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## **Connectivity dynamics and cognitive variability during aging**

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## **Abstract**

Aging is associated with cognitive changes, with strong variations across individuals. One way to characterize this individual variability is to use techniques such as magnetoencephalography (MEG) to measure the dynamics of neural synchronization between brain regions, and the variability of this connectivity over time. Indeed, few studies have focused on fluctuations in the dynamics of brain networks over time and their evolution with age. We therefore characterize aging effects on MEG phase synchrony in healthy young and older adults from the Cam-CAN database. Age-related changes were observed, with an increase in the variability of brain synchronization, as well as a reversal of the direction of information transfer in the default mode network (DMN), in the delta frequency band. These changes in functional connectivity were associated with cognitive decline. Results suggest that advancing age is accompanied by a functional disorganization of dynamic networks, with a loss of communication stability and a decrease in the information transmitted.

**Keywords:** Aging; MEG; Cognition; Cognitive variability; Connectivity

## 1 Introduction

2 With an increasing number of people over 65, the world population is aging. Aging is associated  
3 with a reduced efficiency of cognitive functioning, that primarily affects memory and executive  
4 processes (e.g., Hedden & Gabrieli, 2004). However, some individuals show a major decline  
5 while others maintain cognitive performance similar to young adults (e.g., Hultsch *et al.*, 2008).  
6 Recent research aims to better understand these individual differences during aging. Such  
7 variability across individuals has been associated with concepts of maintenance and cognitive  
8 reserve (Cabeza *et al.*, 2018; Stern *et al.*, 2020). Maintenance (Nyberg *et al.*, 2012) corresponds  
9 to the preservation of similar cognitive and brain functioning to that of younger individuals with  
10 advancing age, while cognitive reserve corresponds to compensatory functional adjustments  
11 associated with the preservation of cognitive performance in the presence of structural changes.  
12 Cognitive reserve and maintenance can account for individual differences in aging- and  
13 pathology-related effects, and have been extensively investigated at both structural and  
14 functional levels (e.g., Stern *et al.*, 2020). However, the contribution of the temporal dynamics  
15 of brain communications underlying cognitive reserve remains under-investigated. As changes  
16 in brain dynamics are expected to occur long before the disconnection associated with atrophy  
17 and brain lesions, this could yield highly sensitive elements on individual differences with age.

18 Neuroimaging research in healthy aging has been primarily conducted using functional methods  
19 with high spatial resolution (e.g., positron emission tomography (PET) or functional MRI  
20 (fMRI)). These methods have provided insights into the anatomical and functional changes that  
21 occur with age, including changes in brain activity (Cabral *et al.*, 2017; Smitha *et al.*, 2017).  
22 These techniques also enable the study of brain connectivity changes. Connectivity measures  
23 are sensitive to cognitive changes and differences between individuals (e.g., Hedden *et al.*,  
24 2016). Studies showed, for example, that the cognitive decline observed in normal aging may  
25 be due to functional connectivity disruptions, particularly in the default-mode network (DMN;  
26 this network is mainly activated when no task is assigned to the participant; Andrews-Hanna *et al.*,  
27 2007). The concept of cognitive reserve itself has also emerged in part from fMRI studies,  
28 as individuals with a higher cognitive reserve showed fewer brain and cognitive alterations than  
29 individuals with a lower level of cognitive reserve (Stern, 2009). The contribution of these  
30 methods in the precise localization of brain activity and in the study of brain networks is  
31 therefore undeniable. However, due to their constrained temporal resolution, age-related  
32 changes on the dynamics of the networks involved remain largely understudied. The use of  
33 methods with high temporal resolutions, such as magnetoencephalography (MEG) and  
34 electroencephalography (EEG; e.g., Baillet, 2017), can provide sensitive and specific elements  
35 on individual differences associated with cognitive aging.

