Modeling the Neurocognitive Dynamics of Language across the Lifespan

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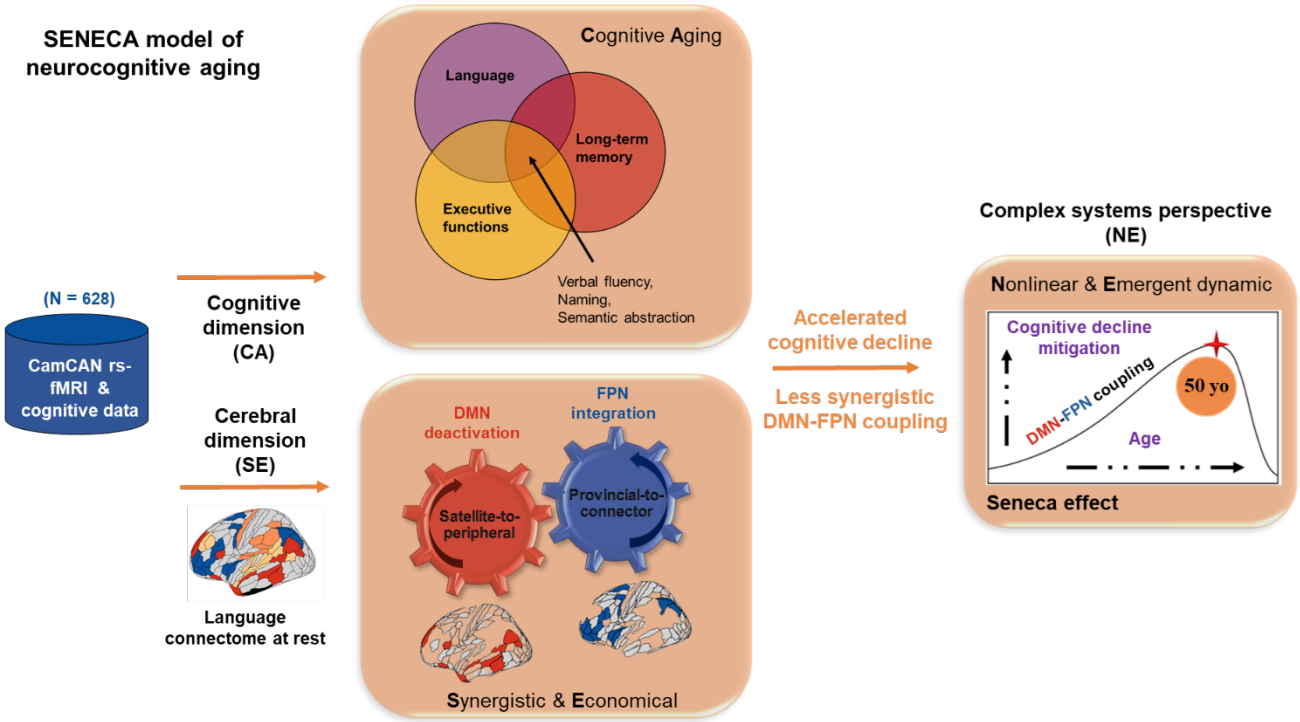
Highlights

- Synergistic interaction of language in interaction with long-term memory and executive functioning modifies along the lifespan
- DMN and FPN coupling is essential to mitigate, with minimal cost and maximum efficiency, the cognitive decline with age
- These changes occur around age 50 with a clear transition in neurocognitive functioning

The Figure hereafter illustrates a novel model entitled SENECA (Synergistic, Economical, Nonlinear, Emergent, Cognitive Aging) which integrates cerebral connectomic and cognitive dimensions. SENECA provides new insights on neural mechanisms that uphold the inter-cognitive functioning during healthy aging.



Abstract

Healthy aging is associated with a heterogeneous decline across cognitive functions, typically observed in language performances. Examining resting-state fMRI and neuropsychological data from 628 healthy adults (age 18-88) from the CamCAN cohort, we performed state-of-the-art graph theoretical analysis to uncover the neural mechanisms underlying this cognitive variability. At the cognitive level, our findings suggest that language processing is not an isolated function but is modulated throughout an individual's lifespan by the extent of inter-cognitive synergy between language, long-term memory, and executive functions. At the cerebral level, we show that the coupling between DMN (Default Mode Network) and FPN (Fronto-Parietal Network) regions may be the way for the brain to compensate for the effects of dedifferentiation at a minimal cost, efficiently mitigating the age-related cognitive decline in language production, fluid processing, and verbal fluency. Notably, the dynamic of cognitive resilience provided by this synergistic coupling seems to follow the Seneca effect typically found in complex systems: a slow rise followed by an abrupt decline. Specifically, we argue that reducing the DMN-FPN coupling could trigger accelerated cognitive decline around age 50. We summarize our findings in a novel SENECA model (Synergistic, Economical, Nonlinear, Emergent, Cognitive Aging), integrating connectomic and cognitive perspectives within a complex system perspective. Our study furthers our understanding of the dedifferentiation-compensation mechanisms that uphold inter-cognitive functioning during healthy aging and suggests that the fifth decade of life could transition towards less synergistic processing.

Keywords: language, healthy aging, synergy, functional reorganization, graph theory

1. Introduction

The crucial need to comprehend the mechanisms that uphold normal cognitive functioning during aging arises from the significant increase in the proportion of older individuals (Antoniou & Wright, 2017). A gradual decline in cognitive abilities typically accompanies aging. However, this decline is heterogeneous across cognitive functions, and some of them, such as language, semantic memory, and vocabulary, tend to be preserved longer (Harada et al., 2013). Therefore, this study aims to shed light on the neural mechanisms that underpin this variability, jointly exploring the functional brain architecture and cognitive performance. Specifically, we hypothesize that changes in language function across the lifespan are subserved by the reconfiguration of the language neurocognitive architecture within the framework of an inter-cognitive interaction between language, long-term memory, and executive functions.

From a cognitive standpoint, language decline under the effect of age is not uniform (Baciu et al., 2021). Although overall language performances tend to be preserved, certain linguistic operations may be impaired with age (Ramscar et al., 2014; Wlotko et al., 2010). Indeed, while language comprehension demonstrates higher resilience to the effects of aging (Diaz et al., 2016; Rossi & Diaz, 2016), language production, which involves word retrieval and generation (Baciu et al., 2016, 2021), tends to be more significantly impaired with age (Evrard, 2002; Ramscar et al., 2014). This is evident in tip-of-the-tongue situations, where individuals experience a feeling of knowing the meaning of a word but struggle to immediately recall and produce the word form (Burke et al., 1991; Condret-Santi et al., 2013). This discrepancy between comprehension and production can be attributed to the advantages of semantic context and the accumulation of verbal knowledge throughout the lifespan (Deary et al., 2009).

From a cerebral standpoint, brain networks may interact with one another, reflecting how language adapts to socio-communicative contexts by drawing memories, knowledge, and

beliefs from long-term memory (Duff & Brown-Schmidt, 2012; Horton, 2007) under the control of executive functions (Corballis, 2019; Hertrich et al., 2020). While long-term memory provides 'traffic' content and coherency, executive functioning provides flexibility and coordination to focus, plan, accomplish tasks, and control emotions. In a previous teamwork (Roger, Banjac, et al., 2022), our team proposed a theoretical framework that conceptualizes the inter-cognitive synergy between language, long-term memory, and executive functions at the cognitive level, L∪M (i.e., Language/union/Memory), and suggested that functional connectivity-based interactions may implement this synergy at the neural level.

Indeed, based on a data-driven approach, the language neurocognitive architecture based on extrinsic brain activity (Roger, Rodrigues De Almeida, et al., 2022) has been highlighted as a language connectome comprising four non-overlapping subsystems, each probabilistically mapping onto known resting-state brain networks (i.e., RSNs; Ji et al., 2019): core Language (Net1), Control-Executive (Net2), Conceptual (Net3), and Sensorimotor (Net4). Interestingly, these findings indicate that age-related decline in language production impacts the extra-linguistic components (Net2 and Net3) beyond the typical core language network (Hertrich et al., 2020). This suggests that language performances in older adults could be determined by synergistic processing (Gatica et al., 2021) or higher-order connectivity-based interactions between regions that support control-executive and conceptual processes. In light of the effect that the reconfiguration of the language connectome has on language function, our team also proposed adopting a 'cognitomic' perspective (Roger et al., 2018), which emphasizes the neuropsychological implications that this connectomic architecture has across the lifespan.

Within this cognitomic perspective, graph theory (Bullmore & Sporns, 2009; Bullmore & Bassett, 2011; Rubinov & Sporns, 2010) is appropriate to identify the neural substrates of this inter-cognitive synergy. Specifically, the brain network can be characterized in terms of integration and segregation properties (Cohen & D'Esposito, 2016; Genon et al., 2018) at

different topological levels (i.e., whole-brain/system-level, modular/subsystem-level, and region/nodal-level) (Farahani et al., 2019; Fornito et al., 2016). Across the lifespan, cognitive efficiency is supported by a balance between integrated and modular information processing (Bullmore & Sporns, 2012; Meunier et al., 2010; van den Heuvel & Sporns, 2013). In other words, optimal coordination of neural activity is based on the homeostasis between integration and segregation properties (Cole et al., 2013; Fornito et al., 2015).

In line with our previous findings (Roger, Rodrigues De Almeida, et al., 2022), a recent systematic review of resting-state data studies reported that reduced local efficiency at the system level, along with reduced segregation and enhanced integration within and between RSNs at the subsystem level, are the connectomic fingerprints of healthy aging with an inflection point around the fifth decade of life (Deery et al., 2023). However, a crucial challenge resides in understanding the mechanisms that bridge reduced segregation with enhanced integration (Stumme et al., 2020) and how these changes induce a dynamic at the system level associated with cognitive performance as age advances.

Indeed, studies report contradictory findings depending on the topological level of analysis. At the system level, age-related enhanced integration (Battaglia et al., 2020) is generally associated with a dedifferentiated system that fails to alternate efficiently between integrative and segregative states of connectivity (Chan et al., 2014; Chan et al., 2017). At a subsystem level, brain regions undergo a similar dedifferentiation process associated with a loss in function specialization (Goh et al., 2010; Park et al., 2004). This is primarily reflected by reduced segregation and enhanced integration in the sensorimotor and higher-order executive networks (Deery et al., 2023; Wig, 2017). However, in contrast with the system level, enhanced integration has been shown to be compensatory (Cabeza et al., 2018) with direct benefits on preserving cognitive performances (Bertolero et al., 2015; Meunier et al., 2010). Specifically, increased coupling between DMN and control-executive regions across subnetworks has also

been linked with better global cognitive performances (Spreng et al., 2018; Spreng & Turner, 2019). Specifically, it appears that the deactivation of DMN regions may be a key ingredient of cognitive resilience across the lifespan or the capacity to mitigate the deleterious effect of dedifferentiation (Deery et al., 2023; Grady et al., 2016; Singh-Manoux et al., 2012; Varangis et al., 2019). Indeed, failing to deactivate the DMN subnetwork seems to worsen performance in synergistic cognitive functions, based on intra-linguistic and control-executive processes, such as verbal fluency (Muller et al., 2016; Whiteside et al., 2016).

Overall, the main objective of this study is to investigate how the reorganization of the language connectome relates to the variability of cognitive performances across the lifespan. By assuming that language is a complex function in synergy with long-term memory and executive functions, we aimed to model how changes in the neural mechanisms that support this inter-cognitive synergy underlie this variability. To address this objective, we leveraged a population-based resting state fMRI dataset from the CamCAN cohort (Cam-CAN et al., 2014) and applied graph theoretical analyses to evaluate the reorganization of the language connectome in terms of segregation and integration properties at multiple topological scales of analysis.

2. Materials & Methods

2.1. Participants

We included 652 healthy adults from the Cambridge Center for Ageing and Neuroscience project cohort (Cam-CAN et al., 2014). Further recruitment information can be found in Taylor et al. (2017). Our analysis focused exclusively on functional fMRI brain data obtained during a resting state period. After careful examination, we had a final sample size of 628 participants (age range: 18-88; 320 females; 208 males). Several participants were excluded from the analysis for various reasons, including missing functional imaging data (N = 4), incomplete

volume acquisition (N = 4; one subject was retained with 74% of the total number of volumes), unreliable CSF mask (N = 9), and having 10% or more outlying volumes after preprocessing (M = 13.6, SD = 3.2, N = 8). Then, we chose eight cognitive tasks to span a continuous spectrum from a high to a low degree of synergy between language, long-term memory, and executive functions (Table 1). Consequently, the dataset was further reduced to 613 participants to analyze the relationship between brain activity and cognition. Specifically, we excluded participants with more than 3 missing neuropsychological scores and replaced the latter with the appropriate median of the age decile for the remaining participants.

Cognitive Task	**Processes involved** (from high to low amount of inter-cognitive synergy)
Verbal Fluency (Lezak et al., 2012)	Language (phonological, semantic) & Executive function (EF)
Hotel task (Shallice & Burgess, 1991)	EF (planning & multitasking)
Proverb comprehension (Huppert et al., 1994)	EF (abstraction) & Language (comprehension)
Naming (Clarke et al., 2013)	Language (phonological access & semantic memory)
Tip-of-the-tongue (Brown & McNeill, 1966)	Language (retrieval) & EF (error monitoring)
Cattell task (Cattell & Cattell, 1960)	EF (Fluid intelligence)
Story recall (Tulsky et al., 2003)	Long-term memory
Sentence comprehension (Rodd et al., 2010)	Language (syntactic, semantic)

Table 1. Presentation of the eight cognitive tasks considered in this study. A detailed description of the tasks can be found in Table S1, Appendix S2

2.2. MR acquisition

For information regarding the MR acquisition and the resting state protocol applied in this study, please refer to Cam-CAN et al. (2014), as the data was sourced from the Cambridge Center for Ageing and Neuroscience project cohort.

2.3. Resting-state fMRI data analysis

2.3.1. Data Preprocessing

The rs-fMRI data underwent preprocessing using SPM12 (Welcome Department of Imaging Neuroscience, UK, http://www.fil.ion.ucl.ac.uk/spm/) within MATLAB R2020b (MathWorks Inc., Sherborn, MA, USA). We employed a standard preprocessing pipeline (including realignment, reslicing, co-registration, segmentation, normalization, and smoothing) similar to that described in our previous work (see Roger et al., 2020) with specific details mentioned in Appendix S1.

