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Neurofunctional Reorganization to Support Semantic Processing during Aging:

An fMRI Study

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Abstract

Language overall is well preserved in aging (Meyer & Federmeier, 2010) whereas semantic memory may even improve (Kavé, Samuel-Enoch, & Adiv, 2009; Prinz, Bucher, & Marder, 2004; Salthouse, 2009; Verhaegen & Poncelet, 2013; Wingfield & Grossman, 2006), despite numerous neurophysiological changes taking place in the brain (Grady, Springer, Hongwanishkul, McIntosh, & Winocur, 2006; Kemper & Anagnopoulos, 1989; Wingfield & Grossman, 2006). The present study focuses on the preservation of semantic memory in aging, the 'cognitive act of accessing stored knowledge about the world' (Binder, Desai, Graves, & Conant, 2009) by means of a semantic judgment task manipulating semantic control with two demand levels (low and high) and two types of semantic relations (taxonomic-thematic). We used a novel task that varied task demands (low versus high) in 39 younger and 39 older adults. More specifically, the aims of this study was 1) to identify whether aging affects the brain activity subserving semantic memory in accordance with the CRUNCH predictions, through a semantic judgment task with two levels of demands (low and high). 2) To bridge the gap in the literature on the existence and evolution of semantic hubs in aging, in light of the dual and single-hub theories, by evaluating the effect of aging on the role of the Anterior Temporal Lobes (ATLs) and the Temporo-parietal junction (TPJ) as neural representations of the semantic hubs responsible for taxonomic and thematic processing, respectively. A submission by registered report was opted for this research project. Our participants, younger and older adults, were overall matched in regards to level of education and as shown in questionnaires assessing engagement in cognitively stimulating activities, MoCA and WAIS-III tests. The behavioral results confirmed that the task was successful in manipulating task difficulty, with error rates and RTs increasing with increasing task demands, namely in the high-demand condition. We found that engaging in cognitively stimulating activities impacted positively on both baseline RTs and accuracy and that higher scores on the WAIS-III and the PPTT tests were positively correlated with accuracy in older adults. There was no statistical difference in accuracy between younger and older participants regardless of the condition, so there was no age effect in accuracy. In terms of RTs, there was a statistically significant difference between younger and older participants for both the task and the baseline conditions, with older adults being slower to

respond in general. RTs increased the more the participant's age increased, which is in line with findings in the literature. As such, the semantic memory task was successful in a) manipulating task difficulty across two levels of demands and b) demonstrating age-invariant behavioural performance for the older group, as requires to test the CRUNCH model (Fabiani, 2012; Schneider-Garces et al., 2010). For objective no 1, the crucial test of CRUNCH model, the fMRI age group by task demand interaction was not found. We did not find statistically significant interaction neither between task demands and age group for RTs or accuracy, nor in regards to brain activation. At the neural level, independently of age, the semantic similarity judgment task activated a large network including bilateral inferior frontal, parietal, supplementary motor, temporal and occipital brain regions, which correspond overall with the semantic network, as suggested in the literature. Region of interest analyses demonstrated task demand effect in these regions, most notably in the left and right inferior frontal gyrus, the left posterior middle temporal gyrus, the posterior inferior temporal gyrus and the pre-frontal gyrus, regions which are typically associated with semantic control requirements. We did not find any significant interactions between task demands and activation in the regions of interest either. Several possible reasons may justify the lack of findings as predicted by the CRUNCH hypothesis. For objective no 2 in regards to the semantic relation effect, the contrast of the taxonomic with the thematic condition directly did not produce any robust activation at a corrected threshold. The taxonomic condition yielded interesting results when contrasted with the baseline one. Seven distinct clusters in the fronto-temporo-parietal cortex were activated across the two hemispheres, including the anterior temporal lobes (ATLs) and the left temporo-parietal junction (TPJ). Additionally, activation was significant in the left frontal syperior gyrus, the left angular gyrus (AG) and the inferior frontal gyrus (orbital part) on the right hemisphere. This finding could be partly in line with the dual-hub theory, that proposes that the ATLs bilaterally and the TPJ act as semantic hubs. Though we did not find the expected double dissociation e.g., significant activation in the ATLs during the taxonomic condition only and in the TPJ during the thematic condition only, we found however that in the taxonomic condition among the seven significantly activated clusters, activation in the left superior frontal gyrus was significantly correlated with performance in both age groups. Activation in the right middle temporal gyrus was also correlated with improved performance, but this was not significant in the