36 Brain activity is characterized by its spectral complexity, and can be distinguished according to  
37 its dominant frequency (delta, theta, alpha, beta, gamma). The delta waves (1-3Hz) are the  
38 slowest, while the gamma waves (40+Hz) are the fastest. Previous work highlighted that these  
39 brain rhythms are associated with different cognitive functions (Buszaki *et al.*, 2006), for  
40 example the gamma frequency band is associated with information processing in higher-order  
41 cognitive tasks. Previous MEG studies show that networks activated at rest are activated  
42 periodically and in different frequency bands (de Pasquale *et al.*, 2010). A decrease in  
43 functional connectivity has been observed during aging (Wig, 2017). Moreover, previous work  
44 has shown that in older individuals, activations and couplings are reduced in the alpha and  
45 gamma frequency bands, and increased in the delta frequency band (Vlahou, 2014). This  
46 slowing of neural activity (Celesia, 1986) has been linked to decreased cognitive performance  
47 (Toth *et al.*, 2014), and slower information processing speed (Anderson & Craik, 2017).  
48 Conversely, the preservation of this neural activity allows cognitive abilities to be maintained  
49 with age. However, previous M/EEG studies have mainly focused on the average of activations

1 and connectivity over long periods of time (see Courtney & Hinault., 2021, for a review), and  
2 therefore do not provide insight into the dynamics of brain activities or their association with  
3 cognitive changes. It is therefore important to study the fluctuations of brain communications  
4 over time.

5 Spontaneous fluctuations of brain activity have long been considered as noise to be eliminated  
6 and/or controlled for. They are now considered as a fundamental aspect of brain  
7 communications (e.g., Uddin, 2020). Recent work has demonstrated the importance of  
8 sustained synchronization between brain regions for performance in complex cognitive tasks  
9 (e.g., Daume *et al.*, 2017). Moreover, disrupted synchronization has been associated with  
10 cognitive decline with age (Hinault *et al.*, 2020). However, fluctuations of activity have not  
11 been considered in light of individual differences during aging. Impaired stability of brain  
12 network dynamics could lead to the neurocognitive changes observed with advancing age  
13 (Voytek & Knight, 2015). The directionality of connectivity between neuronal oscillations may  
14 also play a role in the transmission of neuronal communications. Therefore, changes in dynamic  
15 connectivity would take place in order to maintain cognitive performance, while failure to make  
16 these changes would lead to cognitive decline (Ariza *et al.*, 2015).

17 Here, we investigated the stability and variability of resting brain networks' synchrony over  
18 time in young and older healthy participants from the Cam-CAN (*Cambridge Centre for Ageing  
19 and Neuroscience*) database (e.g., Shafto *et al.*, 2014; Taylor *et al.*, 2017). This database  
20 includes multimodal neuroimaging data (MEG, f/MRI) as well as cognitive performance  
21 assessment in each individual. Analyses were focused on the four main resting-state networks  
22 (default network, salience network, left and right fronto-parietal networks). Our objectives were  
23 twofold: i) To study changes in dynamic connectivity with age: Between young and old  
24 individuals, we hypothesized differences in functional networks, as well as greater variability  
25 in the activity of these networks; ii) To investigate the relationships between changes in  
26 dynamic connectivity and cognitive changes: We expected that stability in synchronization and  
27 directionality of connectivity over time would be associated with better cognitive performance  
28 with age, compared to high variability in these measures. Preservation of this neural activity  
29 would help maintain cognitive abilities with age.

## 30 **Methods**

### 31 Participants

32 We analysed data from 46 young (29 women and 17 men; aged 22-29 years) and 46 older  
33 healthy adults (29 women and 17 men; aged 60-69 years; see participant demographics  
34 characteristic in Table 1). Participants were selected from the Cam-CAN database (e.g., Shafto  
35 *et al.*, 2014; Taylor *et al.*, 2017), in line with demographic characteristics of individuals  
36 recruited in previous work (e.g., Coquelet *et al.*, 2017; Hinault *et al.*, 2020). All participants  
37 were right-handed, showed normal cognitive functioning (Montreal Cognitive Assessment  
38 (MoCA) score >26; Nasreddine. *et al.*, 2005), and no neurological or psychiatric condition.

### 39 Behavioural measures

40 A detailed description of the behavioural measures can be found in supplementary materials  
41 and in Shafto *et al.* (2014) and Taylor *et al.* (2017). Cognitive performance was assessed with  
42 the Mini-Mental State Evaluation (MMSE; Folstein *et al.*, 1975) used as a measure of general  
43 cognitive functioning, the Visual Short-Term Memory (VSTM; Vogel *et al.*, 2001) which  
44 measures working memory, the Cattell test (Horn & Cattell, 1966) which is a measure of  
45 reasoning ability and the Hotel Test (Shallice & Burgess, 1991) which assesses planning  
46 abilities.

