate cortex and the parietal cortex. These areas are required to orchestrate turn-taking or control attention. According to this view, in general, other brain networks are needed to process language (Hagoort, 2019), including interactions with the attentional control multiple demand (MD) system (Duncan, 2010). This system, also known as the frontoparietal attention network, partially covers the control regions of the MUC model. Several studies have examined the relationship between language and the MD system in [younger adults](#). Some of them found that the language system is independent from the MD system (i.e. for language comprehension: Blank et al., 2019). Others reported that the MD regions and core language regions may sometimes interact, in particular in the aging process, when the response to cognitive demands increases (e.g. semantic tasks, both in production and comprehension: Hoffman and Morcom, 2018).

To sum up, although language is relatively preserved from aging, it remains unclear whether age-related differences are characterized by a deterioration of language functional networks, a reorganization of these networks, or to different dynamics with other domains (e.g. the MD system). One hypothesis is that, given the evidence for compensatory recruitment in aging, increased between-network connectivity compensates for disruption within the language network. In the current study, we will attempt to examine network disruption and reorganization in typical aging in relation to language performance. First, we conducted Voxel Based Morphometry (VBM) to analyze volumetric grey matter differences [between a group of younger adults and a group of older adults](#). We expected [grey](#) matter loss in frontal and temporal cortices in the older group (Fjell et al., 2009), correlated with lower fluency performance. Then, we performed functional connectivity analyses. We conducted seed-based analyses, focusing on the dynamic interaction of the LIFG (as defined by Fedorenko et al., 2010) with the rest of the brain under task free conditions. We hypothesized that there are less extended connectivity maps in older adults compared to younger adults. Second, we analyzed local correlations in language networks, assuming that there is lower local connectivity in older adults correlated with [lower](#) language performance. Finally, within-language network connectivity and between-language network-MD-network connectivity were measured. We expected lower within-language network connectivity in older adults but higher between-language network-MD network connectivity, similarly to

Hoffman and Morcom, 2018. We expected positive correlations between language tasks and between language-MD network connectivity in the older group.

2. Materials and Methods

2.1 Participants

All of the volunteers were right-handed and native French speakers with no history of neurological or psychiatric problems. In order to avoid possible reorganization of language networks due to multilingualism, we only included speakers that did not have a good command and/or a frequent use of another language other than French. Twenty-three younger (28 ± 4 years old) and 24 older participants (70 ± 4 years old) were recruited. Both groups were matched for gender (Younger group: 13 women; Older group: 11 women), level of education (years of education, younger group: 14 ± 2 ; older group: 13 ± 4 , $p=0.12$) and global cognition (MMSE, younger group: 28.74 ± 1.01 ; older group: 29.0 ± 1.06 ; $p=0.39$). All the participants provided written, informed consent before participating in the study. The current study was approved by the ethics committee (IDRCB: 2015-A01416-43).

2.2 Cognitive evaluation

Language was assessed with the GREMOTs assessment (Bézy et al., 2016). The GREMOTs is a computerized battery of language tests that evaluates both oral and written language as well as production and comprehension at different levels (i.e. phonological processing, lexical processing, and syntactic processing).

All participants also underwent a comprehensive neuropsychological assessment. Anterograde verbal memory was assessed using the Free and Cued Selective Reminding Test (FCSRT; Van der Linden et al., 2004). Visual recognition memory was assessed with the Doors and People test (Baddeley et al., 1994). Short-term memory and working memory were evaluated with the WAIS-III **Forward** Digit Span and Backward Digit Span subtest (Wechsler, 1997). Cognitive flexibility was assessed with the Trail Making Test (TMT, Reitan, 1958). Praxis was explored with Mahieux's assessment (Mahieux-Laurent et al., 2008) and gnosis

with the Visual Gnosia Evaluation Protocol (Agniel, Joannette, Doyon, & Duchéin, 1992). Apathy and depression were also measured, using the Starkstein scale (Starkstein et al., 1992) and the Beck Depression Inventory (Beck et al., 1961).

Inter-group comparisons of these assessments were performed using the Student's t-test for independent samples. Bonferroni corrections for multiple comparisons were applied.

2.3 MRI-Acquisition

MRI scans were performed for all participants using a 3-T imager (Philips Achieva dStream, Inserm/UPS UMR1214 ToNIC Technical Platform, Toulouse, France). A 3D-T1 image was acquired for anatomical reference with the following parameters: TR = 8 ms, TE = 3.7 ms, flip angle = 8°, matrix size = 256 x 256 mm, 170 slices, voxel size = 0.9 mm x 0.9 mm x 1 mm, slice thickness = 1 mm. Whole-brain resting-state fMRI images were obtained with the following parameters: TR = 2837 ms, TE = 40 ms, flip angle = 90°, 46 interleaved acquisition, slice thickness = 3 mm, matrix size = 80 x 80 mm, 200 volumes, total scan time 10 min. During scanning, participants were instructed to keep their eyes closed but to stay awake and avoid thinking of anything in particular. All participants affirmed that they were fully awake during the 10 minutes of the scanning.

2.4 Preprocessing

Data were analyzed using the Conn toolbox (Version 18b, Whitfield-Gabrieli & Nieto-Castanon, 2012), implemented in Matlab. The preprocessing pipeline of the functional images included: functional realignment and unwarp; slice-timing correction; outlier identification; normalization to the MNI template, smoothing with a Gaussian kernel of 6 mm. This step created a scrubbing covariate (containing the potential outliers scans for each participant) and a realignment covariate (containing the six head motion parameters). Average realignment (Older group: -0.10 ± 0.08 ; Younger group: -0.06 ± 0.08 ; $t(45)=1.82, p=0.08$) and maximum realignment (Older group: 0.52 ± 0.6 ; Younger group: -0.5 ± 0.49 ; $t(45)=0.17, p=0.87$) did not differ significantly between the two groups. Then, the six head motion parameters plus their associated first-order derivatives; the identified

outliers scans; white matter and cerebrospinal fluid signals; and the effect of rest were removed by means of the CompCor method. The resulting preprocessed images were band-pass filtered (0.01 Hz–0.1 Hz) to remove physiological high-frequency noise (e.g. cardiac and respiratory fluctuations). Atlases were then masked with the participant's grey matter mask. With this method, each ROI was restricted to voxels belonging to an estimated grey matter mask derived from the T1 segmentation.