older group. During the thematic condition, when contrasted with baseline, ten distinct clusters were activated, including the temporo-parietal junction (TPJ), whereas the ATLs were not robustly activated during the thematic condition. We aim to pursue additional analyses to explore the relation between task demands, type of semantic relation and age-related neurofunctional reorganization. However, these results in relation to the preservation with age of the abiliites to process the different semantic word relations is associated with a number of neurofunctional reorganizations. These can be specific to the processing of different semantic relations and different task demands. Whether this reorganization is induced by the structural changes in the brain with age, or by the enhanced use of such semantic relations along the trajectory of life is still under exploration.

Keywords: aging, semantic memory, task demands, CRUNCH, semantic hub, taxonomic, thematic, Anterior Temporal Lobes

Résumé

Le langage est dans son ensemble bien préservé pendant le vieillissement (Meyer & Federmeier, 2010) tandis que la mémoire sémantique peut même s'améliorer (Kavé, Samuel-Enoch, & Adiv, 2009; Prinz, Bucher, & Marder, 2004; Salthouse, 2009; Verhaegen & Poncelet, 2013 ; Wingfield & Grossman, 2006), malgré de nombreux changements neurophysiologiques se produisant dans le cerveau (Grady, Springer, Hongwanishkul, McIntosh, & Winocur, 2006 ; Kemper & Anagnopoulos, 1989 ; Wingfield & Grossman, 2006). Cette thèse se concentre sur la préservation de la mémoire sémantique dans le vieillissement, « l'acte cognitif d'accéder aux connaissances stockées sur le monde » (Binder, Desai, Graves et Conant, 2009) à travers une tâche de jugement sémantique manipulant le contrôle sémantique avec deux niveaux de demande (faible et élevé) et deux types de relations sémantiques (taxonomique et thématique). Nous avons développé une nouvelle tâche variant les niveaux de demande (faible et élevé) chez 39 adultes jeunes et 39 adultes âgés. Plus précisément, les objectifs de notre étude étaient 1) d'identifier si le vieillissement affecte l'activité cérébrale liée à la mémoire sémantique conformément aux prédictions du modèle CRUNCH, à travers une tâche de jugement sémantique à deux niveaux d'exigences. 2) de combler le vide de la littérature sur l'existence et l'évolution des hubs sémantiques dans le vieillissement, à la lumière des théories single hub et dual-hub, en évaluant l'effet du vieillissement sur le rôle des lobes temporaux antérieurs (ATL) et du jonction temporo-pariétale (TPJ) en tant que représentations neuronales des centres sémantiques responsables respectivement du traitement taxonomique et thématique. Une soumission par rapport pré-enregistré (registered report) a été utilisée pour ce projet de recherche. Nos participants, adultes plus jeunes et plus âgés, étaient globalement appariés en termes de réserve cognitive, plus précisément en ce qui concerne le niveau d'éducation et comme le montrent les questionnaires évaluant l'engagement dans des activités cognitivement stimulantes, les tests MoCA et WAIS-III. Les résultats comportementaux