## 1 MEG and structural MRI data acquisition

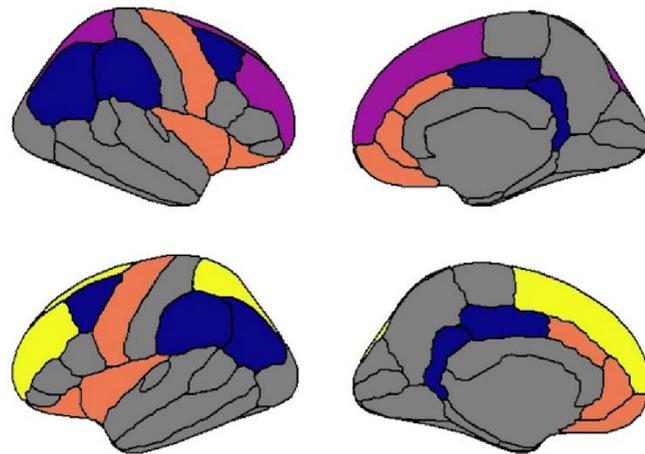
2 Resting brain activity was measured for 10 minutes (sampling rate: 1kHz, bandpass filter: 0.03-  
3 330 Hz) with a 306-channel MEG system. Participants' 3D-T1 MRI images were acquired on a  
4 32-channel 3T MRI scanner. The following parameters were used: repetition time = 2250 ms;  
5 echo time = 2.99 ms; inversion time = 900 ms; flip angle = 9 degrees; field of view = 256 mm  
6 x 240 mm x 192 mm; voxel size = 1 mm; GRAPPA acceleration factor = 2; acquisition time =  
7 4 minutes and 32 seconds.

## 8 Data pre-processing

9 The Elekta Neuromag MaxFilter 2.2 has been applied to all MEG data (temporal signal space  
10 separation (tSSS): 0.98 correlation, 10s window; bad channel correction: ON; motion  
11 correction: OFF; 50Hz+harmonics (mains) notch). Afterwards, artifact rejection, filtering (0.3-  
12 100 Hz bandpass), temporal segmentation into epochs, averaging and source estimation were  
13 performed using Brainstorm (Tadel *et al.*, 2011). In addition, physiological artefacts (e.g.  
14 blinks, saccades) were identified and removed using spatial space projection of the signal. In  
15 order to improve the accuracy of the source reconstruction, the FreeSurfer (Fischl, 2012),  
16 software was used to generate cortical surfaces and automatically segment them from the  
17 cortical structures from each participant's T1-weighted anatomical MRI. The advanced MEG  
18 model was obtained from a symmetric boundary element method (BEM model; OpenMEEG;  
19 Gramfort *et al.*, 2010; Kybic *et al.*, 2005), fitted to the spatial positions of each electrode (Huang  
20 *et al.*, 1999). A cortically constrained sLORETA procedure was applied to estimate the cortical  
21 origin of the scalp MEG signals. The estimated sources were then smoothed and projected into  
22 a standard space (i.e., the ICBM152 model) for comparisons between groups and individuals,  
23 while accounting for differences in native anatomy. This procedure was applied for the entire  
24 recording duration.

## 25 Network segmentation

26 In line with previous work (e.g., Smitha *et al.*, 2017; Van den Heuvel *et al.*, 2009), we  
27 investigated the four main brain networks at rest: the default-mode network (DMN), the  
28 salience network (SN), the left fronto-parietal network (FPL) and the right fronto-parietal  
29 network (FPR). Each network is composed of different brain regions: the DMN is composed of  
30 the posterior cingulate cortex, the medial prefrontal and the inferior parietal cortex. The SN is  
31 composed of the anterior cingulate cortex, the insula and the pre-supplementary motor area.  
32 The FPL is composed of the left dorsolateral prefrontal cortex and the left superior parietal  
33 cortex. Finally, the FPR is composed of the right dorsolateral prefrontal cortex and the right  
34 superior parietal cortex (**Figure 1**). These networks are involved in different cognitive activities  
35 or functions: the DMN is mainly observed at rest and shows lower connectivity levels when  
36 participants are currently performing cognitive tasks (Raichle *et al.*, 2001). The SN is associated  
37 with the processing of salient stimuli in the environment (Seeley *et al.*, 2007). Finally, the  
38 bilateral fronto-parietal network is involved in spatial attention, planning and cognitive control  
39 (Kam *et al.*, 2019). We separately investigated the FPL, which is involved in working memory  
40 (Murphy *et al.*, 2019) and the FPR which is involved in inhibitory processing (Nee *et al.*, 2007).  
41 Regions of interest were selected following segmentation of individual anatomies based on the  
42 Desikan-Killiany atlas (Desikan *et al.*, 2006).