2.5 Voxel based morphometry

Grey matter density was assessed using a voxel-based morphometry method on Statistical Parametric Mapping version 12 (SPM 12, Wellcome Trust Centre for Neuroimaging). For each participant, the 3D-T1 sequence was segmented to isolate grey matter and white matter partitions, modulated for deformation, normalized to the MNI space and smoothed (8×8×8 mm). Inter-group comparisons were then performed (voxel level $p < 0.05$, FWE-corrected, cluster=200 voxels). Whole brain intra-group correlations were performed (threshold for significance: $p = 0.001$, uncorrected; cluster=200 voxels) with language tasks that were demanding for current participants and known to be sensitive to the effect of aging. We selected lexical and syntactic tasks: semantic fluency (total number of words for the category “fruit”), phonemic fluency (total number of words starting with the letter V), grammatical fluency (total number of words with the category verb), and syntactic comprehension (accuracy /24). As these tasks partly involve executive functions, performance on the TMT part B (time in seconds) was also included in the analyses to verify whether results were specific to language processing.

2.6 Seed-based analyses

2.6.1 Definition of the seed

The left Inferior frontal gyrus (LIFG) was used as a seed, based on Fedorenko's parcels of language regions (Fedorenko et al., 2010). This seed encompasses Brodman's areas 44 and 45.

2.6.2 Analyses

Correlation maps were constructed by correlating the averaged BOLD-signal dynamic of the region of interest with the BOLD-signal of every other single voxel. To enforce a Gaussian distribution of the correlation data, Pearson's correlation coefficients were then transformed to z-scores using the Fisher r to z transformation for subsequent t-tests. These individual z values maps were entered into a one-sample t-test to determine the functional network correlated with spontaneous activity of the seed region within each group ($p < 0.05$ FWE at the cluster level). We then performed two-sample t-tests to detect inter-group differences. The threshold for second level maps was set at $p < 0.05$ FWE at the cluster level.

Finally, we extracted connectivity values of each cluster found during the inter-group comparison, to perform partial correlations with language tasks, in each group separately: semantic fluency, phonemic fluency, grammatical fluency, syntactic comprehension, and TMT B. Partial correlations were used to control for participants' age and level of education (in years of education). Bonferroni corrections were applied.

2.7 Local correlations

2.7.1 Definition of the ROIs

Local correlation maps were measured based on the Pearson's correlation coefficient of the time courses between the current and neighboring voxels (Integrated Local Correlation, ILC, Deshpande et al., 2009), using the Conn Toolbox. An 8mm spatial convolution kernel was used for ILC bounds. ILC was determined specifically in the language network. The 13 ROIs from the original parcels of Fedorenko et al. (2010) were chosen (See Supplementary Material). It includes 10 ROIs within the left hemisphere: IFG, IFG-orbitofrontal gyrus, middle frontal gyrus, superior frontal gyrus, anterior temporal gyrus, middle-anterior temporal gyrus, middle-posterior temporal gyrus, posterior temporal gyrus, angular gyrus and cerebellum; 3 ROIs in the right hemisphere: middle-anterior temporal gyrus; middle-superior temporal gyrus and cerebellum.

2.7.2 Analyses

Intergroup comparisons of ILC values from these 13 ROIs were performed using the Student's t-test for independent samples. Bonferroni corrections for multiple comparisons were applied. Partial correlations were then performed between ROIs that significantly differed between the two groups and language tasks, separately in each group. We selected the same language tasks and procedures as those used for the seed-based analysis.

2.8 Within-network and between-network connectivity

2.8.1 Definition of the ROIs

To measure within-language-network connectivity and between-language-MD network connectivity, we selected ROIs from Fedorenko and colleagues. For the language network, the above-mentioned original parcels from Fedorenko et al., (2010) were chosen. For the MD network, the functional parcels from Fedorenko and Blank (available at: <https://evlab.mit.edu/funcloc/download-parcels>) were used (Figure 4, green areas). They include the left and right IFG, middle frontal gyrus, middle frontal-orbitofrontal gyrus, inferior parietal lobe, superior parietal lobe, anterior cingulate cortex, insular cortex, supplementary and presupplementary motor area and precentral gyrus. Both networks are shown Figure 4.

2.8.2 Analyses

Within- and between-network connectivity (average for all the ROIs within each network) was evaluated for each participant. More precisely, **within-network** connectivity is a mean composite network connectivity estimate, calculated by means of pairwise correlations between all the regions comprising an individual network. Between-network connectivity is the result of pairwise correlations between the regions in each pair of different networks. Averages of within- and between-network connectivity were compared between groups with one-tailed t-tests, to analyze whether older adults present higher within- and between-network connectivity. To test the hypothesis that between-network connectivity was positively correlated with language performance in older participants, we performed partial correlations with the same language tasks as the one used for previous analyses, separately in each group.

3. Results

3.1 Cognitive evaluation

3.1.1 Language

As shown in Table 1, older adults performed better than [younger adults](#) for the naming of famous faces and spelling tasks. [On the contrary](#), they were significantly slower [than younger adults](#) for text comprehension.

3.1.2 Other cognitive functions

In the neuropsychological assessment, older participants had a lower anterograde memory performance in the sum of the three free recalls of the FCSRT. They were slower during the TMT A and B. Other results were not significantly different after correction for multiple comparisons. Results are shown in Table 1 below:

Tests		Older Adults	Younger Adults	p value
	Semantic fluency (number fruits in 2 minutes)	19.33±3.38	21.91±4.27	0.03
	Phonemic fluency (number of words starting with R in 2 minutes)	17.29±6.12	20.39±6.28	ns
	Grammatical fluency (number of verbs in 2 minutes)	35.21±11.66	33.61±11.76	ns
Lexical	Naming, Object (/36)	34.70±1.40	34.57±0.99	ns
Processing	Naming, Action (/36)	33.13±3.25	33.65±1.97	ns
	Naming, Famous faces (/10)	8.75±1.15	6.48±1.93	0.001
	Semantic verification (oral) (/18)	17.04±1.27	17.22±0.85	ns
	Semantic verification (written) (/18)	16.30±1.69	16.65±1.11	ns
	Repetition, words (/10)	9.38±1.01	9.91±0.29	0.02
	Reading, words (/30)	29.71±0.55	30.13±1.98	ns
	Spelling, Words (/12)	11.58±0.50	10.78±1.13	0.004
Syntactic	Sentence production (/6)	5.75±0.68	5.96±0.21	ns