2.3.2. Cerebral parcellation: the LANG connectome atlas

The LANG connectome atlas, referred to as the LANG atlas, comprises a collection of 131 regions of interest (ROI) derived from a panel of 13 language fMRI tasks (see Roger, Rodrigues De Almeida, et al., 2022). Each ROI is represented by a spherical region with a diameter of 6 mm, centered on the MNI coordinates as proposed by Power et al. (2011). To transform the LANG atlas, which is based on extrinsic fMRI activation, into a resting-state LANG (rs-LANG) atlas consisting of ROIs derived from the intrinsic activity, we labeled all LANG regions according to their primary resting-state network (RSN) based on the Cole-Anticevic Brainwide Net Partition (CAB-NP; Ji et al., 2019). We utilized a publicly available volumetric version of the CAB-NP that was converted to standard MNI space. By overlaying the volumetric RSN map onto the 131 regions (see Banjac et al., 2021), we determined the number of voxels that overlapped between each region and each RSN. This approach ensured accurate voxel-based labeling of each region to their primary RSN. During the examination of the modular organization of rs-LANG (see Figure 2), the RSN composition of a given subsystem was weighted by the mean percentage of overlap between the primary RSN and each region of the identified subsystem. This improvement led to a 12% increase in mean accuracy.

2.3.3. Resting-state LANG connectomes

Using the CONN toolbox (Behzadi et al., 2007), we conducted an ROI-to-ROI analysis and generated a connectivity matrix of dimensions 131x131 for each participant. These connectivity matrices were subsequently employed for network analysis. We disregarded negative correlations by setting them to zero, consistent with previous studies (Chong et al., 2019; Martin et al., 2022; Wang et al., 2011). Additionally, we applied thresholding to each matrix at five sparsity levels (10, 12, 15, 17, and 20%). This step aimed to reduce the presence of spurious connections and was based on the most likely sparsity levels known to produce a small-world organization, as outlined by Achard and Bullmore (2007). Subsequently, the thresholded matrices were binarized to generate five undirected graphs for each participant.

2.4. Resting state LANG network analysis

The network analysis, or graph analysis, was employed to measure information flow within each connectome (Rubinov & Sporns, 2010). Specifically, we assessed (i) the balance between functional integration and segregation at the system level, (ii) the modularity at the subsystem level, and (iii) the information transfer at the nodal level by evaluating the topological role of each region.

2.4.1. System-level analysis: integration vs. segregation balance assessment

Using the Brain Connectivity Toolbox (BCT) implemented in MATLAB 2020b and available at https://www.nitrc.org/projects/bct/ (Bullmore & Sporns, 2009), we extracted three key graph metrics: (1) global efficiency (Eglob), (2) local efficiency (Eloc), and (3) clustering coefficient (Clustcoeff). Globally, Eglob was calculated as the inverse of the shortest path lengths or the average of unweighted efficiencies across all pairs of nodes (Latora & Marchiori, 2001). This metric quantifies the efficiency of parallel information transmission across the global network

(Bullmore & Bassett, 2011). Locally, Eloc is similar to Eglob but on node neighborhoods. When averaged at the system level, it illustrates the segregation property of a network for processing information (Latora & Marchiori, 2001). For each node, the clustering coefficient (Clustcoeff) was calculated as the fraction of a node's neighbors that are also neighbors of each other (Rubinov & Sporns, 2010) and averaged at the system level. We visually inspected Eglob and Clustcoeff across the five sparsity levels and determined that the optimal threshold that balances integrated and modular processing was 15% (Figure S2, Appendix S2). We further ensured that this threshold was optimal by repeating the procedure for each age decile. Following this, we reduced all graphs to a fixed number of edges by retaining the top 15% (2554 edges). Additionally, we verified that the reduced connectomes maintained full connectivity and sufficiently devoided of isolated nodes, meaning that the largest connected component (LCC) included at least 80% of all nodes. After thresholding at 15%, we characterized the balance between functional integration and segregation at the system level by determining the relative predominance of global (Eglob) versus local efficiency (Eloc). A higher balance reflects a higher predominance of integration or higher integrative/global efficiency.

$$\text{System} - \text{level balance (integration vs. segregation)} = \frac{E_{glob} - E_{loc}}{E_{glob} + E_{loc}}$$

2.4.2. Subsystem-level analysis: modularity assessment

To examine the modular organization of rs-LANG, we employed the Louvain community detection algorithm (Blondel et al., 2008) with a resolution parameter set to $\gamma = 1.295$, aiming to align with the RSNs identified in the CAB-NP Atlas (Ji et al., 2019). As different runs of the algorithm can yield varying optimal partitions, we implemented a consensus clustering approach (Lancichinetti & Fortunato, 2012). This approach involves iteratively clustering co-assignment matrices until convergence, aggregating the frequency of node assignments to the

same module. To reduce spurious node assignments, we applied a threshold of $\tau = 0.5$ to the co-assignment matrices (Jiang et al., 2021). If a node did not consistently belong to the same module in at least 50% of the iterations, its co-assignment weight was set to zero. We executed the algorithm 1000 times for each subject and repeated the entire process 1000 times to generate a group-level consensus partition based on the subject-level partitions. We ensured that this consensus partition accurately represented all individuals across different ages, confirming its suitability for statistical analysis (refer to Appendix S1 for further information).

2.4.3. Nodal-level analysis: topological roles

At the nodal level, we investigated the topological reorganization of each connectome by defining four distinct topological roles: Connector, Provincial, Satellite, and Peripheral (Bertolero et al., 2015; Guimerà & Amaral, 2005). Therefore, the composition of each individual's language connectome is represented by four percentages which add up to 100%. To assign each role to a node (i.e., a region), we employed two graph metrics, (i) the Within-Module Z-score (WMZ; Latora & Marchiori, 2001), which quantifies connectivity within subsystems (intra-modular), and (ii) the normalized Participation Coefficient (PC; Pedersen et al., 2019) which measures connectivity between subsystems (inter-modular) while removing the bias associated with the number of nodes in each module. Consistent with prior research (Roger, Rodrigues De Almeida, et al., 2022; Schedlbauer & Ekstrom, 2019), we standardized both metrics (WMZ and zPCnorm) for each individual and assigned a topological role to each node. In relation to the entire set of 131 regions, a Connector node displays a high proportion of both intra- and inter-modular connections (zPCnorm >= 0, WMZ >= 1e-5). A Provincial node displays a high proportion of intra-modular connections (zPCnorm < 0, WMD >= 1e-5). A Satellite node displays a high proportion of inter-modular connections (zPCnorm >= 0, WMZ < 1e-5). A Peripheral node, on the other hand, displays a low proportion of all modular connections (zPCnorm < 0, WMZ < 1e-5).

2.5. Statistics

We conducted statistical analysis along four steps. Figure 1 illustrates the analytical pipeline. First, we examined the evolution in the proportion of topological roles across the lifespan using compositional analysis techniques (Greenacre, 2021). Second, we modeled the neural mechanisms that drive this evolution using probabilities. This allowed us to uncover the patterns and principles governing the connectivity changes in the language connectome across the lifespan. Third, we employed a canonical correlation analysis (CCA) to examine the many-to-many relationships between these neural mechanisms and the changes in cognitive performances across the lifespan. Finally, CCA analysis helped specify a causal model of how changes in the topological properties of the language connectome, at the system and subsystem levels, may explain the variability in age-related cognitive performances.

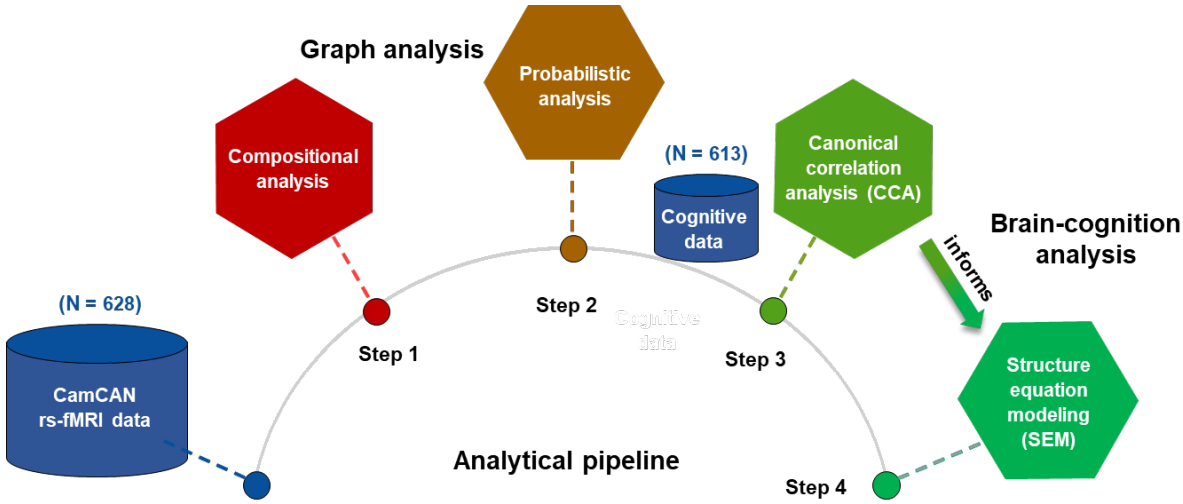


Figure 1. Illustration of the analysis pipeline

2.5.1. Compositional analysis of the language connectome

Due to the high correlation among components and the dependence on pairwise covariance (Greenacre, 2021; Smith et al., 2016), the relative count of topological roles was unsuitable for direct statistical analysis. To address this issue, we used a log-based transformation that mapped

these counts to Euclidean space (i.e., isometric log-ratios (ilr); Egozcue, 2003) (refer to Appendix S1 for more details). This transformation allowed us to construct four log-contrasts, referred to as compositional balances in our study, to capture the dynamics of each role across the lifespan, specifically Connector, Provincial, Peripheral, and Satellite (Eq. 1). To enhance the interpretability of these log-contrasts and address potential issues regarding causality (Ailer et al., 2021), we incorporated the count of all topological roles into the equation. This ensured that an increase in the Connector balance was necessarily driven by an increase in the absolute count of connector nodes. Hereafter Eq.1 describes the compositional balances.

$$\textbf{Connector balance} = \sqrt{\frac{3}{4}}\ \ln\left(\frac{\text{Connector}}{(\text{Provincial}\times\text{Peripheral}\times\text{Satellite})^{\frac{1}{3}}}\right)$$

$$\textbf{Provincial balance} = \sqrt{\frac{3}{4}}\ \ln\left(\frac{\text{Provincial}}{(\text{Connector}\times\text{Peripheral}\times\text{Satellite})^{\frac{1}{3}}}\right)$$

$$\textbf{Peripheral balance} = \sqrt{\frac{3}{4}}\ \ln\left(\frac{\text{Peripheral}}{(\text{Connector}\times\text{Provincial}\times\text{Satellite})^{\frac{1}{3}}}\right)$$

$$\textbf{Satellite balance} = \sqrt{\frac{3}{4}}\ \ln\left(\frac{\text{Satellite}}{(\text{Connector}\times\text{Provincial}\times\text{Peripheral})^{\frac{1}{3}}}\right)$$

Subsequently, for each compositional balance, we used generalized additive models (GAM) with factor-smooth interactions to track the evolution in the proportion of each topological role across the lifespan within each subsystem of the resting-state language connectome (rs-LANG) (Wood, 2006); mgcv package in R, Wood, 2017). For additional information and specifics, please refer to Appendix S1.

2.5.2. Probabilistic analysis of the neural mechanisms

To elucidate the neural mechanisms driving the evolution of the proportion of topological roles (section 2.5.1), we modeled the probability that each region changes its topological role across the lifespan. Based on the compositional results (section 3.2), we determined the most probable role of each region within three distinct age groups: a younger group (18-45 excluded), a middle-aged group (45-55 included), and an older group (>55). Concretely, we first calculated the probabilities for all pairwise trajectories between the younger and middle-aged groups and then repeated the calculation between the resulting non-zero trajectories and the older age group. To account for the inter-individual variability within each age group, we considered all the trajectories whose probability fell within a 5% range from the highest probability for each region. Using this approach, we captured for each region the most likely transitions of topological roles between age groups while considering the variability within each age group.

2.5.3. Canonical correlation analysis

To identify the many-to-many relationships between subsystem-level balances (brain set) and neuropsychological scores (cognitive set), we conducted a canonical correlation analysis (CCA). CCA works by finding the linear combinations within the brain and cognitive set of variables that maximize the correlation between the two sets (Wang et al., 2020). The analysis produces a number of canonical functions equal to the number of variables within the smaller set (viz., eight functions for the eight variables of the cognitive set). Each canonical function is composed of two variates: a latent brain and cognitive variable (Sherry & Henson, 2005). To address the issue of multicollinearity among brain variables inherent to compositional data, we ran two CCA models: one excluding the Satellite balances and the other excluding the Peripheral balances of each subsystem. Both CCA models yielded identical structure coefficients (r_s), representing the correlations between the observed variables and the variates

and identical latent coordinates for the variates, although with different linear combinations (*b;* function coefficients). This approach allowed us to construct a latent correlational space based on the cognitive variate-cognitive variable and cognitive variate-brain variable correlations.

2.5.4. Causal analysis

Based on the results from the CCA analysis, we proposed a causal model that integrates age (X), cognitive performance (Y), subsystem reconfiguration of the resting-state language connectome, as measured by the compositional balances (M), and the balance between integration and segregation properties at the system level (W). Using the lavaan package in R (Rosseel, 2012), we examined how a higher integrative efficiency (W) may mitigate cognitive decline by reducing the mediation effect (X -> M -> Y). To achieve this, we tested for indirect path moderation using an index of moderated mediation and a simple slope analysis should the index be significant (Hayes, 2018). For more details, please refer to Appendix S1.

3. Results

3.1. Modular organization of the Language connectome at rest (rs-LANG)

Applying modularity analysis to the resting-state Language connectome (rs-LANG) uncovered four main subsystems. Figure 2 provides a visual representation of these subsystems. Appendix S2 provides a detailed comparison with the task-based modular organization of the same connectome, described by Roger, Rodrigues De Almeida, et al. (2022).