**Figure 1:** Visualisation of the different regions forming the four studied brain networks; in blue: the DMN; in orange: the SN; in yellow: the FPL; in purple: the FPR

### 11 Study of dynamic connectivity

12 Phase-locking value analyses (PLV; Lachaux *et al.*, 1999) were used to determine the functional  
 13 synchrony between regions of interest. PLV estimates the variability of phase differences  
 14 between two regions over time. If the phase difference varies little, the PLV is close to 1 (this  
 15 corresponds to high synchronisation between the regions), while the low association of phase  
 16 difference across regions is indicated by a PLV value close to zero. To ensure PLV results did  
 17 not reflect volume conduction artefacts, control analyses were conducted using phase lag index  
 18 (weighted PLI analyses). Because PLV is an undirected measure of functional connectivity, and  
 19 to investigate brain dynamics with complementary metrics, analyses of transfer entropy (TE)  
 20 have also been conducted. TE measures of how a signal a can predict subsequent changes in a  
 21 signal b (Ursino *et al.*, 2020). It then provides a directed measure of a coupling's strength. If  
 22 there is no coupling between a and b, then TE is close to 0, while TE is close to 1 if there is a  
 23 strong coupling between a and b.

24 The range of each frequency band was based on the frequency of the individually observed  
 25 alpha peak frequency (IAF), measured as the average of peaks detected with both  
 26 occipitoparietal magnetometers and gradiometers. From previous work (Toppi *et al.*, 2018) the  
 27 following frequency bands were considered: Delta (IAF-8/IAF-6), Theta (IAF-6/IAF-2), Alpha  
 28 (IAF-2/IAF+2), Beta (IAF+2/IAF+14), Gamma1 (IAF+15/IAF+30) and Gamma2  
 29 (IAF+31/IAF+80). To reduce the dimensionality of the data, the first principal component  
 30 analysis (PCA) decomposition mode of the time course of activation in each region of interest  
 31 (ROI) of the Desikan-Killiany atlas brain fragmentation was used. The first component, rather  
 32 than the average activity, was chosen to reduce signal leakage (Sato *et al.*, 2018). Thirty-five  
 33 sliding time windows of 30s each were then extracted for the epochs of interest to calculate the  
 34 variability across time windows (standard deviation) of the PLV. The analyses were conducted  
 35 on the average activity within each network, however additional analyses were conducted at  
 36 the coupling level to further investigate the observed results.

### 37 Statistical tests

38 Permutation analyses were performed in Brainstorm (Tadel *et al.*, 2011), using methods  
 39 originally implemented in Fieldtrip (Maris & Oostenveld *et al.*, 2011). Both toolboxes support

1 open access and scripts are available online. To assess differences between age groups in  
 2 demographic and functional connectivity variables, t-tests and ANOVAs were applied using  
 3 Jamovi software (<https://www.jamovi.org/>; version 1.6.23). Functional data (PLV, TE) were  
 4 analyzed using 2 (age group: young/old) x 4 (networks: DMN, SN, FPL, and FPR) x 6  
 5 (frequency bands: delta, theta, alpha, beta, gamma1, gamma2) repeated-measures ANOVAs to  
 6 determine which network and frequency band showed the greatest young/old changes. The  
 7 Greenhouse-Geisser epsilon correction was used where necessary. Original degrees of freedom  
 8 and corrected p-values are reported. Finally, regressions aimed at determining the association  
 9 between functional connectivity measures and behavioral measures within each group. Results  
 10 were FDR corrected for multiple comparisons (Benjamini & Hochberg, 1995).