processing	Syntactic comprehension (/24)	21.25±2.51	22.78±2.33	0.04
	Spelling, sentences (/27)	25.83±1.05	23.91±2.17	0.001
	Text comprehension (time)	49.30±15.73	39.09±7.54	0.008
Phonological processing	Repetition, non-words (/6)	5.52±0.67	5.87±0.34	ns
	Reading, non-words (/15)	14.67±0.64	14.35±0.83	ns
	Spelling, non-words (/6)	5.50±0.59	5.48±0.51	ns
Other cognitive functions	MMSE (/30)	29±1	28.7±1	ns
	FCSRT - Sum of the three free recalls (/48)	32.29±4.79	38.61±3.85	0.001
	FCSRT - Sum of the three cued recalls (/48)	46.42±1.93	47.52±0.8	0.01
	Doors and People Test, set A (/12)	10.78±1.38	11.3±1.1	ns
	Forward Digit span	6±1	6.3±1.15	ns
	Backward digit span	4.83±1.4	5.13±1.39	ns
	TMT A (speed in seconds)	38.79±12.5	22.1±8.52	0.001
	TMT B (speed in seconds)	92.25±32.44	51.91±16.87	0.001
	Visual Gnosia Evaluation Protocol (/36)	35.26±1.1	35.78±0.52	ns
	Mahieux's assessment (/23)	22.58±0.78	22/96±0.21	0.03
	Beck	2.58±2.2	2.26±2.47	ns
Starkstein	9.5±4.2	6.96±3.17	0.02	

Table 1: Performance during language assessment and neuropsychological assessment

Results correspond to mean ± standard deviation. Significant results after correction for multiple comparisons are in bold.

3.2 Voxel-based morphometry

3.2.1 Inter-group comparisons

Older adults had less grey matter density in several areas, including language regions (e.g. left inferior frontal gyrus and left temporal cortex) as shown Figure 1 below.

[insert Figure 1 about here]

3.2.2 Intra-group correlations

We performed whole brain correlations with language tasks (i.e. semantic fluency, phonemic fluency, grammatical fluency, syntactic comprehension) and TMT B. In the younger group, there were no correlations between performance and grey matter density. In the older group, there were no correlations between language performance and grey matter density. There was a negative correlation between TMT B (execution time in seconds) and grey matter density in the [ventrolateral prefrontal cortex \(VLPFC\)](#) and [dorsolateral prefrontal cortex \(DLPFC\)](#): right pars opercularis and pars triangularis ($p=0.027$), Right frontal pole ($p=0.036$) and Left pars opercularis ($p=0.038$), as shown in Figure 2 below.

[insert Figure 2 about here]

3.3 Seed-based analyses

Both groups showed extended maps of areas connected with the LIFG (Table 2 and Figure 3).

[insert Figure 3 about here]

Cluster	Functional connectivity	K voxels	Peak in MNI Coordinates (x, y, z)	T value
Younger group				
Left frontal regions (i.e. frontal pole, middle and superior frontal gyri, inferior frontal gyri) and temporoparietal regions (i.e. TP, ITG, MTG, SMG, AG, lateral occipital cortex)	positive	30061	-46 +14 +30	31.90

and SPL).				
Right regions mentioned in the cluster above	positive	16908	+44 +12 +28	17.84
Left temporal fusiform cortex	positive	250	-34 -14 -36	8.14
Right cerebellum	positive	2020	+24 -66 -32	8.27
Left cerebellum	positive	366	-18 -76 -52	7.28
Left cerebellum	positive	220	-10 -74 -28	5.34
Precuneus and posterior cingulate	negative	5399	-14 -50 +22	-10.14
Left and Right frontal pole, paracingulate gyrus and frontal medial cortex	negative	1841	-10 +44 -06	-7.40
Right hippocampus and parahippocampal gyrus	negative	649	+38 -38 -04	-9.8
Right ITG, MTG, TP	negative	288	+46 +02 -36	-7.19
Left cerebellum	negative	218	-14 -42 -58	-9.27
Left cerebellum	negative	208	-32 -82 -34	-5.47
Older group				
Left and Right frontal regions (i.e. frontal poles, middle and superior frontal gyri, inferior frontal gyri). Left lateral occipital cortex, SMG, AG, SPL, ITG. Right TP, precuneus	positive	41598	-42 +24 +24	18.82
Right lateral occipital cortex, SMG, AG	positive	2752	+42 -44 +44	8.68
Right ITG, MTG	positive	1050	+60 -38 -18	6.94
Right cerebellum	positive	2367	+32 -70 -52	9.22
Left cerebellum	positive	396	-24 -78 -52	6.92
Left hippocampus, caudate and temporal fusiform cortex	negative	4587	-04 +06 +20	-5.18
Right hippocampus, thalamus, parahippocampal gyrus, PCC	negative	2275	+36 -38 +18	-9.24
Left cerebellum	negative	870	-08 -26 -54	-10.34

Table 2: Summary of regions positively and negatively correlated with the seed (i.e. LIFG) in each group. Abbreviations: PCC= Posterior Cingulate Gyrus; SMG= Supramarginal gyrus; AG = Angular Gyrus; TP= Temporal Pole; ITG= Inferior temporal gyrus; MTG= Middle temporal gyrus; SPL= Superior parietal lobule.

3.3.1 Inter-group comparisons

Three left-lateralized clusters were significantly more correlated with the LIFG in the older group (Figure 4): one cluster involving the posterior cingulate gyrus and the precuneus ($p_{FWE}=0.0007$, 423 voxels), one cluster involving the left temporal pole, inferior temporal pole and middle temporal gyrus ($p_{FWE}=0.001$, 348 voxels), and one cluster within the left angular gyrus ($p_{FWE}=0.015$, 289 voxels). As shown in Figure 4, these clusters are negatively correlated with the LIFG in the younger group but positively correlated in the older group. Two of them are part of the language network we used.

[insert Figure 4 about here]

3.3.2 Intra-group correlations

Connectivity values with clusters that were significantly different between the two groups were correlated with participants' cognitive performance (i.e. semantic fluency, phonemic fluency, grammatical fluency, syntactic comprehension and TMT B). In the older group, the strength of connectivity between the LIFG and the temporal pole/inferior temporal gyrus was positively correlated with grammatical fluency performance ($p=0.037$, $r=0.46$) and semantic fluency performance ($p=0.019$, $r=0.51$). However, these correlations were not significant after Bonferroni correction. In the younger group, no correlation was significant.

3.4 Local correlations

3.4.1 Inter-group comparisons

ILC values extracted from the 13 Language ROIs that were previously chosen, were compared between the two groups. One ROI, the left Superior frontal gyrus; had significantly lower ILC in the older group (Older group: 0.5 ± 0.01 ; Younger group: 0.53 ± 0.02 , $p < 0.001$). Another frontal ROI, the left IFG-orbitofrontal gyrus, had lower ILC in the older group, but this difference was not significant after correction for multiple comparisons (Older group: 0.61 ± 0.03 ; Younger group: 0.64 ± 0.03 , $p = 0.013$). Other ROIs were not significantly different between the two groups.