Considering the composition, the largest subsystem, RS NET1 (40 regions), is composed of 66.4% of DMN regions known to be involved in higher-level cognitive function and can thus be regarded as the associative subsystem. The second largest subsystem, RS NET2 (34 regions), is saturated by sensorimotor regions (SMN; 77.1%) along with contributions from CON regions (15.3%) and can thus be regarded as the sensorimotor subsystem. The third largest subsystem,

RS NET3 (32 regions), engages the cingulo-opercular network (CON; 56.4%), a broader network encompassing the salience network (SAL) and known to support low-level attentional redirection. It can thus be regarded as the low-level attentional subsystem. The smallest subsystem, RS NET4 (22 regions), is saturated by FPN regions (63.1%), with nontrivial contributions from CON regions as well (17.2%), and can thus be regarded as the control-executive subsystem. In addition, RS NET1 & 3 are supported by FPN regions (13.8% & 11.8%), and RS NET1, 3, and 4 by Language regions (13%, 10.8%, 8.6%).

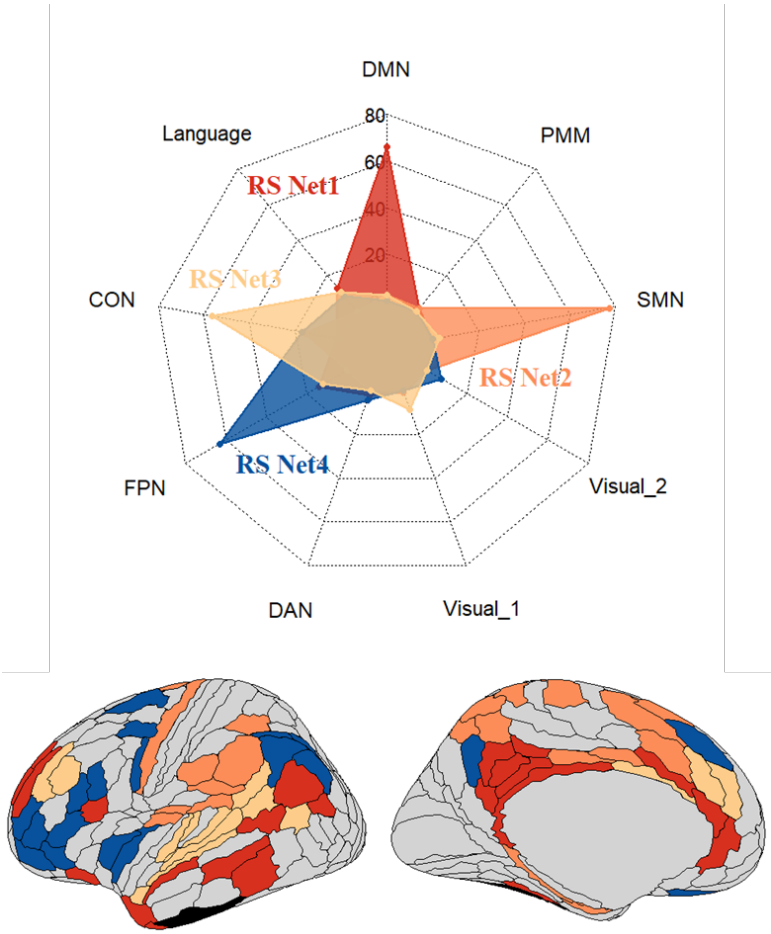


Figure 2. Illustration of the modular organization of the language connectome at rest (rs-LANG). Projection of on a multimodal parcellation (HCP_MMP1.0; Glasser et al., 2016). Only the left hemisphere (LH) is represented here (see Figure S1, Appendix S2 for a whole-brain projection). An additional 3-region module (black) associated with the VMM network has been identified but not considered for analysis due to its instability as a stand-alone module across the lifespan. Brain visualization created with the package *ggseg* in R (Mowinckel & Vidal-Piñeiro, 2020)

3.2. Compositional analysis of the language connectome

Overall, we found that healthy aging is associated with reduced local efficiency (t = -10.37, p < .001, η_{2p} = .15, 95% CI [.11; Inf]) and preserved global efficiency (t = -1.14, p = .26), which tilts the balance between integration and segregation towards a higher integrative efficiency as age increases (t = 9.71, p < .001, η_{2p} = .13, 95% CI [.09; Inf]) (see Figure 3A).

Considering the evolution of topological roles (Figure 3B), we found that healthy aging is associated with a decrease in the proportion of provincial nodes (b = -0.07 95% CI [-0.09; -0.05]; F(1, 624) = 52.5; p < .001; η_p^2 = .08) and satellite nodes (b = -0.03 95% CI [-0.04; -0.01]; F(1, 624) = 20.3; p < .001; η_p^2 = .03), which is contrasted by an increase in the proportion of connector nodes (b = 0.04 95% CI [0.02; 0.05]; F(1, 624) = 31.5; p < .001; η_p^2 = .05) and peripheral nodes (b = 0.04 95% CI [0.02; 0.05]; F(1, 624) = 25.6; p < .001; η_p^2 = .04).

Considering the significant changes at the subsystem level (Figure 3C), we found that, in RS NET4, the rate of loss of provincial nodes (F = 29.8, p < .001, *edf* = 1), the rate of gain of connector nodes (F = 13.6, p < .001, *edf* = 1) and peripheral nodes (F = 6.5, p = .02, *edf* = 1) remains constant across the lifespan, while the loss of satellite nodes stabilizes around age 50 (F = 5.1, p = .007, *edf* = 2.1). Interestingly, in RS NET1, we observed a dynamic of reconfiguration centered around this age window: while the rate of loss of satellite nodes remains constant (F = 15.5, p < .001, *edf* = 1), the rate of gain of peripheral nodes in RS NET1 (F = 6.7, p = .001, *edf* = 2.27) gets slower and the rate of gain of connector nodes tends to accelerate (F = 2, p = .18, *edf* = 2.37). In contrast, while the rate of loss of provincial nodes being quite constant (F = 6.8, p = .01, *edf* = 1.31), the rate of gain of connector nodes (F = 3.81, p = .034, *edf* = 2.23) slows down but that of peripheral nodes tends to accelerate (F = 1.9, p = .17, *edf* = 2.42). Overall, this suggests that, around age 50, RS NET4 stops losing satellite nodes and that changes in the connectivity patterns of RS NET1 and 2 are mirrored.

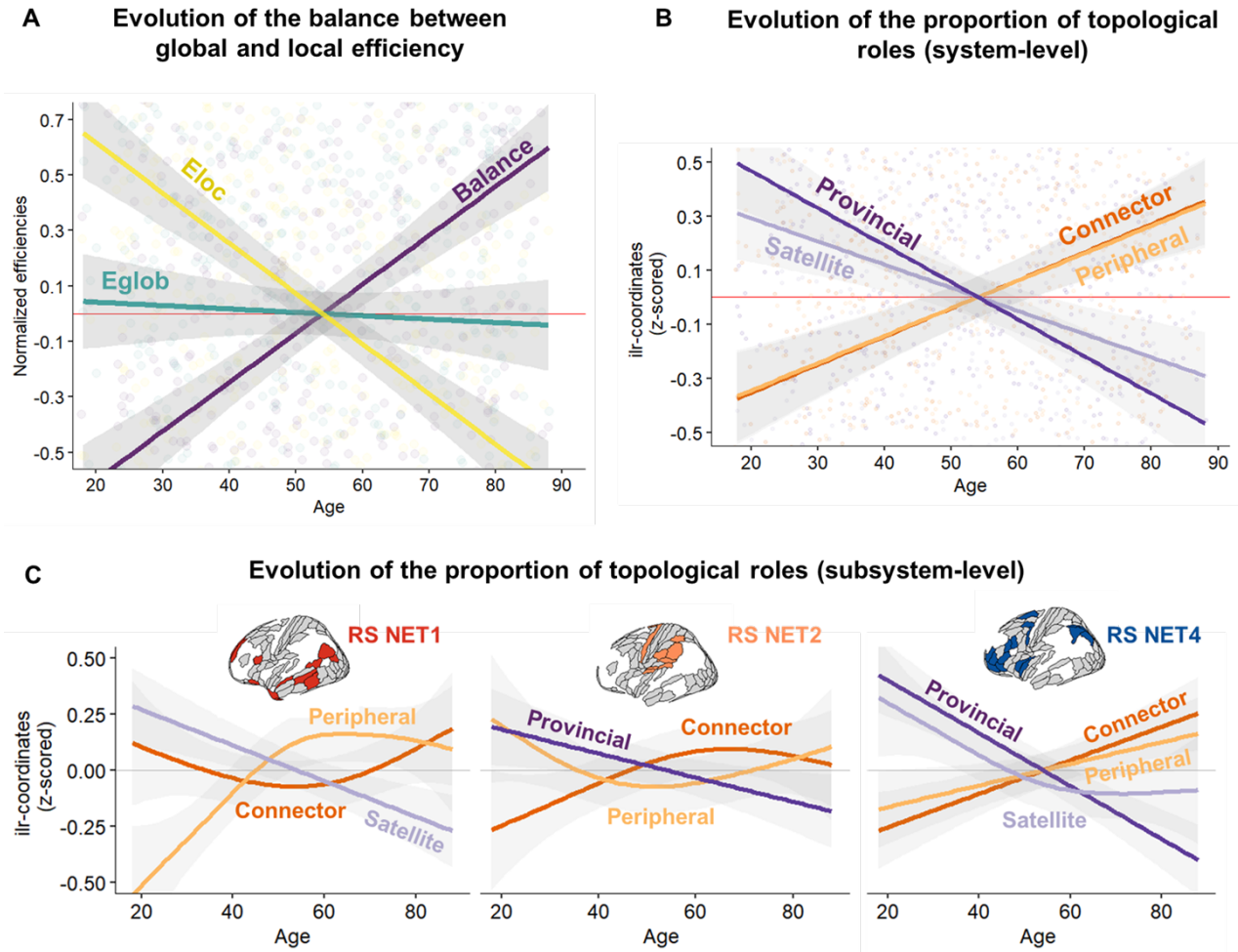


Figure 3. System-level topological dynamics across the lifespan. **Panel A.** Normalized efficiencies as a function of age. Eloc = Local efficiency; Eglob = Global efficiency; Balance = dominance of global efficiency calculated as (Eglob – Eloc) / (Eglob + Eloc). **Panel B and C.** Evolution of the proportion of topological roles as a function of age. For the subsystem level, only significant changes are illustrated.

3.3.Probabilistic analysis of the neural mechanisms

Probabilistic analysis revealed that 35.8% of the language connectome (47 regions) undergoes a topological reorganization across the lifespan. Across subsystems, 50% of RS NET4, 50% of RS NET2, and 34% of RS NET1 regions reconfigure, whereas regions in RS NET3 are more inflexible (24.3%). A web app is available to explore the reconfiguration cross-sectionally: https://lpnc-lang.shinyapps.io/seneca/. To account for inter-individual variability, we consider 16 additional trajectories, which are also highly probable (see section 2.5.2 for details on the calculations), which amounts to 63 trajectories in total and is the number of references for the results below.

As suggested by compositional analysis, we found that functional integration, via the gain of connector nodes, is driven by the reconfiguration of provincial and satellite nodes.

Considering provincial nodes, the decrease is mostly due to the acquisition of new between-subsystem connections or inter-modular links (i.e., provincial-to-connector; 30.1% of all reconfigurations), 52.6% before and 47.4% after age 45-55. Specifically, we notice that RS NET4, which accounts for 31.5% of these acquisitions, tends to acquire them before age 45-55 (83.3%), whereas RS NET2, which accounts for 57.8% of these acquisitions, continues to acquire them after age 45-55 (63.6%). In addition, we notice that the number of regions failing to acquire these properties doubles across the lifespan for RS NET4 (i.e., provincial-to-satellite reconfigurations instead of provincial-to-connector) and starts appearing in RS NET1. This highlights the greater instability of intra-modular links after age 45-55 in RS NET1 & 4.

Interestingly, we observed that this dynamic correlates a change in the way reduced segregation is conducted across the lifespan (i.e., provincial-to-peripheral; 9.5% of all reconfigurations). Indeed, reduced segregation is dominated by RS NET1 (right MTG; 92% FPN, right BA44; 72% DMN) and complemented by RS NET4 (left IFG; 99% FPN) before age 45-55, and after age 45-55 is dominated by RS NET2 (right SMA; SMN, left paracentral lobule; 74% DMN) and complemented by RS NET1 (left insula; 72% DMN).

Considering satellite nodes, we found the opposite pattern. The decrease is mostly due to the acquisition of new within-subsystem connections or intra-modular links (i.e., satellite-to-connector; 20.6% of all reconfigurations), 69.2% of which occur after age 45-55. Specifically, RS NET3 and RS NET4, which respectively account for 38.4% and 15.3% of these acquisitions, tend to acquire them after age 45-55 (80% and 100%), whereas RS NET2 and 1, which respectively accounts for 30.7%, and 15.3% of these acquisitions, tends to acquire them in equal proportions across the lifespan. In addition, we notice that this acquisition may be inefficient

after age 45-55, given the opposite connector-to-satellite reconfigurations in RS NET1, 2, and 4 (8% of all reconfigurations).

Interestingly, we observed that this dynamic correlates with a change in the way deactivation is conducted across the lifespan (i.e., satellite-to-peripheral; 9.5% of all reconfigurations). Indeed, this mechanism occurs exclusively before age 45-55 (5 out of 6 trajectories: 83.3%; 1 out of 6 being in RS NET4) and is most likely to be implemented by RS NET1 (left fusiform area; 63% DAN, 37% DMN; left paracentral lobule; 93% DMN; left pCC 68% DMN) as well as in bilateral postcentral regions in RS NET3 (95% SMN).

To summarize, probabilistic analysis helps us clarify the dynamic of reconfiguration of the language connectome across the lifespan based on the reallocation of inter- and intra-modular links. As illustrated in Figure 4, this suggests two strategies for acquiring connector properties across the lifespan: (i) an efficient, synergistic strategy based on inter-modular links and the coupling between RS NET1 and RS NET4, which is implemented before age 45-55; (ii) an inefficient strategy based on intra-modular links, which occurs primarily in older adults. The detail of the regions involved in all mechanisms can be found in Appendix S3.