## 11 **Results**

### 12 **Age-related differences in cognitive performance**

13 The main behavioral and demographic data from the Cam-CAN database are summarized in  
 14 **Table 1.**

15 Variables	Young adults	Older adults	p-value
16 Number of participants	46	46	-
17 Number of females	29	29	-
18 Age	26.5	64.5	-
19 <b>Years of education</b>	<b>22.2 (2.873)</b>	<b>19.1 (3.262)</b>	<b>0.001</b>
20 <b>MMSE</b>	<b>29.5 (0.863)</b>	<b>28.9 (1.173)</b>	<b>0.013</b>
21 <b>VSTM</b>	<b>0.5 (0.088)</b>	<b>0.4 (0.069)</b>	<b>0.001</b>
22 <b>Cattell</b>	<b>37.8 (3.628)</b>	<b>30.5 (6.285)</b>	<b>0.001</b>
23 <b>Hotel_Num_rows</b>	<b>4.7 (0.585)</b>	<b>4.3 (1.008)</b>	<b>0.018</b>
24 <b>Hotel_Time</b>	<b>227.7 (119.796)</b>	<b>326.9 (194.305)</b>	<b>0.005</b>

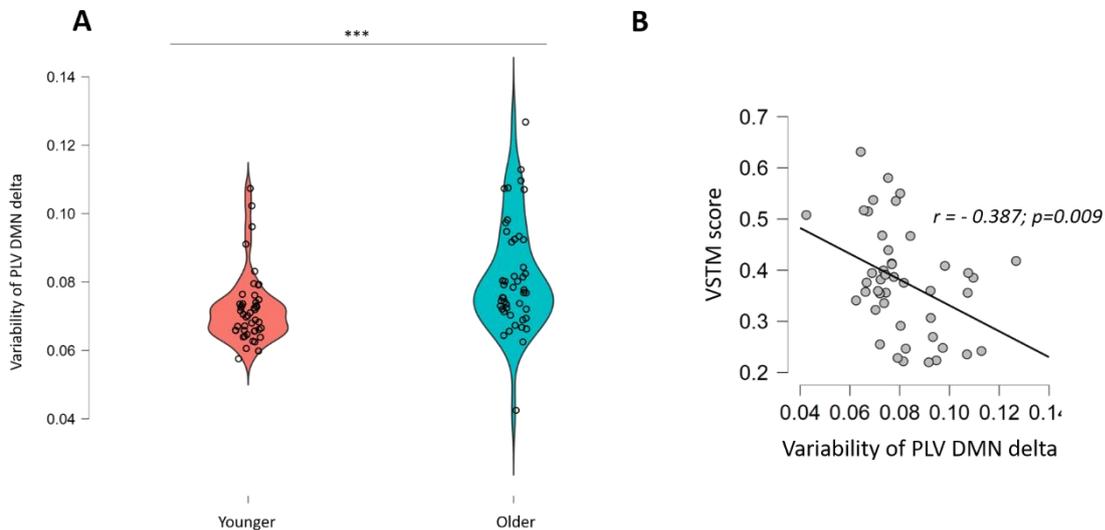
**Table 1:** Demographics and scores for both groups younger and older participants

26 Relative to younger individuals, older adults showed lower scores in the MMSE ( $p=0.013$ ),  
 27 VSTM ( $p<0.001$ ), Cattell ( $p<0.001$ ) and hotel test ( $p=0.018$  for number of rooms; and  $p=0.005$   
 28 for time) scores. For the hotel test, a decrease in the rate of correct answers was observed  
 29 ( $p=0.018$ ). A significant increase in response time for the hotel test was also observed in older  
 30 individuals ( $p=0.005$ ).