3.4.2 Intra-group correlations

In the older group, the Left Superior frontal gyrus ILC was positively correlated with grammatical fluency performance ($p = 0.01$, $r = 0.54$). Other correlations were not significant after correction. In the younger group, no correlation was significant.

3.5 Within-network and between-network connectivity

3.5.1 Inter-group comparisons

Both groups showed positive functional connectivity between regions comprising the language network and the MD network. The average connectivity within the language network (Older group: 0.26 ± 0.11 ; Younger group: 0.23 ± 0.09 ; $t(45) = 0.7$, $p = 0.23$) or within the MD network (Older group: 0.38 ± 0.13 ; Younger group: 0.35 ± 0.08 ; $t(45) = 1.1$, $p = 0.13$) was not significantly different between the two groups. However, the strength of connectivity between these two networks was higher in the group of older adults (Older group: 0.17 ± 0.13 ; Younger group: 0.11 ± 0.08 ; $t(45) = 1.7$, $p = 0.04$)¹.

3.5.2 Intra-group correlations

Between-network connectivity was positively correlated with phonemic fluency performance ($p = 0.009$, $r = 0.55$, Figure 5) in the group of older adults. Correlation with grammatical fluency performance was not significant after Bonferonni correction ($p = 0.016$, $r = 0.52$). In the younger group, no significant correlations were identified.

¹ Some ROIs overlapped between the language and the MD network (e.g., parts of IFG or MFG). We therefore conducted another set of analyses, excluding these ROIs, and it did not affect results.

[insert Figure 5 about here]

4. Discussion

In the current study, we showed that healthy older adults have preserved language capacity but structural and functional differences that encompass language regions. Notably, their naming and fluency scores were not lower than those of [younger adults](#), contrary to previous studies (e.g. Connor et al., 2004; Meinzer et al., 2009) in which participants had a similar age and level of education. While it is known that language comprehension is usually preserved from aging whereas language production declines (Burke et al., 2018), current results show that both aspects were relatively preserved in this group of older adults. On a structural level however, this group had widespread atrophy, including language areas. A mismatch between age-related structural changes and the preservation of language abilities has already been mentioned in the literature (Ansado et al., 2013), which suggests neurofunctional reorganization.

4.1 Structural imaging and aging

Older participants had widespread atrophy, including frontal and temporal cortices but also other areas (e.g. cerebellum, thalami), contrary to what was expected. These results are consistent with Ramanoël et al., 2018, who showed a similar pattern of atrophy in older adults with a similar age and [level of education](#) as older participants in the current study. However, contrary to what was expected, grey matter loss was not correlated with language performance in the group of older adults, while it was with performance to TMT B. This implies that, in the older group, fluency and syntactic tasks were not associated [with](#) structural changes, even if atrophy encompassed language areas (e.g. LIFG, LSTG). On the contrary, TMT B (execution time) was correlated with grey matter atrophy within bilateral VLPFC and right DLPFC. In a functional near-infrared spectroscopy study, Müller et al., 2014, compared [younger](#) and older adults' performance to TMT. They showed that in both groups, TMT B required bilateral VLPFC, DLPFC. They also showed that older adults had additional

activation in right DLPFC, in particular BA 10 and BA 46. The current study indicates that not only functional activations, but also grey matter density within DLPFC could contribute to better performance to TMT B during typical aging.

To reinforce the absence of correlation with language tasks, it is important to emphasize that older adults had significantly lower performance than younger adults during the neuropsychological assessment (e.g. FCSRT, TMT A, TMT B) but not during the language assessment (i.e. not after correction for multiple comparisons). The discrepancy between atrophy and language performance suggests that language differs from other cognitive functions. It probably relies on a distributed functional network rather than individual structures. This postulate has been further investigated during functional connectivity analyses. Indeed, given the significant atrophy in the older group, we applied individual masks of grey matter on the ROIs we used. By doing this, we restricted functional analyses to voxels within the estimated grey matter mask for each subject. Results show that despite grey matter loss, older adults did not present functional alteration, as discussed in the following subsections. They support the idea that the distributed nature of language enables several functional compensations.

4.2 Comparison with current literature on functional connectivity and aging

Resting-state functional analyses indicate that during seed-based analyses, three clusters were positively correlated with the LIFG in older adults, while negatively correlated with the LIFG in [younger adults](#). In other words, contrary to our hypotheses, we did not find a less extensive pattern of correlations and anti-correlations in typical aging. In both groups, connectivity maps of regions functionally connected to the LIFG included bilateral frontotemporal as well as subcortical regions in both groups, similarly to previous studies in [younger adults](#) (e.g. Muller & Meyer, 2014; Tomasi, 2012). Moreover, connectivity between LIFG and two language areas (i.e. left angular gyrus and left inferior temporal gyrus/temporal pole) as well as with the PCC/precuneus were positive in the group of older adults, which implies that more areas are recruited in the language network at rest during typical aging. It can be assumed that this pattern of connectivity is related to the preservation of language ability during aging. Most of the literature in which functional connectivity in healthy aging

was analyzed showed decreased connectivity with age (e.g. default mode network, salience network, attentional network: Sala-Llonch, Bartrés-Faz, & Junqué, 2015) but increases in the connectivity of a network toward regions of other resting-state networks. One previous study compared functional networks of language in [younger participants](#) and older participants using BA44 as a seed (Antonenko et al., 2013). They revealed stronger intra-hemispheric functional connectivity in the [younger adults](#) compared to older adults, which was correlated with superior language task performance (i.e. evaluated through syntactic tasks only). On the contrary, older adults' networks showed higher connections with areas outside the core language network (i.e. with the right hemisphere). According to the authors, there could be a beneficial effect of higher intra-network connection on behavior, (which would reflect the efficiency of communication within a given brain network), and lower inter-network connection, (which would reflect specificity and selectivity of the network under study), for preserved cognitive functions. This statement is in keeping with the literature concerning other cognitive networks (e.g. Damoiseaux 2017; Sala-Llonch, Bartrés-Faz, & Junqué, 2015). Although the current study does not show a similar pattern of connectivity in older adults, results partly support this idea, given that the older group had a stronger intra-hemisphere correlation within language regions, correlated with superior language performance (i.e. connectivity between the LIFG and the temporal pole/inferior temporal gyrus was positively correlated with grammatical fluency performance and semantic fluency performance in the older group). The relatively high level of education of older participants we recruited might partly explain why they presented higher intra-network connection, contrary to Antonenko et al., 2013. However, because participants' level of education was not mentioned in their study, we cannot further discuss this hypothesis. Similar to Antonenko et al., 2013, the specificity of the language network differed somewhat in the group of older adults we tested: the LIFG was also positively correlated with the PCC/precuneus, a region that is not part of language network, while the correlation was negative in the younger group.