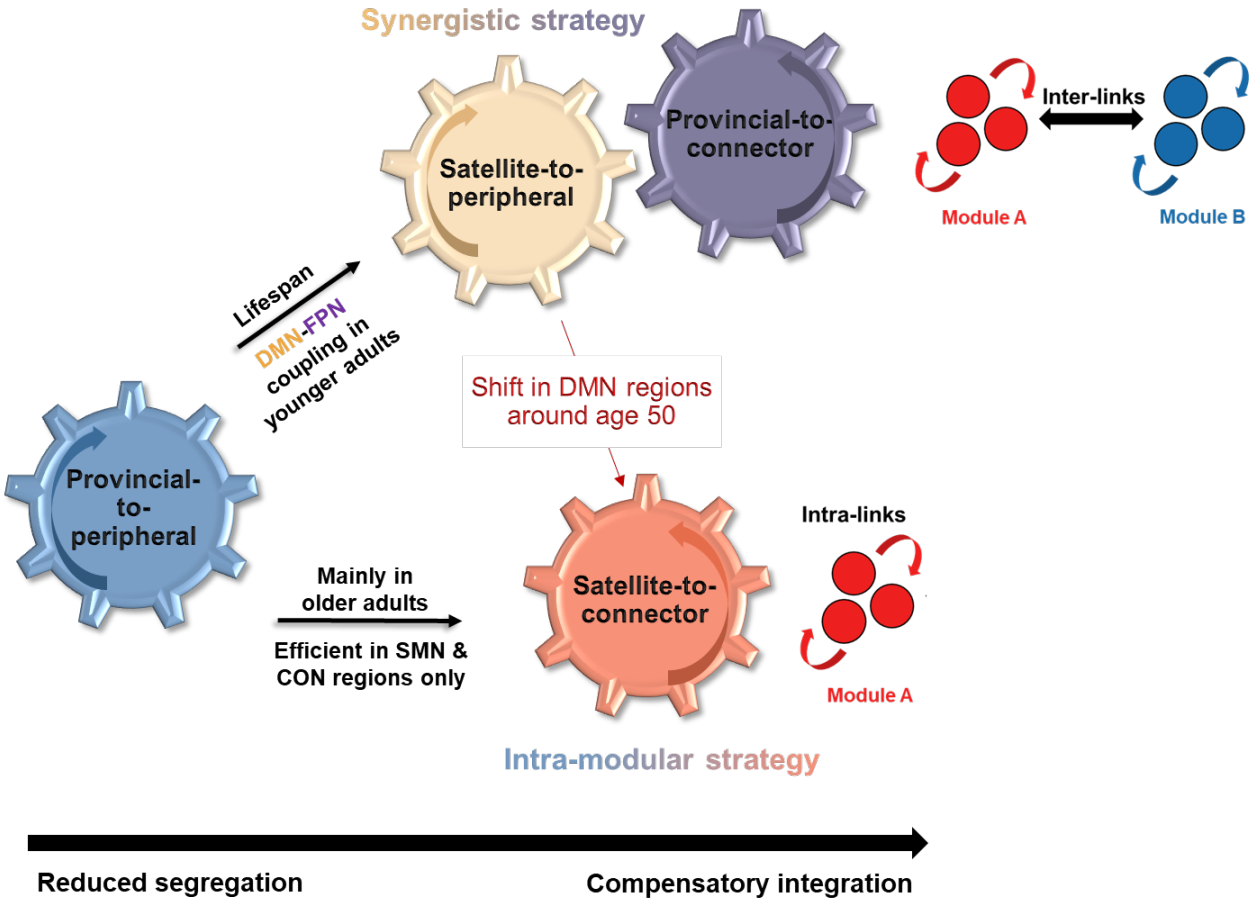


Figure 4. Topological model of compensatory integration. We propose two compensatory strategies to acquire connector properties across the lifespan: (i) a synergistic strategy based on links between subsystems (inter-links) and the coupling between DMN and FPN regions which is most efficient in younger adults. (ii) an inexpensive strategy based on links within subsystems (intra-links) which occurs primarily in older adults

3.4.Canonical correlation analysis

Canonical correlation analysis (CCA) yielded two significant canonical functions, each composed of a cognitive and brain variate, which maximize the correlation between the brain and cognitive set of variables (R_{c1} = .28; ${R_{c1}}^2$ = 8%, p < .001; R_{c1} = .25; ${R_{c2}}^2$ = 6%, p < .001). We examine these results in two steps. In the first step, we analyze the organization of the age-related performances in the eight cognitive tasks based on the two cognitive variates (section 3.1.1.). In the second step, we identify the brain variables associated with this organization (section 3.1.2.).

3.1.1. Effect of age on cognitive functions

Based on the correlations between the two cognitive variates and each cognitive variable (i.e., structure coefficients; r_s), we built the corresponding cognitive map shown in Figure 5A. By relating the age-related performances of the eight cognitive tasks (Figure 5C, Table 2) with the cognitive map, we found that cognitive decline can be predicted by two factors.

Cognitive variables	*Goodness-of-fit of Age as a predictor (Deviance explained in %)*
Cattell	42.9
Naming	41.4
LTM	14.8
Verbal Fluency	14.1
Tip-of-the-tongue	13
Multitasking	8.75
Sentence Comprehension	6.02
Proverb	3.74

Table 2. Estimates from generalized additive models (GAMs): Cognitive variable ~ s(Age). All models are significant at p < .001 '***'. Deviance explained is used as a proxy for the amount of age-related cognitive decline

The first factor may correspond to the amount of semantic processing associated with a task. Given the high correlation between the deviance reported in Table 2 (r = -.94, p < .001) and the coordinates of cognitive tasks on this factor, we suggest that semantic processing is the main predictor of age-related cognitive performances. In other words, the first factor discriminates non-semantic tasks, which tend to decline the most (fluid processing: $r_{_Cattell} = -.8$; phonological access: $r_{_Naming} = -.78$) from semantic tasks which tend to decline the least (semantic access: $r_{_Comprehension} = -.27$; lexical retrieval: $r_{_ToT} = -.26$; semantic abstraction: $r_{_Proverb} = .06$).

Based on the description of the processes recruited for each cognitive task (see Table 1, section 2.1), the second factor may correspond to the amount of synergy between language, long-term memory, and executive functions associated with a task. Interestingly, synergistic task performances have a nonlinear relationship with age. Indeed, Figure 5B illustrates a shift around age 50 from an increase to a decrease in performance (F = 5.6, p < .001, *edf* = 2.7). Therefore,

this second factor may discriminate the highly synergistic tasks which follow this shift ($r_{_Proverb}$ = -.68, $r_{_Multitasking}$ = -.59, $r_{_Verbal_Fluency}$ = -.53) from the less synergistic tasks which do not ($r_{_Comprehension}$ = -.04, $r_{_LTM}$ = -.07, and $r_{_Cattell}$ = -.08). In addition, this decrease in synergistic task performances is associated with accelerated cognitive decline in non-semantic tasks around the same age window (F = 119, p < .001, *edf* = 4.9; Figure 5B).

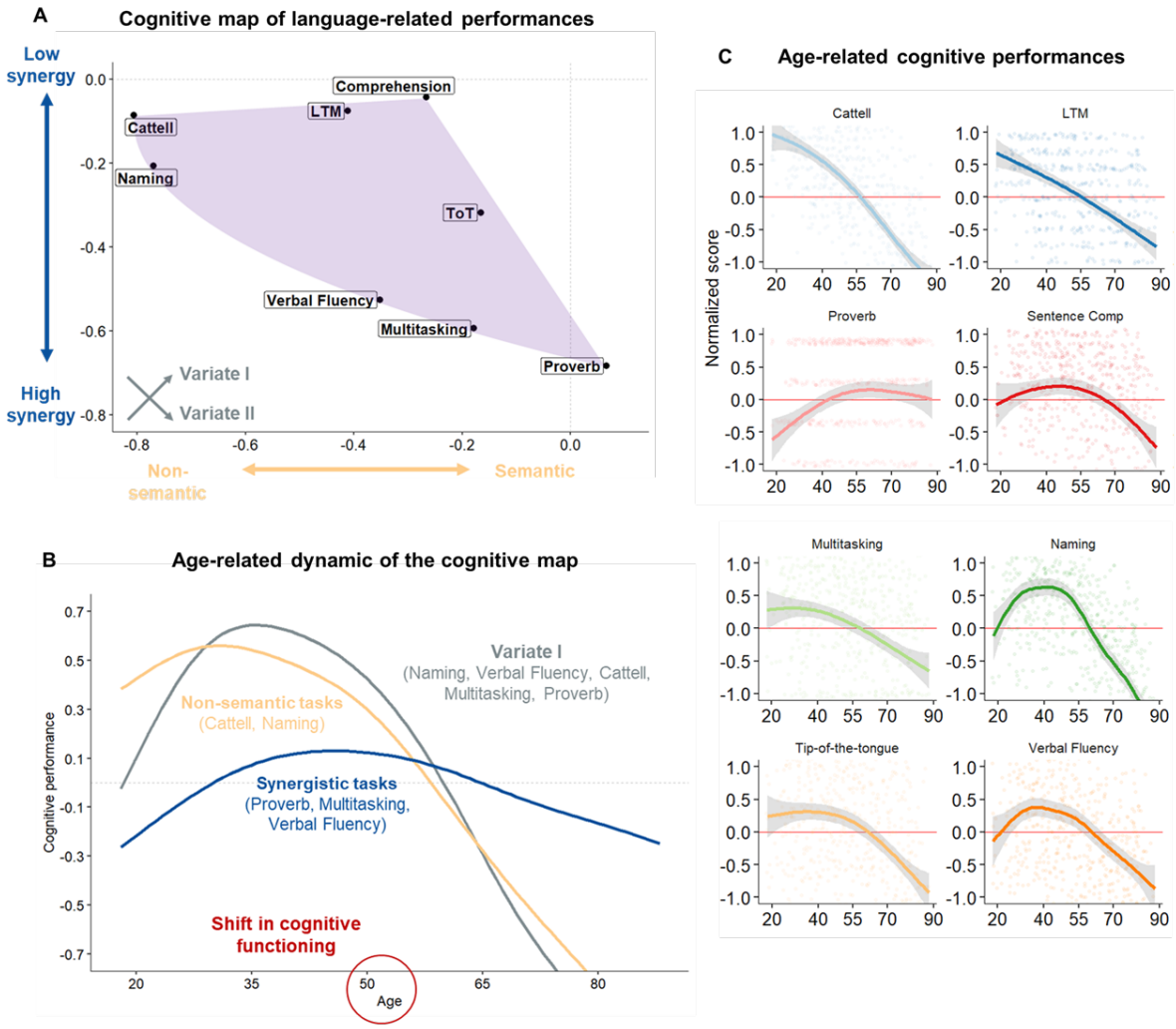


Figure 5. Illustration of the predictors of age-related cognitive performances. Panel A. Cognitive map of language-related performances based on the correlations between each cognitive task and the two predictors; semantic (yellow) and synergistic processing (blue). These factors are calculated as the two cognitive variates' cross-products (i.e., diagonals). Language-related performances tend to self-organize in a triangular pattern to maximize the correlations with topological mechanisms (not shown here). Panel B. Illustrates the age-related dynamic of the cognitive map. As age increases, synergistic task performances shift from better to worse performances (blue). This shift is associated with an acceleration of the cognitive decline in non-semantic tasks (yellow), suggesting that the amount of synergy mitigates the decline in non-semantic tasks before age 50. Panel C. Age-related performances of the eight cognitive tasks using GAMs

3.1.2. Effect of age on cognitive functions and cerebral correlates

We identified the brain variables that correlate with the task performances of the first cognitive variate, which is the variate that combines the factors identified in the previous section. As illustrated by the grey trajectory in Figure 5A, a high correlation with the first cognitive variate (e.g., $r_{_Naming}$ = -.7, $r_{_Cattell}$ = -.63, $r_{_Verbal_Fluency}$ = -.62) suggests that performances tend to increase before accelerating around age 50-55. Therefore, the brain changes that are also highly correlated with this variate may be associated with this dynamic.

Below, we only considered the brain variables that showed a significant or tendency for change across the lifespan (see section 3.2). In line with probabilistic analysis (section 3.3), Figure 6 illustrates that the dynamic of the first cognitive variate is primarily associated with provincial-to-connector reconfigurations in RS NET4 and satellite-to-peripheral reconfigurations in RS NET1. This further suggests that a coupling between deactivation in RS NET1 and integration in RS NET4 is responsible for cognitive performance variations across the lifespan. Moreover, Figure 6 suggests that the shift around age 50 in the performances of synergistic tasks driven by a shift in the connectivity patterns in RS NET1 from deactivation towards integration. This particularly highlights the pivotal role of satellite nodes, as previously identified in Figure 4 (section 3.3).