### 31 **Increased variability of delta phase synchrony frequency band in older adults**

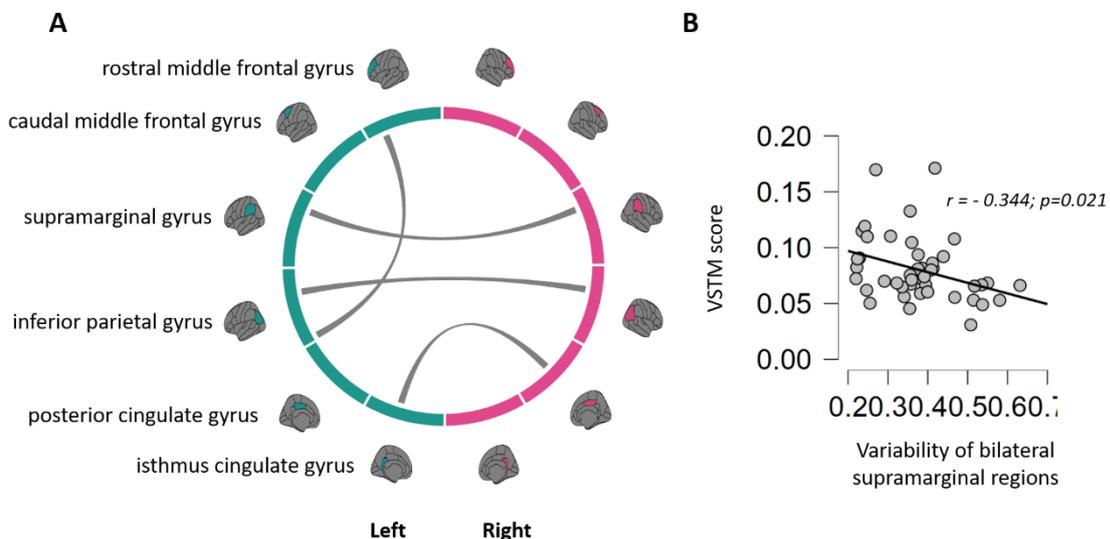
32 We first observed a significant effect of network,  $F(3, 270) = 8.085$ ,  $p<0.001$ ,  $\eta^2 = 0.082$ ,  
 33 frequency,  $F(5, 450) = 202.748$ ,  $p<0.001$ ,  $\eta^2 = 0.693$ , and age,  $F(1,90) = 4.698$ ,  $p= 0.033$ ,  $\eta^2=$   
 34  $0.05$ . The interaction between frequency and age,  $F(5,450) = 6.57$ ,  $p<0.001$ ,  $\eta^2 = 0.068$ , revealed  
 35 that this difference in variability between young ( $M = 0.076$ ,  $SE = 0.002$ ) and older adults ( $M$   
 36  $= 0.087$ ,  $SE = 0.002$ ) was stronger for the delta frequency band. This effect was not observed  
 37 in other frequency bands. The Age x Networks interaction for the delta frequency band was  
 38 also significant,  $F(3,270) = 6.823$ ,  $p<0.001$ ,  $\eta^2 = 0.07$ , with the DMN network showing the

1 largest difference. These results indicate an increased variability of the delta DMN activity with  
 2 advancing age (**Figure 2**). We observed a significant negative regression between such  
 3 variability and cognitive performance (VSTM,  $p = 0.009$ ,  $r = -0.387$ ). The rest of the analyses  
 4 was therefore focused on the DMN network, in the delta frequency band.



**Figure 2:**  
**A:** Increased variability of the DMN network in the delta frequency band for the older group ( $p = 0.001$ ) compared to younger individuals; **B:** Negative association between increased PLV DMN variability and VSTM score (regression test,  $r = -0.387$ ,  $p = 0.009$ ) in older adults

5 We then performed permutation t-tests on the DMN couplings between age groups. Different  
 6 couplings were found to be significantly more variable for the older group compared to the  
 7 younger group especially for interhemispheric and fronto-parietal couplings (**Figure 3**). In the  
 8 older group, the interhemispheric coupling (bilateral supramarginal regions) was found to be  
 9 negatively correlated with cognitive performance (VSTM test;  $r = -0.344$ ,  $p = 0.021$ ). These  
 10 data suggest an increase in variability in the overall DMN network in the delta frequency band,  
 11 but also an increase in the significant variability of specific couplings in this network, both  
 12 being associated with lower cognitive performance.



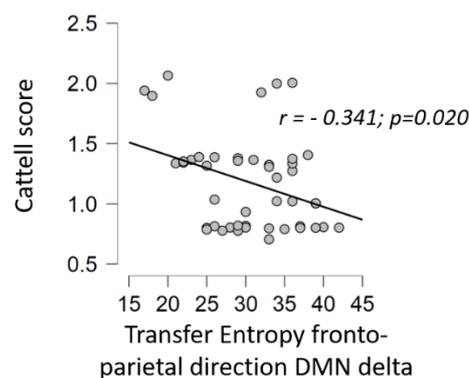
**Figure 3:**

**A:** DMN couplings in the delta frequency band showing increased PLV variability in the older group (t-test,  $p = 0.001$ ); **B:** Negative association between increased variability of PLV DMN coupling (bilateral supramarginal regions) and Cattell score (regression test,  $r = -0.344$ ,  $p = 0.021$ ) in older adults