Similarly, the analyses we conducted on within- and between-network connectivity indicated that the older group did not have lower within-language network connectivity but an increase in between-language network-MD system connectivity compared to the younger group. This finding reinforces the idea mentioned above: although network efficiency is not

weaker, older adults have higher inter-network connections. While Blank et al., 2014 showed a functional dissociation between the language and MD systems at rest in [younger adults](#), our results indicate that aging may change this dissociation, in line with Hoffman and Morcom, 2018. Correlation analyses indicate that inter-network connectivity might have a beneficial effect: the strength of connectivity between the language system and the MD system was positively correlated with phonemic and grammatical fluency scores in the older group. Those tasks are well known to be at least as demanding in lexical abilities as in executive functions (Piatt et al., 1999), especially in older participants (Shao et al., 2014). In sum, the current study results in slightly different conclusions than in the previous literature. Seed-based analyses and between-network connectivity show a reorganization of language network in healthy aging, but not a deterioration. These results differ from those in the literature concerning other cognitive networks but also from those provided by Antonenko et al., 2013. However, given that these authors did not conduct a neuropsychological and language assessment, we cannot further examine why our results differ on a functional level.

Therefore, it would appear that older participants use functional compensatory mechanisms before major alterations can be visible through seed-based analyses and within-network connectivity. This is an interesting finding in the light of the scaffolding theory of aging and cognition (STAC, Park and Reuter-Lorenz 2009; Reuter-Lorenz and Park 2014). As mentioned in the introduction, this theory aims to understand the high level of cognitive processing that can be maintained by older adults during neurobiological changes. Increased functional activity (e.g. HAROLD, PASA, etc.) could be due to compensatory scaffolding (i.e. the recruitment of additional circuitry that shores up declining structures). According to this view, scaffolding is not only the brain's response to normal aging but, in fact, the brain's normal response to cognitive challenges, which occur more often during aging. In other words, humans develop scaffolds as a result of stimulating experiences. According to these authors, this is why the maintenance of language in aging may result from the continuous use of language throughout life and from a particularly elaborate scaffolding network for this overlearned behavior. This could explain why our findings are different from findings on other functional networks (e.g. Damoiseaux 2017; Sala-Llonch, Bartrés-Faz, & Junqué, 2015), with increased inter-network connections without lower intra-network connections. This

could also explain why older adults' grey matter atrophy does not have an impact on their language performance.

Although we cannot fully explain the reorganization we observed, measurement of the integrated local correlation in core regions of the language network brought complementary findings. In fact, this measurement showed alterations related to aging that were not noticeable with other analyses. The integrated local correlation assesses local network connectivity alterations. It determines the strength or change in the "local coherence" of functional networks which are not visible through large-scale network analyses. Results suggest that local connectivity is reduced in the language network during typical aging. Some clusters had lower ILC values in the group of older adults, the left superior frontal gyrus being the most significant cluster. Its ILC preservation was positively correlated with grammatical fluency performance in older participants. This pattern contrasts with the one found in Alzheimer's disease. In fact, Liu et al. (2008) identified altered functional connectivity patterns in Alzheimer's patients, decreased local coherence in the PCC/Precuneus correlated with lower MMSE, but increased local coherence in other areas, which could be interpreted as compensation. On the contrary, in the current study, we can assume that the increased functional connectivity observed in the older group is linked to local coherence alterations in several areas of the language system. This could also imply that ILC measures are more sensitive to the effects of healthy aging.

4.3 Limitations

This study has several limitations. First, the sample size is rather small, due to its homogeneity. For example, we did not include bilingual participants, which restricted the group of participants. This also explains why we did not apply FWE corrections on structural correlations. Further studies are therefore required to examine structural and functional differences of language networks in typical aging and reinforce current findings. Second, we did not use a functional language task to control whether participants were left hemisphere dominant, or to define our ROIs. Although we exclusively included right-handed participants, we cannot be sure that their language was left lateralized. Moreover, the use of a predefined atlas might have influenced the results. However, the atlas we chose provides a

good representation of the language function, since it includes language areas that are not always part of other atlases, such as different sections of the left temporal lobe. We also decided to use a seed that was functionally defined, since they are more likely to represent brain regions effectively involved in language processing than anatomical seeds (Muller et al., 2014). Nonetheless, the seed we chose is quite large compared to other studies (e.g. Antonenko et al., 2013, generated a 3mm-radius sphere in the left pars opercularis). It is therefore possible that we lose information by averaging BOLD signal from this type of seed.

4.4 Future directions

The current study focused on the MD system, but the connectivity between language and other networks could also be examined. In fact, it is possible that increased connectivity between the language network and other networks participates in language preservation at a behavioral level. Additionally, phonemic and grammatical fluency may be sensitive measures in aging that should be further investigated. In fact, all functional measures were correlated with at least one of these two measures. Given the important executive component of these tasks, one hypothesis might be that compensation is mainly possible for the executive control of language. In the future, it might be interesting to further examine compensatory mechanisms for distinct language abilities, both for language production and language comprehension.

Finally, given the scarcity of literature on language functional networks in aging, we decided to use a priori defined brain regions instead of data-driven approaches to focus on language-specific areas, but future work could use methods that take into account the whole brain rather than a specific network. In the future, it would also be crucial to compare the language functional network with other cognitive networks for a more in-depth analysis of its specific effect during aging. Finally, we focused on resting-state data but further work is required to examine fMRI data acquired during different language production tasks to elucidate the modulations in the network when the brain is actively processing specific language tasks and the differences related to age-groups.

4.5 Conclusions

In conclusion, the current study is the first to examine language networks in younger and older participants, using several levels of analysis. We showed that the increase in the number of areas positively correlated with the LIFG in older adults, as well as the higher connectivity between the language network and the MD network in this group probably explains why their performance during language assessment was not lower than younger adults despite significant atrophy. This compensation seems particularly helpful for the executive control of language.

Acknowledgments

This study was supported by a grant from the Occitania Region and the Toulouse Mind and Brain Institute to MJ (TellMA project grant number: 15050480). We would like to thank the Inserm/UPS UMR1214 Technical Platform for the MRI acquisitions. The authors would also like to thank the patients and control participants who participated in the study, as well as the promoter of the study, Toulouse University Hospital (CHU). There are no conflicts of interest to report.