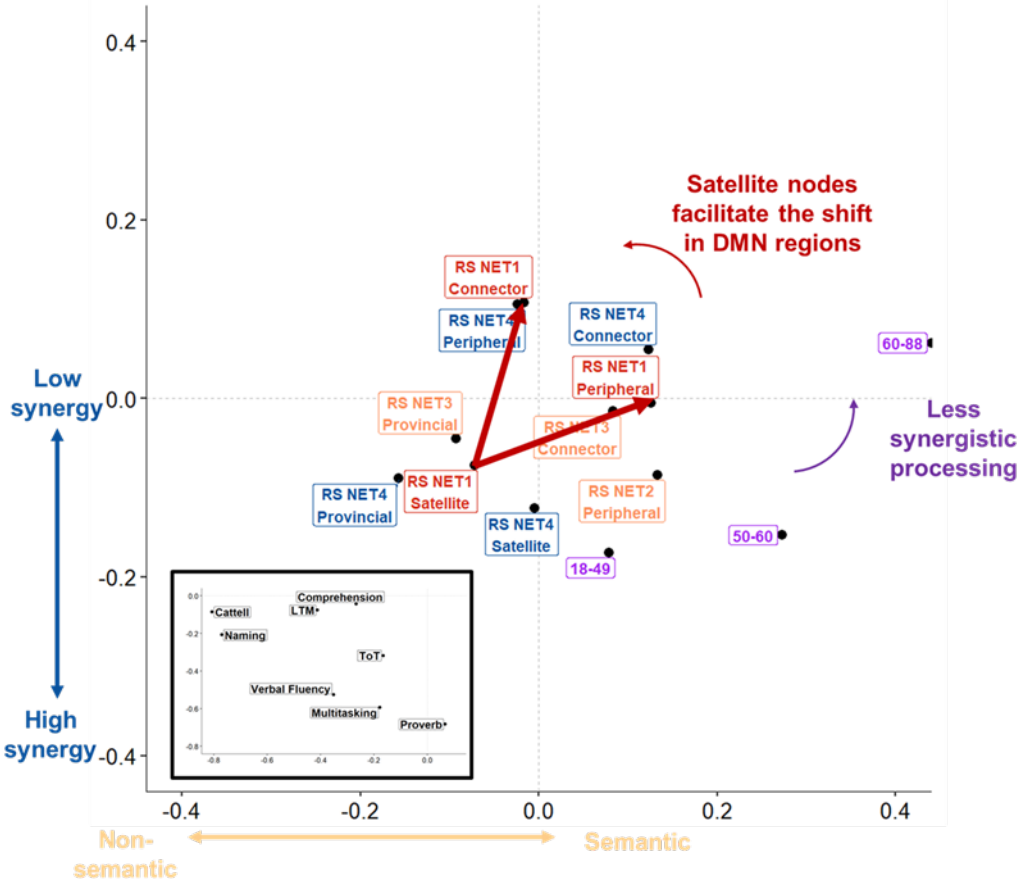


Figure 6. Neurocognitive map of healthy aging. Coordinates represent the correlations between topological changes in the language connectome and the cognitive variates (i.e., cross-loadings). The shift around age 50 corresponds to a shift from deactivation to integration of DMN regions which disrupts the DMN-FPN coupling that mitigates cognitive decline. The black box in the bottom left can be viewed in full size in Figure 5A

3.5.Causal analysis

Based on the results of canonical correlation analysis, we hypothesized that the synergy between deactivation in RS NET1 and integration in RS NET4 may mitigate cognitive decline before age 50, whereas a loss of this coupling may accelerate cognitive decline after age 50. Therefore, we examined whether the reorganization at the subsystem level, which we described in the previous section, induces a high integrative efficiency at the system level (balance integration/segregation) to mitigate this decline (see Figure S4, Appendix S2 for an illustration of the model).

As expected, at the subsystem level, we found that the reorganization of the language connectome (i.e., less provincial nodes in RS NET4 and 2 and more connector nodes in RS

NET4 coupled with more peripheral nodes in RS NET1) mediates cognitive decline (mediation (a*b1): z = 3.672, p < .001) in non-semantic or highly synergistic tasks ($r_{_Naming}$ = -.69, $r_{_Cattell}$ = -.63, $r_{_Verbal_Fluency}$ = -.62, $r_{_Multitasking}$ = -.55, $r_{_Proverb}$ = -.43). Nonetheless, it seems that this reorganization also induces a high integrative efficiency at the system level (a*d1: z = -2.21, p = .003) which partially mitigates this decline (moderated mediation (a*b2): z = -2.2, p = .03). Indeed, Figure 7 clarifies that a high integrative efficiency gradually mitigates cognitive decline until a tipping point around age 54 (Figure 7; full tensor product: *edf* = 7.377, F = 50.1, p < .001). line with our previous analyses, this could suggest a sudden loss in synergistic processing between RS NET1 and RS NET4.

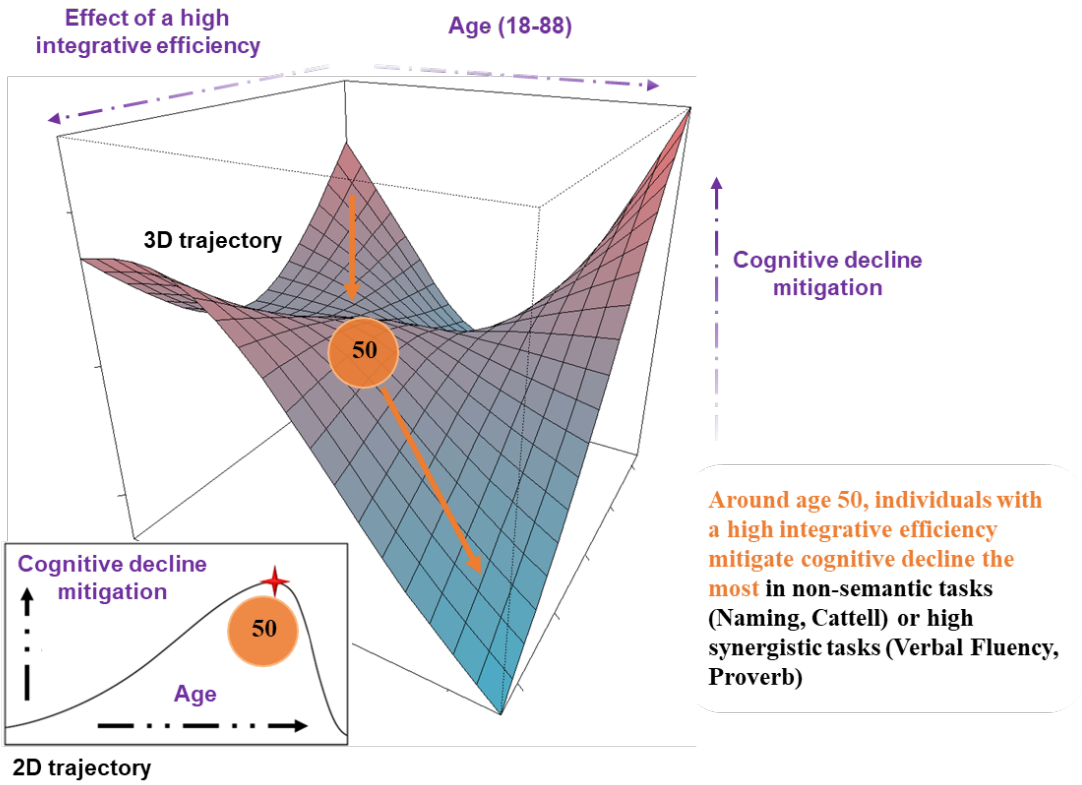


Figure 7. Illustration of the lifespan trajectory of cognitive resilience provided by functional reorganization. The hyperplane shows where the most substantial impacts of moderated mediation (b2) on cognitive performances (Y) are. The orange arrow shows the shortest path to mitigate cognitive decline optimally. In the mediation model, age is the predictor (X), topological reorganization is the mediator at the subsystem level (M), and the balance between integration and segregation at the system level is the moderator (W)

4. Discussion

Healthy aging is associated with a heterogeneous decline across cognitive functions, including language. However, the neural mechanisms underlying this variability still need to be understood. In this study, we leveraged resting-state fMRI and neuropsychological data from the population-based CamCAN cohort (Cam-CAN et al., 2014) to investigate the functional reorganization of the language connectome and its association with age-related cognitive variability. Employing state-of-the-art graph theoretical analysis, we developed a data-driven pipeline that integrates both cerebral and cognitive levels of analysis.

Our findings can be summarized in two categories, shedding light on the mechanisms that underlie the evolution of neurocognitive functioning across the lifespan. First, at the cognitive level, we demonstrate that language processing is not an isolated function but is modulated throughout an individual's lifespan by the extent of inter-cognitive synergy between language, long-term memory, and executive functions. This modulation offers a potential explanation for the observed variability in language performances. Second, at the cerebral level, we reveal that the synergistic coupling between DMN and FPN regions may act as a compensatory mechanism to mitigate the loss in the specialization. Importantly, we propose that a loss in this synergistic processing around the fifth decade of life may trigger a transition in neurocognitive functioning associated with accelerated cognitive decline.

Taken together, the present study contributes to ground neurocognitive aging as the study of a dynamical system which provides the basis for 'studying the emergent function and its efficiency' (Naik et al., 2017; O'Byrne & Jerbi, 2022). Our findings can be formalized as a novel SENECA model (Synergistic, Economical, Nonlinear, Emergent, Cognitive Aging), integrating connectomic and cognitive dimensions within a complex system perspective.

SENECA furthers our understanding of the brain's language processes and their implication on inter-cognitive functioning in healthy aging.

Evidence for inter-cognitive functioning across the lifespan

At a cognitive level, our results from canonical correlation analysis (section 3.4) offer a new quantitative framework that emphasizes the implication of synergistic processing on age-related variability in language abilities (Gatica et al., 2021; Muller et al., 2016).

Indeed, we found that cognitive performances in healthy adults are primarily influenced by the amount of semantic processing demanded by a task. However, we also observed a dynamic interplay between language and executive functions, suggesting that the amount of inter-cognitive synergy could modulate the effect of semantic processing on age-related cognitive decline. Indeed, our findings also suggest that a sudden shift around age 50 from better to worse performances in synergistic processes (i.e., verbal fluency, semantic abstraction, multitasking) is associated with accelerated cognitive decline around the same age window in non-semantic processes (i.e., phonological for language production and fluid processing for the Cattell task). Overall, this provides empirical support for the LARA model (Banjac et al., 2021), highlighting the involvement of executive processes during language production across the lifespan (Hoyau et al., 2018; Pistono et al., 2021; Shafto & Tyler, 2014). This also reinforces the idea that language is more than just intra-linguistic processes, and interacts with other cognitive functions (Hagoort, 2016, 2023).

Dedifferentiation-Compensation mechanisms

At a cerebral level, our study aligns with previous team work (Roger, Rodrigues De Almeida, et al., 2022), suggesting language is an interactive function whose neurocognitive architecture at rest (rs-LANG) involves an associative (RS NET1), sensorimotor (RS NET2), low-level attentional (RS NET3), and control-executive (RS NET4) subsystems (see section 3.1).

Within a lifespan perspective, compositional analysis (section 3.2) suggests that the cognitive decline observed in non-semantic processes (i.e., language production and fluid processing) is associated with reduced local efficiency of rs-LANG (Cao et al., 2014; Chong et al., 2019; Martin et al., 2022; Song et al., 2014) and reduced segregation in the control-executive, and sensorimotor subsystems (Dosenbach et al., 2007; Grady et al., 2016). It highlights that a loss in functional specialization, or dedifferentiation, drives cognitive decline in healthy aging adults (Chan et al., 2014, 2017; Deery et al., 2023). In contrast, enhanced integration of control-executive and sensorimotor regions within the language connectome may act as a compensatory mechanism, countering the effects of dedifferentiation (Cabeza et al., 2018). This compensatory integration is characterized by increased connector nodes across the lifespan, essential for information transfer (Bagarinao et al., 2020) and task processing flexibility (Bertolero et al., 2015). Specifically, connector nodes confer integrative properties to the network by tuning the connectivity of their neighbors to preserve modularity or functional specialization (Bertolero et al., 2018), which leads to better cognitive performances (Meunier et al., 2010), especially during healthy aging (Meunier et al., 2009; Setton et al., 2021).

While previous studies focused exclusively on how dedifferentiation mediates poorer performances in fluid intelligence (Mitchell et al., 2023) and long-term memory (Koen et al., 2020), this study aimed to model the neural mechanisms that bridge dedifferentiation and compensation (section 3.3), and how the changes in this dedifferentiation-compensation dynamic relate to the age-related variability in language abilities discussed previously. Overall, we suggest that dedifferentiation-compensation follows the principle of the economy of brain network organization (Bullmore & Sporns, 2012). To clarify, the reorganization of the language connectome may be governed by the balance efficiency-cost, which seeks to maximally mitigate cognitive decline for the minimal integration cost (Barbey, 2018). Specifically, we identified two compensatory strategies that satisfy this principle of economy. The first

compensatory strategy relies on acquiring long-distance connections (i.e., inter-modular links) and is most efficient in younger adulthood thanks to the coupling between DMN and FPN regions. The second compensatory strategy relies on acquiring short-distance connections within subsystems and is primarily implemented in older adulthood.

Accelerated cognitive decline emerges from the loss of DMN-FPN coupling

As age increases, we discuss how a change in the dedifferentiation-compensation dynamic will likely trigger an acceleration in cognitive decline in non-semantic (e.g., language production) and synergistic tasks (e.g., verbal fluency).

In younger adults, differentiation is implemented by deactivating provincial nodes within subsystems, which provide segregative properties to the network (Bertolero et al., 2015; Guimerà & Amaral, 2005). In contrast, compensatory integration may be implemented by the synergy between the DMN and FPN regions. Indeed, DMN regions may deactivate (i.e., satellite-to-peripheral) to offset the integration cost of long-distance connections in the FPN regions (i.e., provincial-to-connector), thus satisfying the principle of economy. It aligns with numerous studies indicating that the deactivation of DMN regions via peripheral hubs (Dohmatob et al., 2020) enhances the coupling of DMN-FPN (Muller et al., 2016; Pistono et al., 2021).

Interestingly, our results suggest that this DMN-FPN coupling may be disrupted in older adults due to the increased scarcity of satellite nodes in the associative subsystem (RS NET1). Indeed, satellite nodes initiate deactivation in the synergistic strategy (i.e., satellite-to-peripheral) and enhanced integration in the other strategy (i.e., satellite-to-connector). Hence, satellite nodes get more scarce as age increases in RS NET1. Based on our study, we suggest that this scarcity could change the way compensatory integration is carried out as age increases. Indeed, DMN regions may shift their connectivity patterns from deactivation (i.e., satellite-to-peripheral) to

integration (i.e., satellite-to-connector), favoring the most direct reconfiguration mechanism which provides an inexpensive way to mitigate cognitive decline. Interestingly, control-executive regions in older adults may also switch to this strategy based on short-distance connections (i.e., satellite-to-connector) as inter-modular links are no longer pre-allocated by DMN regions. Nonetheless, the switch of this strategy in DMN and FPN regions may be less efficient in mitigating cognitive decline in the long-term due to the instability of short-distance, intra-modular connections. This is particularly manifest of a greater dedifferentiated system in older adults and also aligns with a more inefficient integration of long-distance connections (i.e., provincial-to-satellite instead of provincial-to-connector), further reducing the mitigating effect of integration.