## 1 Reversal of the direction of information transfer of delta band in older adults

2 As phase synchrony measures are undirected, transfer entropy was used to determine whether  
3 a specific direction of connectivity was associated with age-related differences. We performed  
4 a repeated measures ANOVA (Age x Networks x Frequencies x Direction) to determine which,  
5 network, which frequency band and in which direction the largest young-to-old changes were  
6 found. We showed a significant effect of frequency,  $F(5, 450) = 361.1$ ,  $p < 0.001$ ,  $\eta^2 = 0.801$ . A  
7 significant effect of age,  $F(1, 90) = 17.7$ ,  $p < 0.001$ ,  $\eta^2 = 0.165$  was also observed. Results revealed  
8 an increase in the direction of information transfer variability in the delta frequency band, in  
9 older adults relative to young adults. An interaction between frequency and age was also  
10 observed,  $F(5, 450) = 14.61$ ,  $p < 0.001$ ,  $\eta^2 = 0.140$ . This significant interaction effect indicates  
11 larger coupling strength in delta frequency in the older group ( $M = 1.218$ ,  $SE = 0.0231$ )  
12 compared to the younger group ( $M = 0.921$ ,  $SE = 0.0231$ ).

13 Student's t-tests were performed to determine the direction of information transfer for young  
14 and older adults in the DMN. We saw a significant difference between the fronto-parietal and  
15 parieto-frontal direction ( $p = 0.013$ ), with a significantly larger coupling strength parieto-frontal  
16 direction relative to the opposite direction for young adults that was not observed in older  
17 participants. This decrease in communication can be linked to the cognitive performance  
18 observed in this group. Indeed, we conducted regressions analyses to determine the association  
19 between these entropy transfer measures and behavioural measures within each group. We  
20 found negative regressions of information transfer with cognitive performance in each direction  
21 (VSTM,  $p = 0.031$ ,  $r = -0.319$ ; Cattell,  $p = 0.020$ ,  $r = -0.341$ ) in the delta frequency band for older  
22 adults (**Figure 4**).



**Figure 4:** Negative association between increased of parieto-frontal direction in DMN network and Cattell score (regression test,  $r = -0.341$ ,  $p = 0.020$ )

## 30 Discussion

31 Our main objective was to investigate changes in the stability and variability of brain  
32 communication dynamics with age and the relationship of these changes with age-related

1 cognitive changes. Our connectome-based approach, based on MEG data in healthy young and  
2 older participants from the Cam-CAN database, allowed us to investigate changes of  
3 connectivity dynamics with aging. Two time-resolved connectivity aspects were studied: the  
4 stability of synchronized communications over time, and directed connectivity. Brain activity  
5 was studied at rest, as previous work suggested a link between the activity of specific networks  
6 at rest and cognitive abilities (e.g. Nashiro *et al.*, 2017). In this study, we first showed an  
7 increased variability of phase synchrony over time with age, especially in the delta frequency  
8 band. We also showed a reversal of the main direction of synchronized connectivity with age:  
9 connectivity in the fronto-parietal direction was found to be increased in older participants,  
10 whereas it was stronger in the parieto-frontal direction for younger participants. These  
11 observations are in line with the available literature on functional connectivity during non-  
12 pathological aging (e.g. Geerligs *et al.*, 2015). The results also show for the first time that the  
13 stability or variability of functional networks, as well as information exchange over time, are  
14 associated with individual cognitive differences during aging. This was made possible by the  
15 excellent temporal resolution of MEG, combined with advanced source reconstruction  
16 analyses.

17 The study of oscillatory activity allowed us to specify age-related changes in the variability of  
18 phase synchrony over time, and the specific frequency band associated with these differences.  
19 Phase synchrony between brain regions is a critical parameter of neural communications (e.g.,  
20 Fries, 2015). Indeed, with advancing age, changes in synchronized network communications  
21 have been observed (see Courtney & Hinault, 2021, for a review). Our results reveal an  
22 increased variability of phase synchrony in the default network, mainly in the delta frequency  
23 band with age. Such variability of neural synchrony was negatively correlated with cognitive  
24 performance (measures of general cognition, and working memory). This result is consistent  
25 with MRI work showing that an age-related decrease in connectivity within the DMN is related  
26 to a decrease in memory and executive functions (e.g. Andrews-Hanna *et al.*, 2007). Our results  
27 are also consistent with previous M/EEG work reporting an overall slowing of brain activity  
28 with advancing age (e.g., Celesia, 1986), with an increase of slow rhythms relative to faster  
29 rhythms. Increased slow waves seem to be associated with the cognitive decline observed with  
30 advancing age. Here, we show that this slowing of brain rhythms with age is associated with a  
31 loss of stability in neuronal communications, and poorer performance.