ont confirmé que la tâche varie correctement la difficulté de la tâche puisque les taux d'erreur et les temps de réponse (RT) augmentent de manière linéaire avec l'augmentation des exigences de la tâche, à savoir dans la condition de forte demande. Nous avons constaté que la participation à des activités stimulantes sur le plan cognitif avait un impact positif à la fois sur les RT de référence et sur la précision. Nous n’avons pas observé de différence statistiquement significative dans la précision entre les participants jeunes et plus âgés, quelle que soit la condition. Nous avons constaté que des scores plus élevés aux tests WAIS-III et PPTT étaient positivement corrélés avec la précision chez les personnes âgées. En termes de RT, nous avons observé une différence statistiquement significative entre les participants jeunes et plus âgés pour la tâche et les conditions de référence, les adultes plus âgés étant plus lents à répondre en général. Les RT augmentent linéairement avec l'âge du participant. En tant que telle, la tâche de mémoire sémantique a réussi à a) manipuler la difficulté de la tâche sur deux niveaux d'exigences et b) démontrer une performance comportementale invariante selon l'âge pour le groupe plus âgé, comme l'exige le test du modèle CRUNCH (Fabiani, 2012 ; Schneider-Garces et al., 2010). Pour l'objectif n°1, les tests cruciaux du modèle CRUNCH, l'interaction IRMf groupe par difficulté, n'étaient pas cohérents avec les prédictions du modèle. Malgré nos résultats comportementaux, lorsque nous avons comparé directement la condition de faible demande avec la condition de forte demande, il n'y avait pas de différence statistiquement significative dans l'activation entre les conditions de faible et de forte demande. Nous n'avons pas non plus obtenu d'interaction entre tranche d'âge et difficulté. Nous avons obtenu des interactions significatives en comparant les conditions de demande faible et élevée avec la ligne de référence. Au niveau neuronal, indépendamment de l'âge, la tâche de jugement de similarité sémantique a activé un large réseau bilatéral fronto-temporo-pariétal. Pour l'objectif n°2 concernant l'effet de relation sémantique, le contraste de la condition taxonomique avec la condition thématique directement n'a pas trouvé d'activation robuste à un seuil corrigé. La condition taxonomique a donné des résultats intéressants par rapport à la condition de base. Sept groupes distincts dans le cortex fronto-temporo-pariétal ont été activés dans les deux hémisphères, y compris les lobes temporaux antérieurs (ATL) et la jonction temporo-pariétale gauche (TPJ). De plus, l'activation était significative dans le gyrus supérieur frontal gauche, le gyrus angulaire gauche (AG) et le gyrus

frontal inférieur (partie orbitale) sur l'hémisphère droit. Cette découverte pourrait être en partie conforme à la théorie du double-hub, qui propose que les ATL bilatéralement et le TPJ agissent comme des hubs sémantiques. Bien que nous n'ayons pas trouvé d'activation significative dans les ATL pendant la condition taxonomique et dans le TPJ pendant la condition thématique, nous avons cependant constaté que dans la condition taxonomique parmi les sept clusters significativement activés, l'activation dans le gyrus frontal supérieur gauche était significativement corrélée avec la performance dans la condition taxonomique pour les deux groupes d'âge. L'activation dans le gyrus temporal moyen droit était également corrélée à l'amélioration des performances, mais cela n'était pas significatif dans le groupe plus âgé. En ce qui concerne la condition thématique, par contraste avec condition de référence, dix groupes distincts ont été activés, y compris la jonction temporo-pariétale (TPJ), alors que les ATL n'ont pas été activés de manière robuste pendant la condition thématique. Plus précisément, les régions activées comprenaient bilatéralement le gyrus angulaire, le gyrus temporal moyen, le gyrus frontal inférieur (partie triangulaire) et le gyrus frontal moyen. Nous visons à poursuivre des analyses supplémentaires pour explorer la relation entre les exigences de la tâche, le type de relation sémantique et la réorganisation neurofonctionnelle liée à l'âge. Cependant, ces résultats relatifs à la préservation avec l'âge des capacités à traiter les différentes relations sémantiques de mots sont associés à un certain nombre de réorganisations neurofonctionnelles. Celles-ci peuvent être spécifiques au traitement de différentes relations sémantiques et de différentes demandes de tâches. Il reste à déterminer si cette réorganisation est induite par les changements structurels du cerveau avec l'âge, ou par l'utilisation accrue de telles relations sémantiques tout au long de la trajectoire de la vie.