These findings align with a recent study suggesting that a youth-like network architecture is associated with more economical processing (Martin et al., 2022). Therefore, our findings (i) supports that an efficient reorganization most likely follows the principle of economy of brain network organization, and also (ii) highlight that satellite nodes may play a pivotal role in this economical reorganization across the lifespan, responsible for the shift of connectivity patterns of DMN regions. This aligns with the DECHA model (Default Executive Coupling Hypothesis of Aging), which reports that older adults with reduced deactivation in DMN regions fail to modulate control-executive regions (Spreng & Turner, 2019; Varangis et al., 2019). This also echoes recent theoretical (Grasso et al., 2021; Varley et al., 2022) and empirical studies (Luppi et al., 2022; Santos et al., 2023; Varley et al., 2023) suggesting that higher-order interactions facilitate higher-level cognitive performances (Williams et al., 2022) such as cognitive control (Varley et al., 2023), particularly during healthy aging (Gatica et al., 2021).

A novel integrative and connectomic model: SENECA

As Livneh (2023) suggested, we combine the cerebral and cognitive levels of analysis within a single integrative model: SENECA. The SENECA model articulates a cerebral (SE) and cognitive (CA) dimension, which embraces a complex system perspective (NE). We borrow the name from the Seneca effect, generally found in complex systems, which denotes a slow rise followed by an abrupt decline (Bardi, 2017). Hereafter, we refer to the model as SENECA in uppercase and to the Seneca effect in lowercase letters.

Along the cerebral dimension (SE), we confirm that dedifferentiation and compensation are two sides of the same coin (Deery et al., 2023; Naik et al., 2017; Stumme et al., 2020; Tognoli & Kelso, 2014). Specifically, we show that higher-order interactions between subsystems are the way for the brain to satisfy the balance between maximal cognitive efficiency and a minimal cost of integration across the lifespan. In sum, the synergistic (S) coupling between DMN and FPN regions seems to follow the principle of the economy (E) of brain network organization (Bullmore & Sporns, 2012; Martin et al., 2022).

Along the cognitive dimension (CA), we suggest that satellite nodes are the currency of this economy. Specifically, accelerated cognitive (C) decline in healthy aging (A) adults may stem from an increased scarcity of satellite nodes within the language connectome, which disrupts the way dedifferentiation and compensation are implemented, in turn disrupting the DMN-FPN coupling that promotes mitigate cognitive decline mitigation.

Considering both dimensions together, we suggest that the synergistic (S) and economic (E) reorganization of the language connectome produces a nonlinear (N) and emerging (E) dynamic of cognitive aging (CA). The 'nonlinear' aspect is associated with the acceleration of the cognitive decline in non-semantic and synergistic tasks, which could mark a transition in neurocognitive functioning during the fifth decade of life. The 'emergent' aspect suggests that

the reorganization at the subsystem level induces a dynamic at the system level that is more than the sum of its parts (Pessoa, 2022; Piccinini, 2022). In line with Stumme et al. (2022), this makes significant progress toward reconciling cognitive efficiency across topological levels of analysis.

Perspectives and limitations

Theoretically, SENECA embraces the notion of cognitomics (Roger et al., 2018) which proposes to consider the neuropsychological implications that the connectomic architecture imposes on human cognition and behavior. Specifically, we provide evidence that changes in the language architecture mediates cognitive performances supported by intra- (language) and extra-linguistic sub-processes (long-term memory, executive functions), as reported conceptually (Hagoort, 2023; Roger, Banjac, et al., 2022) and empirically (Roger, Rodrigues De Almeida, et al., 2022). Within this cognitomic perspective, it seems that the re-allocation of inter- and intra-modular connections between subsystems provides an appropriate topological framework to investigate the cognitive efficiency of compensatory integration across the lifespan. In further studies, we suggest that this framework could serve as the basis to examine how the mechanisms underlying this dedifferentiation-compensation dynamic may differ in clinical populations.

Our study also shows several methodological novelties. First, we propose a data-driven pipeline that makes extensive use of compositional data analysis (Greenacre, 2021; Smith et al., 2016) and demonstrate that isometric log-ratio transformation (ilr) is a valuable tool to model the dynamic of network communication within and between subsystems. Second, the data-driven map presented in Figure 5A supports that simple bivariate correlations are sufficient to identify the amount of inter-cognitive synergy as a critical determinant of language function. The map also provides a latent geometry of age-related language function, which particularly

discriminates between key landmarks of language processing: sentence comprehension (semantic, low synergy), language production (phonological, mid-low synergy), and semantic abstraction (semantic, high synergy). This map suggests that topological roles (Guimerà & Amaral, 2005) provide a parsimonious framework to track the mechanisms that implement the inter-cognitive synergy and can also discriminate between critical language tasks. Therefore, rs-LANG may be appropriate to investigate the age-related variability in language abilities, despite being based on a task fMRI atlas (Roger, Rodrigues De Almeida, et al., 2022).

Our study also shows several limitations. Descriptively, the probabilistic analysis may only model the most potential topological role for each region and age group. Therefore, it cannot identify all the regions involved in the underlying mechanisms and fails to account for inter-individual variability, especially in older adulthood (Stumme et al., 2020). To clarify, two individuals may have the exact relative count of connector nodes, but different regions may implement these roles. To mitigate this issue, we introduced a tolerance parameter in our analysis for modeling the trajectories with a probability very close to the top one. Nonetheless, longitudinal studies would be more appropriate to investigate the reconfiguration between topological roles.

We considered GAMs for estimating how the system-level dynamic modulates the mediation effect of topological changes on age-related cognitive tasks. Although a direct estimation of nonlinear smooth functions within an ordinary SEM framework would make the causal model more rigorous, such a framework has yet to be reported in the literature and is likely to be computationally challenging. Although cross-sectional data may also bias estimates in mediation analysis (Cole et al., 2013; Lindenberger et al., 2011), a recent study comparing longitudinal, cross-sectional, and cohort effects on cognitive aging revealed that using cross-sectional data is perfectly reasonable as long as no cohort effect is assumed (Sørensen et al., 2021). In the present study, no cohort effect is assumed, given that we estimated universal

lifespan trajectories only. Nonetheless, this opens up future perspectives to investigate how idiosyncratic mechanisms (Baciu et al., 2021) associated with a high cognitive reserve (Pitarque et al., 2016; Solé-Padullés et al., 2009) could provide the basis for a more graceful decline as age advances. Our findings suggest that subcortical structures such as the bilateral thalamus and putamen could also play a crucial role in these mechanisms in late adulthood.

Topologically, current methods in graph theory follow the predicate that inter-regional interactions of interest are limited to dyadic relationships: two regions connected by an edge (Battiston et al., 2020, 2021). Therefore, graphs need help to fully account for the topological characteristics intrinsic to higher-level interactions, which cannot always be modeled as the sum of dyadic interactions. Although dyadic patterns can often describe the structural architecture, the functional dynamics underlying complex cognitive functions such as language are implemented by a distributed network of cortico-subcortical regions and their multilevel interactions (Gazzaniga et al., 2019; Giusti et al., 2016) suggesting higher-order coupling. In addition, several studies have highlighted the redundant nature of specific higher-order motifs (Merchan & Nemenman, 2016), which can sometimes be fully described in dyadic relationships. Therefore, modeling higher-level interactions has a robust statistical (Schneidman et al., 2006; Yu et al., 2011), topological (Gardner et al., 2021; Giusti et al., 2015), and theoretical justification for quantifying how the synergy-redundancy balance evolves across the lifespan to mitigate cognitive decline (Gatica et al., 2021; Luppi et al., 2022, 2023; Stanford et al., 2022).

Considering the breadth of current neuroimaging datasets, the use of sophisticated techniques designed to yield high inter- and low intra-individual variability is timely. The proportional thresholding for the topological structure (Jiang et al., 2023) may lead to the exclusion of weaker edges that are neurobiologically meaningful (van den Heuvel et al., 2017). Therefore, assessing how a data-driven topological filtering scheme such as OMST (Orthogonal Minimum

Spanning Tree; Dimitriadis et al., 2017; Martin et al., 2022) compares to proportional thresholding would provide new insight into how older adults navigate the trade-off between cognitive efficiency and the cost of synergistic reorganization.

5. Conclusion

Language is an interactive function that embodies the complexity of human cognition. In this study, we aimed to clarify how language function is implemented at the cerebral level across an individual's lifespan. We found that synergistic coupling between DMN and FPN regions may be the way for the brain to maximally mitigate cognitive decline in language production and verbal fluency while limiting the reorganization cost. Relatedly, a disruption of this coupling could mark a transition in neurocognitive functioning towards less synergistic processing around the fifth decade of life. We summarize these findings in a novel integrative and connectomic model called SENECA, which articulates a cerebral (S- synergistic E- economical) and cognitive (C- cognitive A- aging) dimension within a complex systems perspective (N- nonlinear E- emergent).

Data availability

Raw data can be made available by the authors upon request. Scripts for analysis and visualizations are available at: https://github.com/LPNC-LANG/SENECA