32 In association with synchrony analyses, transfer entropy analyses allow the quantification of  
33 directed connectivity (see Ursino *et al.*, 2020). This quantifies the information flow between  
34 brain regions more precisely than functional connectivity, thus allowing the detection of causal  
35 interactions (i.e., *A* must precede *B*) between brain regions. Such investigation of directed  
36 connectivity revealed a decrease in the parieto-frontal direction of brain communications  
37 relative to the fronto-parietal direction in the default network and the delta frequency band with  
38 age. This reversal of information transfer between young and old participants was negatively  
39 associated with cognitive performance (especially for working memory and fluid intelligence).  
40 The reversal of information transfer and decreased variability in phase synchrony observed here  
41 may help furthering the age-related pattern described in the PASA model (Cabeza *et al.*, 2018).  
42 According to this model, the increase in the recruitment of frontal regions in older adults would  
43 be an indicator of their attempts to compensate for the decrease in their cognitive abilities. Here,  
44 we show a decrease in information transfer to these frontal regions, which is negatively  
45 associated with cognitive performances. Reduced connectivity of these frontal regions has been  
46 found to be negatively correlated with cognitive performance (Toth *et al.*, 2014), which may  
47 reflect a decrease in recruitment to these frontal regions. Indeed, frontal regions are the first  
48 regions to see their neuroanatomy impacted by aging (Dennis & Cabeza, 2008). These results  
49 allow us to understand this concept at the network communication dynamics levels. Further

1 investigation of investigation transfer during task completion will be necessary to specify its  
2 associations with the direct implementation of cognitive processes.

3 Several methodological considerations must be discussed regarding the reported results. First,  
4 the investigation of resting-state activity prevents in part the direct investigation of the neural  
5 bases of cognitive processes, which may explain the small number of associations with  
6 cognition. This could also reflect the fact that the Cam-CAN database does not include tasks  
7 directly testing executive functions. However, studying dynamic network connectivity at rest  
8 furthers our knowledge on the stability of these networks and help better characterize their  
9 individual variations. Second, the use of the Desikan-Killiany atlas, which has a less precise  
10 spatial resolution than other atlases, could limit the interpretations of SN results. However, the  
11 spatial resolution of the MEG does not enable a much higher spatial resolution. The Desikan  
12 atlas limits the degrees of freedom and has been frequently reported in previous work (e.g.,  
13 Ceisnaite et al., 2021; Canal-Garcia et al., 2022). Third, eta-squares for the effect of age on  
14 variance and transfer entropy show small to medium effects. Nevertheless, because we observed  
15 these effects in healthy older adults, at rest, suggests they are sensitive to early age-related  
16 changes. Future work is necessary to assess longitudinal changes of dynamic connectivity.  
17 Finally, the use of PLV for M/EEG data can be problematic because of volume conduction  
18 effects. However, volume conduction effects are unlikely to explain couplings between distant  
19 brain regions, and cannot account for between-group differences or correlations with behavioral  
20 performance. Using the first mode of principal component analysis (PCA) of the activation time  
21 course in each region of interest, rather than mean activity, reduces signal leakage (e.g., Sato et  
22 al 2018). Finally, even alternative measures (such as Phase Lag Index (PLI), or coherence), do  
23 not fully control for this risk of conduction volume (Palva et al 2017). Additional weighted PLI  
24 analyses were conducted, and results were replicated for the DMN network in the delta  
25 frequency band.

26 Empirically, the variability of brain communications has received little investigation, as it was  
27 long considered as noise, but is now recognized as contributing to brain functions (Uddin *et al.*,  
28 2020). Here, we show that healthy aging is associated with an increased variability in  
29 synchronized brain communications, and with changes of the main connectivity directions  
30 between brain regions. Results highlight that even when brain networks are not engaged in a  
31 particular cognitive activity, significant changes occur with age regarding connectivity  
32 dynamics and information flow between regions of different functional brain networks.  
33 Advancing age appears to be accompanied by a functional disorganization of dynamic  
34 networks, with a loss of communication stability and a decrease in the information transmitted.  
35 The study of dynamic connectivity contributes to a better understanding of the cognitive decline  
36 with aging. The stability of communications and its alteration should be considered in the  
37 framework of maintenance, reserve and resilience (Cabeza, 2018; Stern, 2020).

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