Mots-clés : vieillissement, mémoire sémantique, exigences de tâches, CRUNCH, hub sémantique, taxonomique, thématique, Lobes temporaux antérieurs

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Liste of abbreviations

AG: Angular Gyrus

ANOVA: ANalysis Of Variance

ATLs: Anterior Temporal Lobes

BA: Brodmann Area

BET: Brain Extraction Tool

BOLD: Blood Oxygen Level Dependent

CRUNCH: Compensation-Related Utilization of Neural Circuits Hypothesis

dACC: Dorsal Anterior Cingulate

DLPFC: DorsoLateral PreFrontal Cortex

DMN: Default Mode Network

ET: Echo Time

fMRI: functional Magnetic Resonance Imaging

FOV: Field of View

FWHM: Full Width at Half Maximum

GLM: General Linear Model

HAROLD: Hemispheric Asymmetry Reduction in OLDer adults

HRF: Hemodynamic Response Function

IFG: Inferior Frontal Gyrus

IFS: Inferior Frontal Sulcus

IPS: Intra-Parietal Sulcus

LOC: Lateral Occipital Cortex

MFG: Middle Frontal Gyrus

MNI: Montréal Neurological Institute

MoCA: Montreal Cognitive Assessment

MRI: Magnetic Resonance Imaging

PASA: Posterior-Anterior Shift in Aging

PFC: Prefrontal Cortex

PFC: Prefrontal Cortex

pMTG: posterior Middle Temporal Gyrus

PPTT: Pyramids and Palm Trees Test

pre-SMA: pre-supplementary motor area

ROI: Region of Interest

RS: Resting State

RT: Response time

STAC: Scaffolding Theory of Aging and Cognition

TPJ: Temporo-Parietal Junction

VLPFC: VentroLateral Prefrontal Cortex

WAIS: Wechsler Adult Intelligence Scale

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Introduction

The world's population is aging, living longer and healthier lives thanks to improved quality of life and medical advances, but at the same time, age-related diseases such as dementia have also increased. It is estimated that by 2050 the world population over 60 will be 2 billion and that the total number of people living with dementia is currently 55 million (World Health Organization (WHO), 2017). In Canada, it is estimated that by 2030 the number of individuals over 65 will make up 23 percent of Canadians (Government of Canada, 2014), that as of 2016-7 there are 432,000 Canadians diagnosed with dementia and that the annual healthcare cost would arise to $16.6 billion by 2031 (PHAC, 2020). In 2012, the World Health Organization declared dementia a public health priority (WHO, 2012), focusing on its impact on individuals but also their families and caregivers, socially and economically. Like younger individuals, older adults, regardless of their health status, want to live meaningful lives and contribute positively to their families, social networks, and communities. There is more and more research, medical and political attention focusing on healthy aging, prevention of cognitive decline and preservation of cognitive abilities, including communication skills.

The current research project was meant to describe the age-related neurofunctional reorganization phenomena. More specifically, how inter- or intra-hemispheric brain activations increase or decrease to maintain performance during a task of semantic processing, which is thought to minimally require other cognitive skills such as attention and memory. Forty older adults (60-75 years old) are compared with forty younger adults (20-35 years old) while they perform a task of semantic similarity judgment (deciding which of the two words is more related to a third word), in the MRI scanner. The word triads are designed to compare taxonomic versus functional semantic relations while the semantic distance of the triads is manipulated (close vs. distant), to reflect task demands. The results will allow to better understand how neurofunctional reorganization phenomena reported for older adults in numerous cognitive domains are applicable to the semantic processing of words, an ability usually well preserved.