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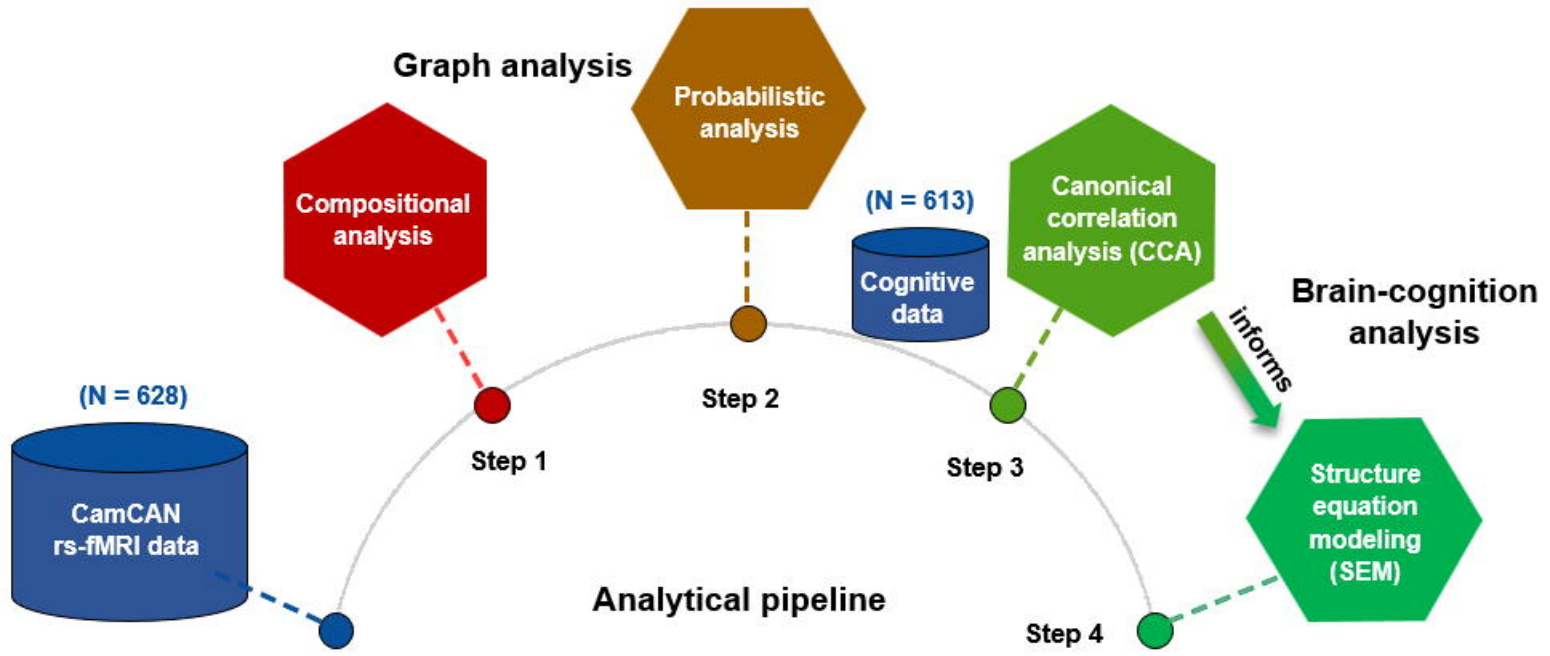
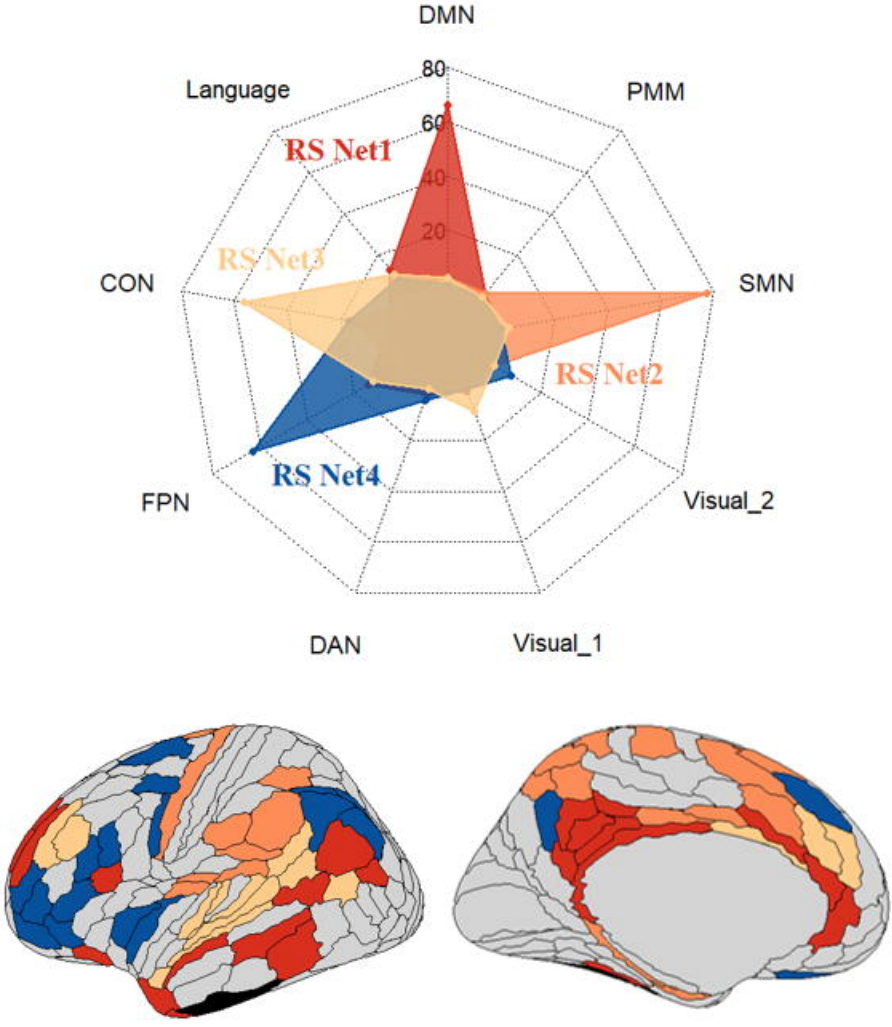
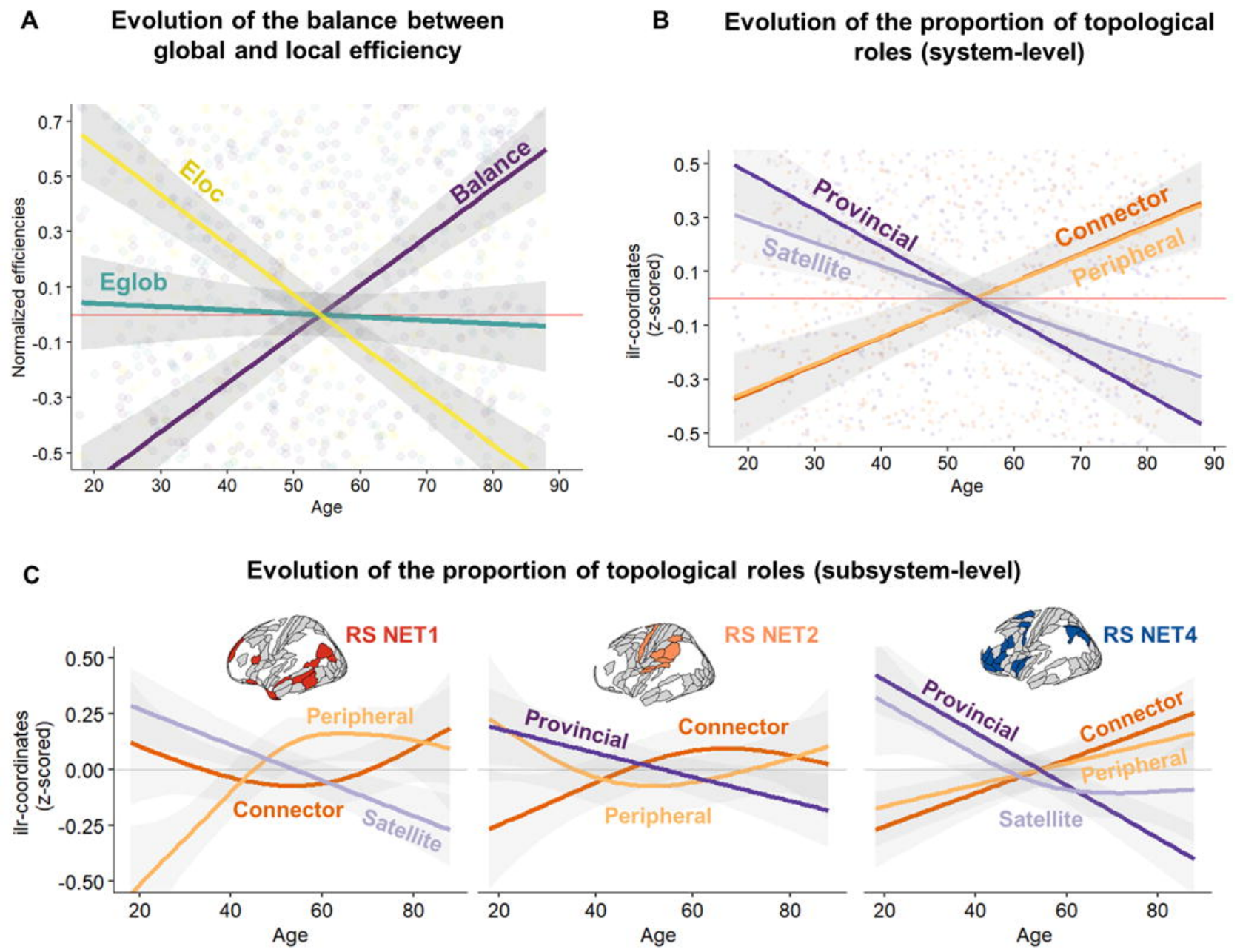
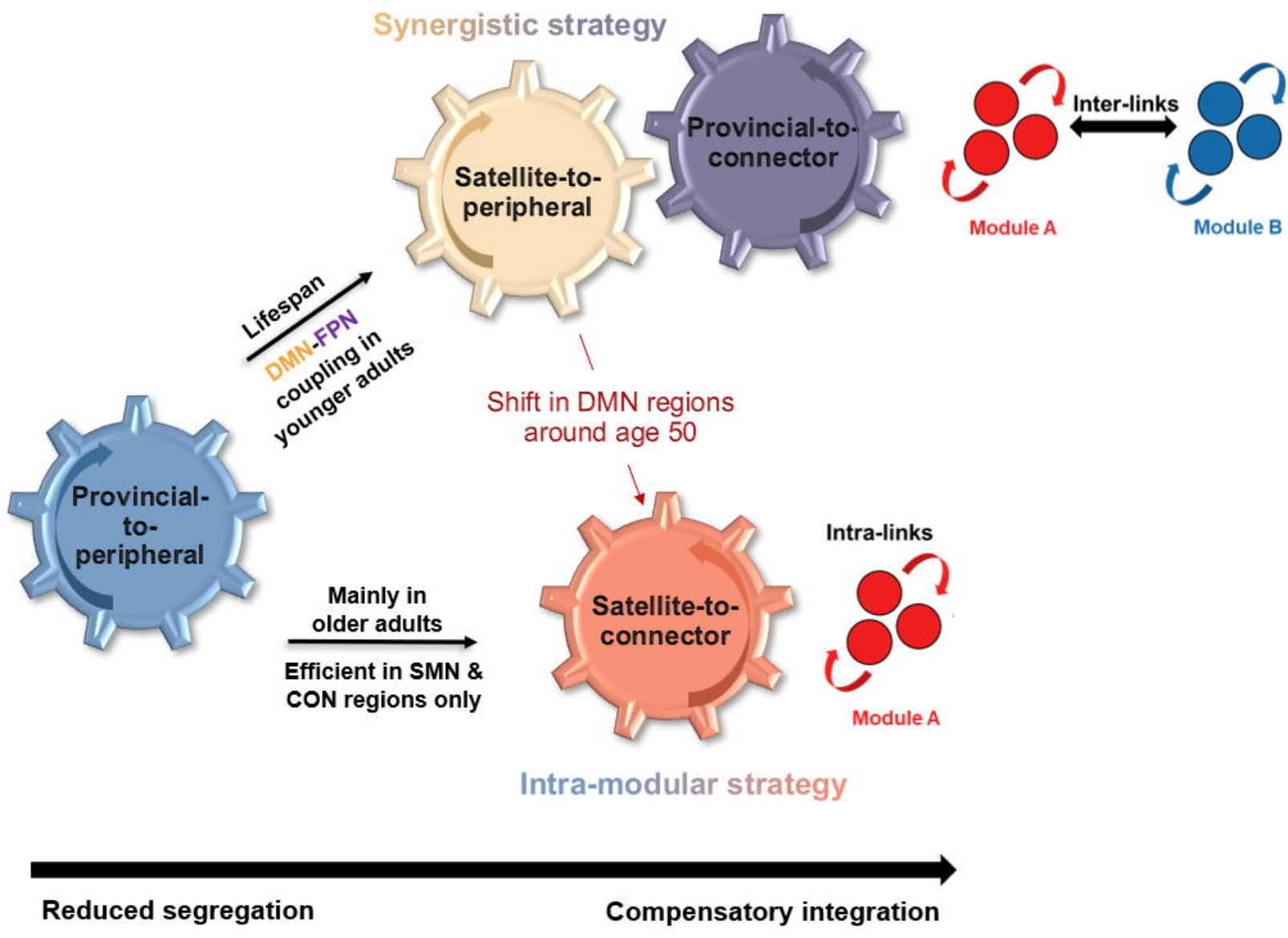
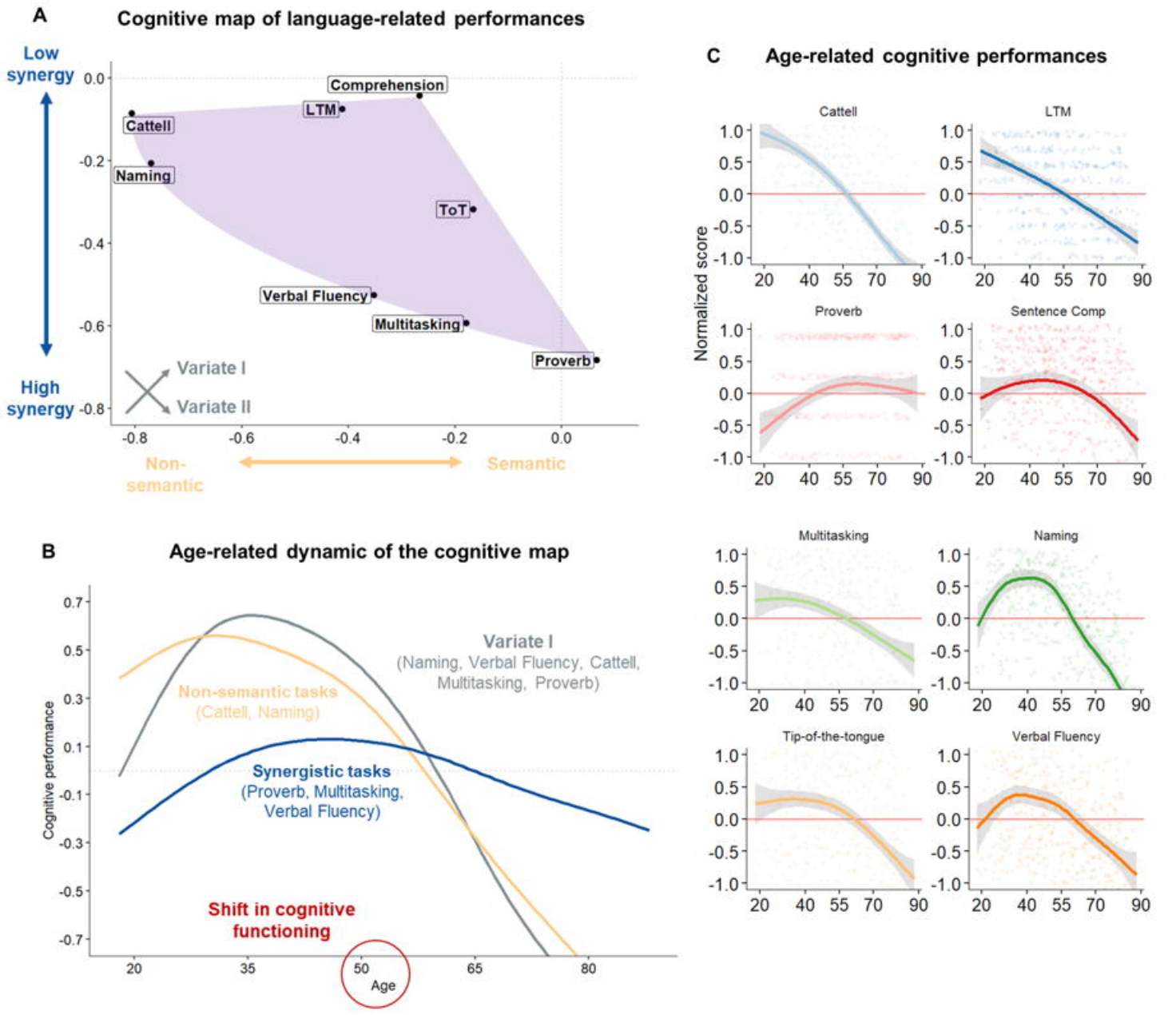
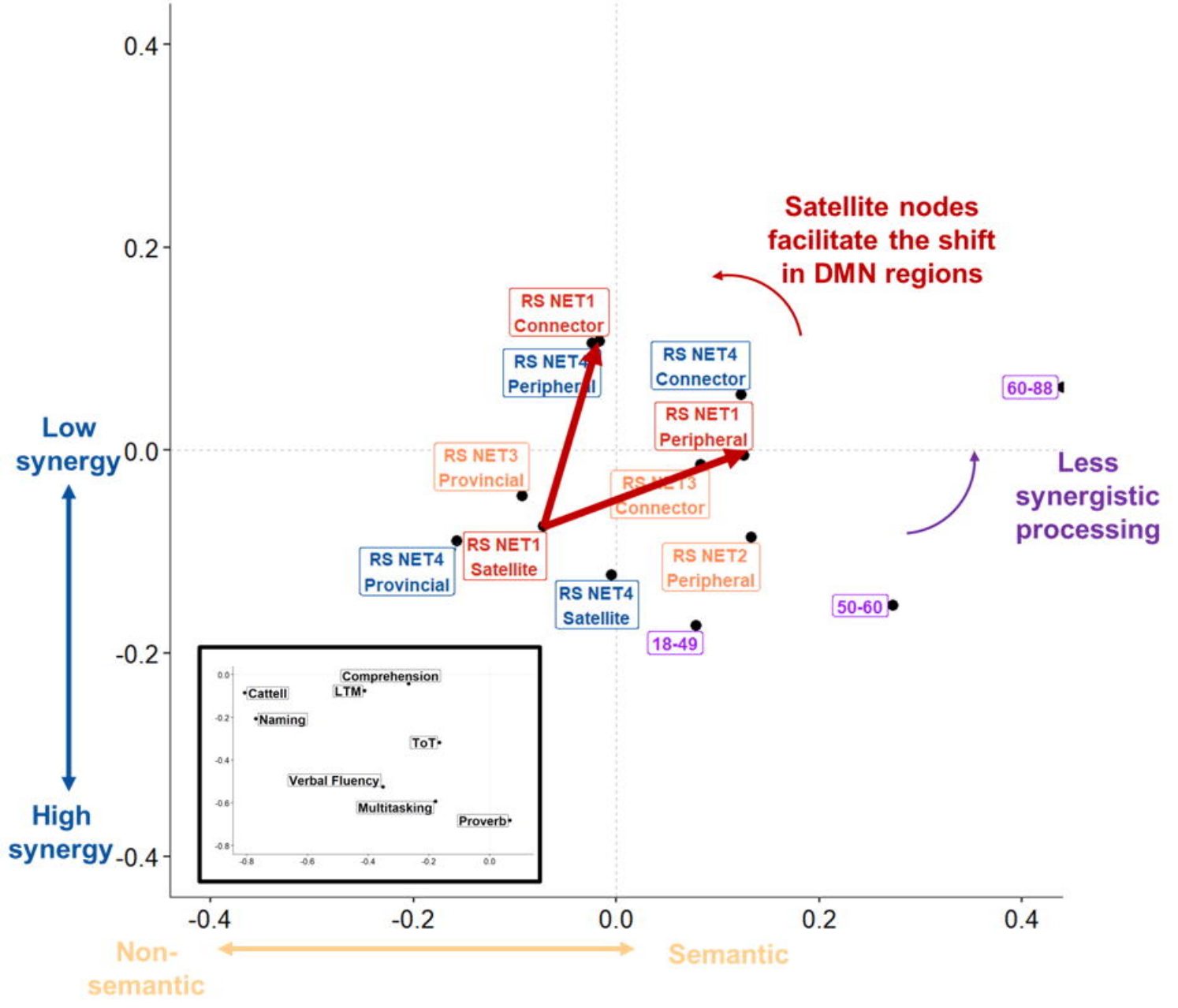