References

- Agniel, A., Joannette, Y., Doyon, B., & Duchéin, C. (1992). *Protocole Montréal-Toulouse : Évaluation des gnosies visuelles et auditives* (O. Edition (ed.)).
- Ansado, J., Marsolais, Y., Methqal, I., Alary, F., & Joannette, Y. (2013). The adaptive aging brain: Evidence from the preservation of communication abilities with age. *European Journal of Neuroscience*, 37(12), 1887–1895. <https://doi.org/10.1111/ejn.12252>
- Antonenko, D., Brauer, J., Meinzer, M., Fengler, A., Kerti, L., Friederici, A. D., & Flöel, A. (2013). NeuroImage Functional and structural syntax networks in aging. *NeuroImage*, 83, 513–523. <https://doi.org/10.1016/j.neuroimage.2013.07.018>
- Baddeley, A. D., Emslie, H., Nimmo-Smith, I., & Company, T. V. T. (1994). *Doors and People: A Test of Visual and Verbal Recall and Recognition. Manual*. Thames Valley Test Company. <https://books.google.fr/books?id=bK4xAAAACAAJ>

- Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry*, *4*, 561–571.
- Bézy, C., Renard, A., & Pariente, J. (2016). *GREMOTS Batterie d'évaluation des troubles du langage dans les maladies neurodégénératives*. De Boeck supérieur.
- Blank, I., Kanwisher, N., & Fedorenko, E. (2014). A functional dissociation between language and multiple-demand systems revealed in patterns of BOLD signal fluctuations. *J Neurophysiol.*, *112*(5), 1105–1118. <https://doi.org/10.1152/jn.00884.2013>
- Bonakdarpour, B., Hurley, R. S., Wang, A. R., Ferreira, H. R., Basu, A., Chatrathi, A., Guillaume, K., Rogalski, E. J., & Mesulam, M. M. (2019). Perturbations of language network connectivity in primary progressive aphasia. *Cortex*, *121*, 468–480. <https://doi.org/10.1016/j.cortex.2019.08.010>
- Burke, D. M., MacKay, D. G., & James, L. E. (2018). Theoretical Approaches to Language and Aging. In *The Routledge Handbook of Language and Politics* (Perfect &, Issue October 2012). Oxford, U.K.: Oxford University Press. <https://doi.org/10.4324/9781315183718-2>
- Cabeza, R. (2002). Hemispheric asymmetry reduction in older adults: the HAROLD model. *Psychology and Aging*, *17*(1), 85–100. <https://doi.org/10.1037//0882-7974.17.1.85>
- Connor, L. T., Spiro, A., Obler, L. K., & Albert, M. L. (2004). Change in Object Naming Ability During Adulthood. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, *59*(5), P203–P209. <https://doi.org/10.1093/geronb/59.5.P203>
- Damoiseaux, J. S. (2017). Effects of aging on functional and structural brain connectivity. *NeuroImage*, *160*(February), 32–40. <https://doi.org/10.1016/j.neuroimage.2017.01.077>
- Deshpande, G., LaConte, S., Peltier, S., & Hu, X. (2009). Integrated local correlation: A new measure of local coherence in fMRI data. *Human Brain Mapping*, *30*(1), 13–23. <https://doi.org/doi:10.1002/hbm.20482>
- Duncan, J. (2010). The multiple-demand (MD) system of the primate brain: mental programs for intelligent behaviour. *Trends in Cognitive Sciences*, *14*(4), 172–179. <https://doi.org/https://doi.org/10.1016/j.tics.2010.01.004>

- Fedorenko, E., Hsieh, P., Nieto-castañón, A., Whitfield-gabrieli, S., & Kanwisher, N. (2010). *New Method for fMRI Investigations of Language : Defining ROIs Functionally in Individual Subjects*. 1177–1194. <https://doi.org/10.1152/jn.00032.2010>.
- Fjell, A. M., Walhovd, K. B., Fennema-Notestine, C., McEvoy, L. K., Hagler, D. J., Holland, D., Brewer, J. B., & Dale, A. M. (2009). One-year brain atrophy evident in healthy aging. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 29(48), 15223–15231. <https://doi.org/10.1523/JNEUROSCI.3252-09.2009>
- Geschwind, N. (1970). The Organization of Language and the Brain. *Science*, 170(3961), 940 LP – 944. <https://doi.org/10.1126/science.170.3961.940>
- Hagoort, P. (2005). On Broca, brain, and binding: A new framework. *Trends in Cognitive Sciences*, 9(9), 416–423. <https://doi.org/10.1016/j.tics.2005.07.004>
- Hagoort, P. (2017). Neuroscience and Biobehavioral Reviews The core and beyond in the language-ready brain. *Neuroscience and Biobehavioral Reviews*, 81, 194–204. <https://doi.org/10.1016/j.neubiorev.2017.01.048>
- Hagoort, P. (2019). The neurobiology of language beyond single-word processing. *Science*, 58(October), 55–58.
- Hoffman, P., & Morcom, A. M. (2018). Age-related changes in the neural networks supporting semantic cognition: A meta-analysis of 47 functional neuroimaging studies. *Neuroscience and Biobehavioral Reviews*, 84(November 2017), 134–150. <https://doi.org/10.1016/j.neubiorev.2017.11.010>
- Li, S.-C., Lindenberger, U., & Sikström, S. (2001). Aging cognition: from neuromodulation to representation. *Trends in Cognitive Sciences*, 5(11), 479–486. [https://doi.org/https://doi.org/10.1016/S1364-6613\(00\)01769-1](https://doi.org/https://doi.org/10.1016/S1364-6613(00)01769-1)
- Liu, Y., Wang, K., Yu, C., He, Y., Zhou, Y., Liang, M., Wang, L., & Jiang, T. (2008). Regional homogeneity, functional connectivity and imaging markers of Alzheimer's disease: a review of resting-state fMRI studies. *Neuropsychologia*, 46(6), 1648–1656. <https://doi.org/10.1016/j.neuropsychologia.2008.01.027>
- Mahieux-Laurent, F., Fabre, C., Galbrun, E., Dubrulle, A., & Moroni, C. (2008). Validation

d'une batterie brève d'évaluation des praxies gestuelles pour consultation Mémoire. Évaluation chez 419 témoins, 127 patients atteints de troubles cognitifs légers et 320 patients atteints d'une démence. *Revue Neurologique*, 1519(6), 511 YP – 611.