Examining the interplay of brain activation differences provoked by both age-related neurofunctional reorganization and semantic processing itself between younger and older participants will help understand both the quantitative aspect of differential processing for different task demands (low-high) and the qualitative aspect of differential processing for different types of semantic relations (taxonomic-thematic). Three articles are proposed to contribute to the question above. The first article provides an overview of functional reorganization phenomena reported in the literature, and serves as a background of existing knowledge. The second article is a registered report protocol (https://www.cos.io/initiatives/registered-reports) and as such, focuses on the methodology for testing our hypotheses. A submission by Registered Report is a relatively recent type of publication. It was selected as it aims to address publication biases by focusing more on the methodology before data are collected, rather the results obtained (Chambers, 2013; Chambers, Feredoes, Muthukumaraswamy, & Etchells, 2014). As such, an initial manuscript was submitted, peer reviewed and published prior to data collection, named as Registered Report Protocol. This focused on introduction, hypotheses, experimental procedures, analyses and statistical power analysis. It aimed to test the Compensation-Related Utilisation of *Neural* Circuits Hypothesis (CRUNCH) model, which was chosen as it emphasizes the importance of task demands as a factor in age-related reorganization. The article 2 thus describes the methodology *proposed* of examining how two levels of semantic task demands (low-high) impact performance and neurofunctional activation in younger and older adults. The third article is the registered report which details the methodology that was followed, as well as the results, refering additionally to any deviations that took place from the protocol. The fourth article focuses on the study of different types of semantic relations (taxonomic-thematic) by younger and older adults, and the existence of semantic hubs, as suggested in the literature, using the same participants and the same methodology as the one described in articles 2 and 3.

Understanding how the brain reorganizes and adapts to aging through a task of semantic processing of words can provide knowledge for the early recognition, preservation and rehabilitation of semantic memory in older adults, knowledge that can further be applied to other cognitive skills as well. Preserved semantic memory can further contribute to maintaining quality of life and social interactions, a factor known to favor healthy aging.

Chapter 1 – Literature review

The current research project literature review is separated in three parts. The first part focuses on neurofunctional reorganisation in aging. It describes several neurofunctional reorganization phenomena, possible explanations that have been expressed to justify reorganisation in aging, brain regions that are particularly concerned and finally, factors that affect aging, cognititive performance and neurofunctional reorganisation. The second part looks at semantic processing as a cognitive function that uses semantic memory, aiming to describe how words are organised, accessed and processed in our brain, hemispheric activation asymmetries related to semantic processing of words and finally, factors and word features that affect performance and activation in tasks of semantic processing. The third part looks at semantic processing during aging, research findings and factors that affect performance of older adults in semantic processing tasks. The review closes with a summary of the problem refering to existing gaps in current research and the objective of this study, which is to better understand the interplay of neurofunctional reorganization and semantic processing of different types of semantic relations and of different semantic distance in aging.

Neurofunctional reorganization in aging

Aging and neurofunctional reorganization phenomena

Several neuroscientific proposals have attempted to describe and explain how the brain is affected by aging, as well as how the brain dynamically re-organises itself to maintain optimal cognitive abilities. Probably the most impressive element in an optimally-performing aging brain is that despite numerous biological and structural changes taking place, behavioral performance can be sustained (Grady, Springer, Hongwanishkul, McIntosh, & Winocur, 2006; Prinz, Bucher, & Marder, 2004). Huge variability however exists among older individuals regarding maintenance of cognitive abilities, with the exact reasons or mechanisms not yet being clear (Park & Reuter-