Graph analysis
Probabilistic analysis
Compositional analysis
(N = 613)
Cognitive data
Canonical correlation analysis (CCA)
Brain-cognition analysis
informs
(N = 628)
Step 2
Step 1
Step 3
CamCAN rs-fMRI data
Structure equation modeling (SEM)
Analytical pipeline
Step 4

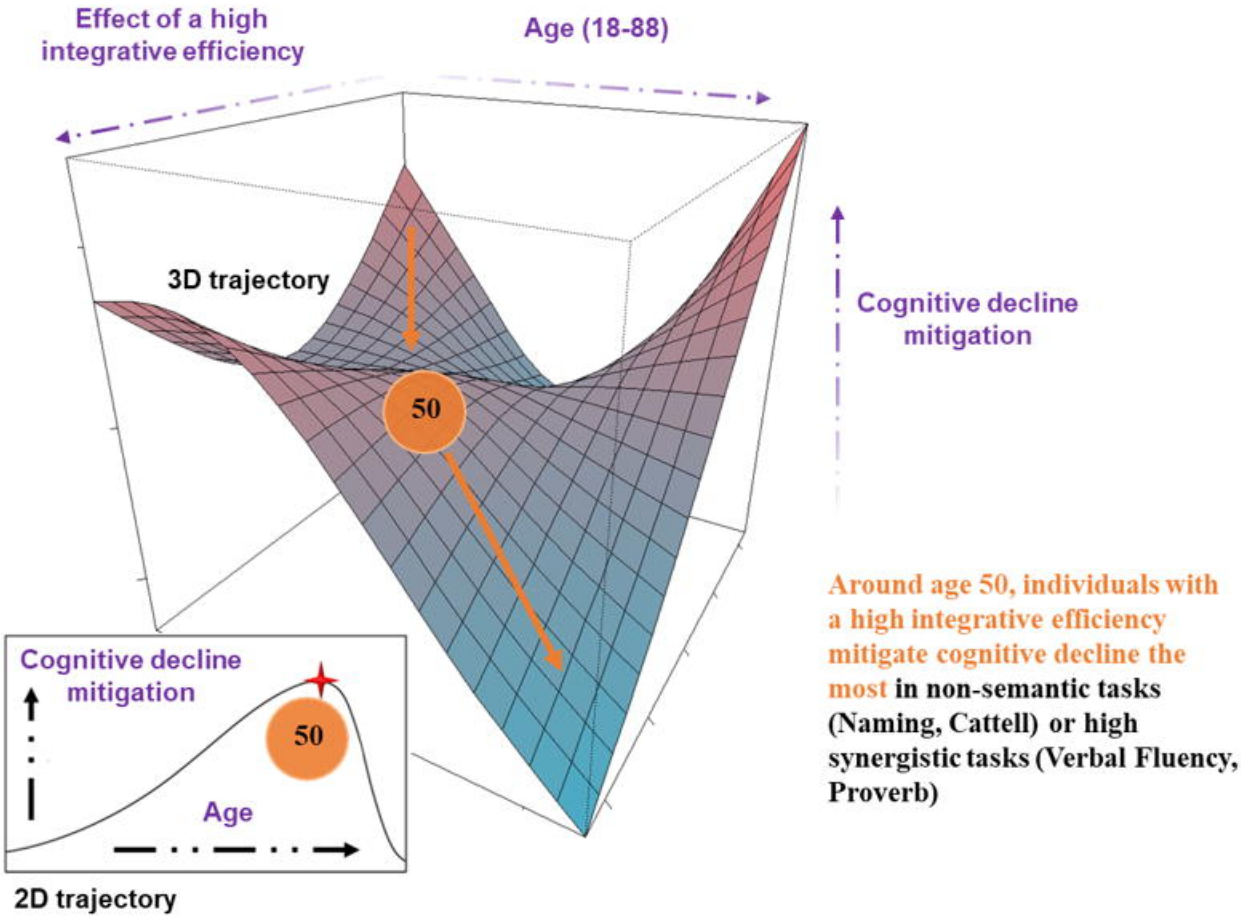

DMN
PMM
SMN
Visual_2
Visual_1
DAN
FPN
CON
Language
80
60
40
20
RS Net1
RS Net2
RS Net3
RS Net4

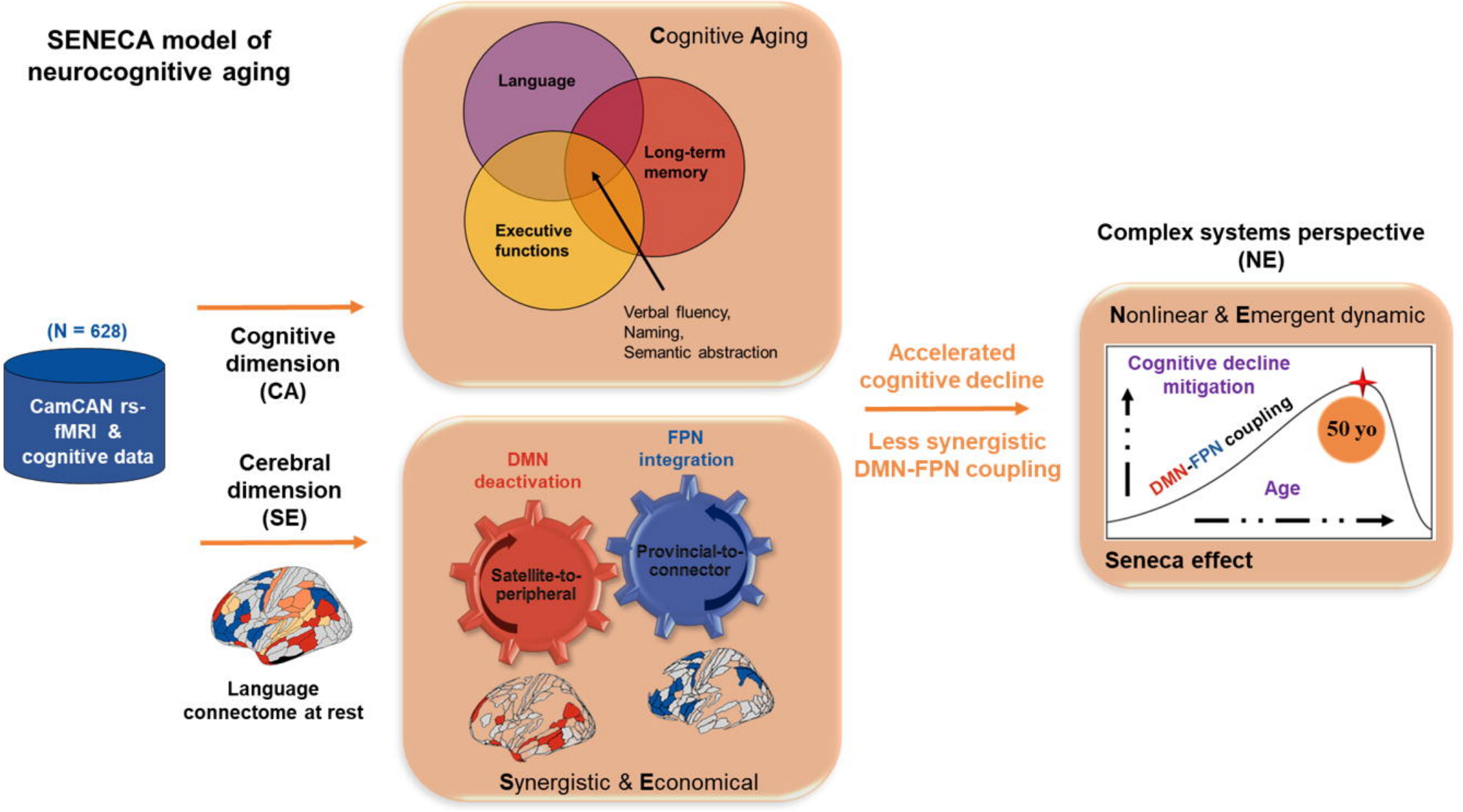

A
Evolution of the balance between global and local efficiency
Normalized efficiencies
Eloc
Balance
Eglob
Age
B
Evolution of the proportion of topological roles (system-level)
ilr-coordinates (z-scored)
Provincial
Connector
Satellite
Peripheral
Age
C
Evolution of the proportion of topological roles (subsystem-level)
RS NET1
RS NET2
RS NET4
ilr-coordinates (z-scored)
Peripheral
Connector
Satellite
Provincial
Connector
Peripheral
Provincial
Connector
Peripheral
Satellite
Age
Age
Age


Synergistic strategy
Satellite-to-peripheral
Provincial-to-connector
Inter-links
Module A
Module B
Lifespan
DMN-FPN coupling in younger adults
Shift in DMN regions around age 50
Provincial-to-peripheral
Mainly in older adults
Efficient in SMN & CON regions only
Satellite-to-connector
Intra-links
Module A
Intra-modular strategy
Reduced segregation
Compensatory integration


A
Cognitive map of language-related performances
Low synergy
High synergy
Comprehension
LTM
Cattell
Naming
ToT
Verbal Fluency
Multitasking
Proverb
Variate I
Variate II
Non-semantic
Semantic
B
Age-related dynamic of the cognitive map
Variate I
(Naming, Verbal Fluency, Cattell, Multitasking, Proverb)
Non-semantic tasks
(Cattell, Naming)
Synergistic tasks
(Proverb, Multitasking, Verbal Fluency)
Shift in cognitive functioning
Cognitive performance
Age
C
Age-related cognitive performances
Normalized score
Cattell
LTM
Proverb
Sentence Comp
Multitasking
Naming
Tip-of-the-tongue
Verbal Fluency


Satellite nodes facilitate the shift in DMN regions
RS NET1 Connector
RS NET4 Peripheral
RS NET4 Connector
RS NET1 Peripheral
RS NET3 Provincial
RS NET3 Connector
RS NET1 Satellite
RS NET4 Provincial
RS NET4 Satellite
RS NET2 Peripheral
60-88
50-60
18-49
Less synergistic processing
Low synergy
High synergy
Non-semantic
Semantic
0.4
0.2
0.0
-0.2
-0.4
Comprehension
Cattell
LTM
Naming
ToT
Verbal Fluency
Multitasking
Proverb


Effect of a high integrative efficiency
Age (18-88)
3D trajectory
50
Cognitive decline mitigation
Cognitive decline mitigation
50
Age
2D trajectory
Around age 50, individuals with a high integrative efficiency mitigate cognitive decline the most in non-semantic tasks (Naming, Cattell) or high synergistic tasks (Verbal Fluency, Proverb)


SENECA model of neurocognitive aging
(N = 628)
CamCAN rs-fMRI & cognitive data
Cognitive dimension (CA)
Cerebral dimension (SE)
Language connectome at rest
Cognitive Aging
Language
Long-term memory
Executive functions
Verbal fluency, Naming, Semantic abstraction
DMN deactivation
FPN integration
Satellite-to-peripheral
Provincial-to-connector
Synergistic & Economical
Accelerated cognitive decline
Less synergistic DMN-FPN coupling
Complex systems perspective (NE)
Nonlinear & Emergent dynamic
Cognitive decline mitigation
DMN-FPN coupling
50 yo
Age
Seneca effect

Cognitive Task	**Processes involved** (from high to low amount of inter-cognitive synergy)
Verbal Fluency (Lezak et al., 2012)	Language (phonological, semantic) & Executive function (EF)
Hotel task (Shallice & Burgess, 1991)	EF (planning & multitasking)
Proverb comprehension (Huppert et al., 1994)	EF (abstraction) & Language (comprehension)
Naming (Clarke et al., 2013)	Language (phonological access & semantic memory)
Tip-of-the-tongue (Brown & McNeill, 1966)	Language (retrieval) & EF (error monitoring)
Cattell task (Cattell & Cattell, 1960)	EF (Fluid intelligence)
Story recall (Tulsky et al., 2003)	Long-term memory
Sentence comprehension (Rodd et al., 2010)	Language (syntactic, semantic)

Table 1. Presentation of the eight cognitive tasks considered in this study. A detailed description of the tasks can be found in Table S1, Appendix S2

Cognitive variables	*Goodness-of-fit of Age as a predictor (Deviance explained in %)*
Cattell	42.9
Naming	41.4
LTM	14.8
Verbal Fluency	14.1
Tip-of-the-tongue	13
Multitasking	8.75
Sentence Comprehension	6.02
Proverb	3.74

Table 2. Estimates from generalized additive models (GAMs): Cognitive variable ~ s(Age). All models are significant at $p < .001$ '***'. Deviance explained is used as a proxy for the amount of age-related cognitive decline