<https://doi.org/http://dx.doi.org/10.1016/j.neurol.2008.11.016>

Mascali, D., Dinuzzo, M., Serra, L., Mangia, S., & Maraviglia, B. (2018). Disruption of Semantic Network in Mild Alzheimer ' s Disease Revealed by Resting-State fMRI. *Neuroscience*, 371, 38–48. <https://doi.org/10.1016/j.neuroscience.2017.11.030>

Meinzer, M., Wilser, L., Fleisch, T., Eulitz, C., Rockstroh, B., Conway, T., & Crosson, B. (2009a). Neural Signatures of Semantic and Phonemic Fluency in Young and Old Adults. *Journal of Cognitive Neuroscience*, 21(10), 2007–2018.

Meinzer, M., Wilser, L., Fleisch, T., Eulitz, C., Rockstroh, B., Conway, T., & Crosson, B. (2009b). *NIH Public Access*. 21(10), 2007–2018. <https://doi.org/10.1162/jocn.2009.21219>. Neural

Muller, A. M., & Meyer, M. (2014). Language in the brain at rest: new insights from resting state data and graph theoretical analysis. *Frontiers in Human Neuroscience*, 8(April), 228. <https://doi.org/10.3389/fnhum.2014.00228>

Müller, L. D., Guhn, A., Zeller, J. B. M., Biehl, S. C., Dresler, T., Hahn, T., Fallgatter, A. J., Polak, T., Deckert, J., & Herrmann, M. J. (2014). Neural correlates of a standardized version of the trail making test in young and elderly adults: A functional near-infrared spectroscopy study. *Neuropsychologia*, 56(1), 271–279. <https://doi.org/10.1016/j.neuropsychologia.2014.01.019>

Park, D. C., Lautenschlager, G., Hedden, T., Davidson, N. S., Smith, A. D., & Smith, P. K. (2002). Models of visuospatial and verbal memory across the adult life span. *Psychology and Aging*, 17(2), 299–320. <https://doi.org/10.1037/0882-7974.17.2.299>

Park, D. C., & Patricia Reuter-Lorenz. (2009). The Adaptive Brain: Aging and Neurocognitive Scaffolding. *Annu Rev Psychol.*, 60, 173–196.

Park, D. C., Polk, T. A., Park, R., Minear, M., Savage, A., & Smith, M. R. (2004). Aging reduces neural specialization in ventral visual cortex. *Proceedings of the National Academy of Sciences of the United States of America*, 101(35), 13091–13095.

<https://doi.org/10.1073/pnas.0405148101>

- Piatt, A. L., Fields, J. A., Paolo, A. M., & Tröster, A. I. (1999). Action (verb naming) fluency as an executive function measure: Convergent and divergent evidence of validity. *Neuropsychologia*, *37*(13), 1499–1503. [https://doi.org/10.1016/S0028-3932\(99\)00066-4](https://doi.org/10.1016/S0028-3932(99)00066-4)
- Ramanoël, S., Hoyau, E., Kauffmann, L., Renard, F., Pichat, C., Boudiaf, N., Krainik, A., Jaillard, A., & Baci, M. (2018). Gray matter volume and cognitive performance during normal aging. A voxel-based morphometry study. *Frontiers in Aging Neuroscience*, *10*(AUG), 1–10. <https://doi.org/10.3389/fnagi.2018.00235>
- Reitan, R. M. (1958). Validity of the Trail Making Test as an indicator of organic brain damage. *Perceptual and Motor Skills*, *8*, 271–276. <https://doi.org/10.2466/PMS.8.7.271-276>
- Reuter-Lorenz, P. A., & Cappell, K. A. (2008). Neurocognitive aging and the compensation hypothesis. *Current Directions in Psychological Science*, *17*(3), 177–182. <https://doi.org/10.1111/j.1467-8721.2008.00570.x>
- Reuter-Lorenz, P. A., & Park, D. C. (2014). How Does it STAC Up? Revisiting the Scaffolding Theory of Aging and Cognition. *Neuropsychology Review*, *24*(3), 355–370. <https://doi.org/10.1007/s11065-014-9270-9>
- Sala-Llonch, R., Bartrés-Faz, D., & Junqué, C. (2015). Reorganization of brain networks in aging: a review of functional connectivity studies. *Frontiers in Psychology*, *6*(May), 1–11. <https://doi.org/10.3389/fpsyg.2015.00663>
- Shafto, M. A., & Tyler, L. K. (2014). Language in the aging brain: The network dynamics of cognitive decline and preservation. *Science*, *346*(6209), 583–588.
- Shao, Z., Janse, E., Visser, K., & Meyer, A. S. (2014). What do verbal fluency tasks measure? Predictors of verbal fluency performance in older adults. *Frontiers in Psychology*, *5*(JUL), 1–10. <https://doi.org/10.3389/fpsyg.2014.00772>
- Starkstein, S. E., Mayberg, H. S., Preziosi, T. J., Andrezejewski, P., Leiguarda, R., & Robinson, R. G. (1992). Reliability, validity, and clinical correlates of apathy in Parkinson's disease. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *4*(2), 134–139.

<https://doi.org/10.1176/jnp.4.2.134>

Tomasi, D., & Volkow, N. D. (2012). Resting Functional Connectivity of Language Networks: Characterization and Reproducibility Dardo. *Mol Psychiatry*, 17(8), 841–854.

Van der Linden, M., Coyette, F., Poitrenaud, J., Kalafat, M., Calicis, F., Wyns, C., & Adam, S. (2004). L'épreuve de rappel libre / rappel indicé à 16 items (RL/RI-16). In *L'évaluation des troubles de la mémoire: Présentation de quatre tests de mémoire épisodique avec leur étalonnage* (Solal, pp. 25–47). France.

Wechsler, D. (1997). *WAIS-III: Administration and Scoring Manual*. The Psychological Corporation.

Whitfield-Gabrieli, S., & Nieto-Castanon, A. (2012). Conn: A Functional Connectivity Toolbox for Correlated and Anticorrelated Brain Networks. *Brain Connectivity*, 2(3), 125–141.
<https://doi.org/10.1089/brain.2012.0073>

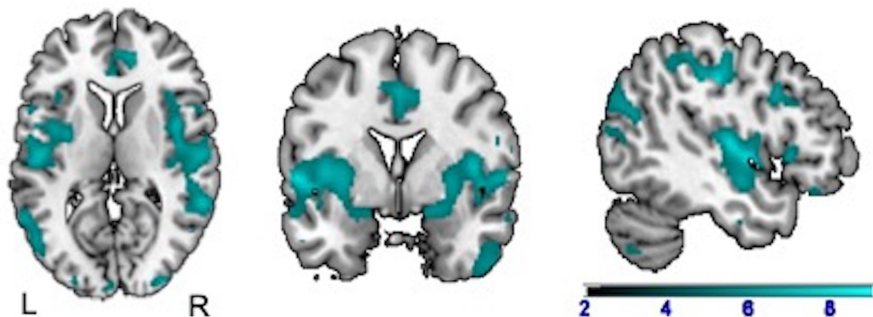
Figure 1: Regions showing less density of grey matter in older participants in comparison to younger participants. The statistical threshold is $p_{FWE-corr} < 0.05$ ($k > 200$ voxels). Abbreviations: STG= superior temporal gyrus; SMA= supplementary motor area; SMG= supramarginal gyrus; IFG= inferior frontal gyrus; MTG= middle temporal gyrus.

Figure 2: Negative correlations between TMT B (in seconds) and grey matter density in the older group.

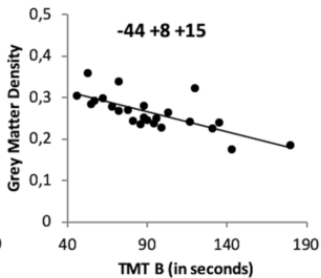
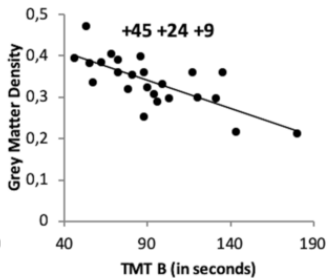
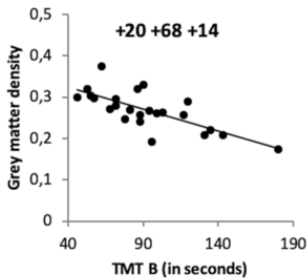
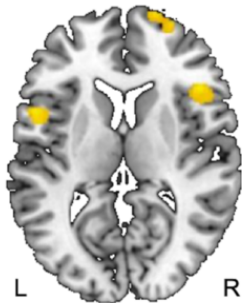
Figure 3: Cluster map for LIFG in [younger adults](#) (A) and older adults (B). Yellow to red color for clusters positively correlated to LIFG activity; blue to pink color for clusters negatively correlated to LIFG activity

Figure 4: (A) Significant clusters (in red) following inter-group comparisons, are partly related to language network (in yellow) but not part of the MD network (in green). (B) Violin plots show connectivity values for each participant in each group. Abbreviations: PCC= Posterior Cingulate Gyrus; AG= Angular Gyrus; TP/ITG= Temporal Pole/Inferior Temporal gyrus; MD network= Multiple-demand network; L= Left.

Figure 5: Intra-group correlation between grammatical fluency performance (A) and phonemic fluency performance (B) and between-network connectivity in the group of older adults.



Areas	Coordinates (x,y,z)	T-values	K voxels
Right superior and middle occipital gyrus	32 -84 24	9.16	1993
Left planum polare, STG	-56 -3 3	8.97	10648
Left and Right SMA, middle cingulate gyrus	0 15 39	8.27	9196
Right pre and post-central gyrus, SMG	39 -24 45	8.26	18471
Left pre and post-central gyrus, SMG	-45 -21 39	8.19	2605
Left cerebellum	-14 -71 -38	7.46	11079
Left and Right Thalamus	0 -14 3	7.26	616
Left IFG	-57 12 17	7	564
Left MTG, temporal pole	-51 -3 -29	5.73	583



Areas (Brodmann areas)

Right frontal pole (BA10, BA46)

Right pars opercularis, Right pars triangularis (BA44, BA45)

Left pars opercularis (BA44)

Coordinates

+20 +68 +14

+45 +24 +9

-44 +8 +15

T values

5.08

5.04

4.86

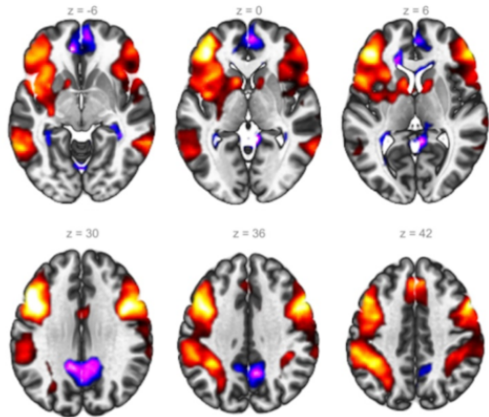
K voxels

554

633

546

A) Younger adults

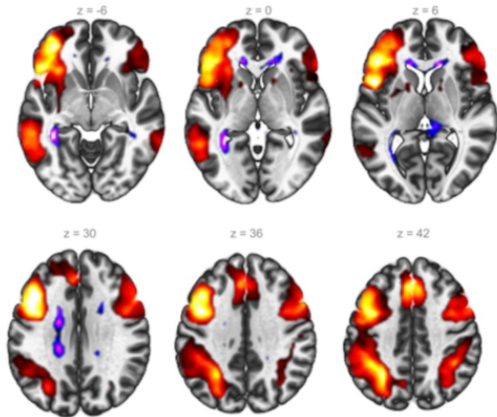


B) Older adults

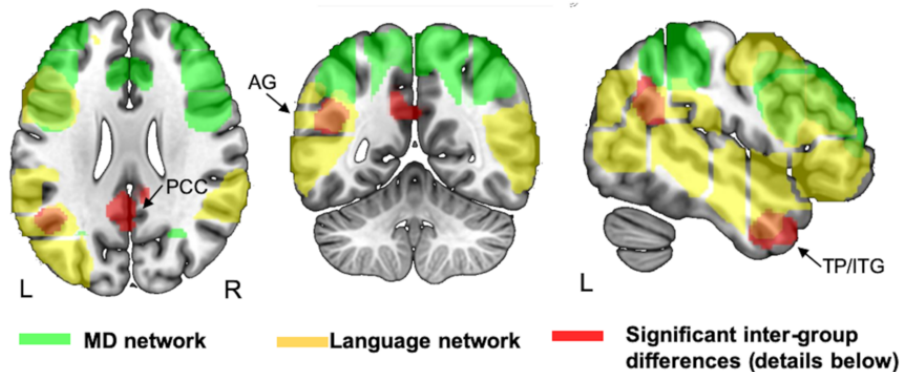
23.43



-10.23



A) Inter-group differences during seed-based analyses



B) Distribution of connectivity values in the three significant clusters