Lorenz, 2009). Memory and attention are more affected than other cognitive domains for example (Salthouse, 2004; Schaie & Willis, 1993; Valdois, Joanette, Poissant, Ska, & Dehaut, 1990). In comparison to younger individuals, aging provokes complex changes to brain activity which can be reduced or increased (Grady, 2012). Underactivation can be seen in the hippocampus which is associated with memory (Nadel, Samsonovich, Ryan, & Moscovitch, 2000) whereas overactivation can be seen in the prefrontal cortex (PFC), which is typically considered to be key for executive functions (Grady, 2008). Language skills on the other hand, remain largely intact or can even improve during aging (Wingfield & Grossman, 2006). Modern neuroimaging techniques such as fMRI provide the necessary insight on how the brain neurofunctionally activates, adapts and re-organises across ages, tasks, and individuals to maintain its cognitive capabilities, including communication (Cabeza et al., 1997; Grady et al., 1994).

One of the first descriptions of different neurofunctional reorganization between younger and older adults referred to the HERA (Hemispheric Encoding/Retrieval Asymmetry) phenomenon (Nyberg, Cabeza, & Tulving, 1996). The HERA asymmetry seen in younger, manifested through left PFC lateralization during encoding of episodic memory and right PFC lateralization during retrieval of episodic memory (Nyberg et al., 1996; Tulving, Kapur, Craik, Moscovitch, & Houle, 1994), was not confirmed for older adults. The latter demonstrated little PFC activity during encoding and more bilateral PFC activation during retrieval in a verbal task of encoding and recalling word pairs (Cabeza et al., 1997). This finding would indicate that older age is associated with neural changes in brain activation during encoding, retrieval and other memory functions (Cabeza et al., 1997). Both increasing and decreasing regional activation related to memory function seen in the older as compared to younger adults could be attributed to age-related less efficient processing (Grady et al., 1994; Madden et al., 1996). However, it could also be attributed to functional compensation, in the sense that to counteract neurocognitive deficits, older adults recruit both hemispheres for a task that would require only one hemisphere in younger adults (Cabeza, 2002; Grady et al., 1994).

Another approach describing neurofunctional reorganization in aging was captured by the HAROLD (Hemispheric Asymmetry Reduction in Older adults) phenomenon. The HAROLD phenomenon refers to a hemispheric asymmetry reduction or else, a neurofunctional reorganization across the two hemispheres and specifically the PFC of older adults with the objective of maintaining high performance (Cabeza, 2002). To reduce the asymmetry, brain activation can increase and/or decrease in certain brain areas by recruiting additional and alternative neuronal circuits from the contralateral hemisphere. The resulting asymmetry reduction was found to optimize performance, whereas older adults who maintained a unilateral or asymmetrical activation pattern similar to the younger, did not perform as well (Cabeza, 2002). The HAROLD phenomenon was observed in numerous cognitive tasks, including episodic memory retrieval, episodic encoding/semantic retrieval, working memory, perception and inhibitory control (Cabeza, 2002). HAROLD was considered to be a general aging phenomenon regardless of the cognitive task (Cabeza, 2002; Cabeza, Anderson, Locantore, & McIntosh, 2002).

Though a popular pattern of reorganization in the literature of cognitive aging, the HAROLD proposition has also received critiques. Several studies have not confirmed the HAROLD phenomenon in a consistent manner (Berlingeri, Danelli, Bottini, Sberna, & Paulesu, 2013; Manenti, Cotelli, & Miniussi, 2011; Nenert et al., 2017; Rossi et al., 2004) whereas some have even found the opposite effect (Duverne, Motamedinia, & Rugg, 2009). The fact that HAROLD focuses mainly on the PFC has been questioned, as the PFC is typically activated during executive functions, and while it reduces in size during aging, at the same time it presents the biggest task-related activations (Greenwood, 2007). An important critique of HAROLD lies on the circularity of the proposed model, as the memory tasks used to test it typically depend on the PFC, making it therefore difficult to test the model on the entire brain (Berlingeri et al., 2013). The authors criticized that the model lacks robust statistical evidence for functional asymmetry by using for example laterality indices. They conducted a study comparing younger vs. older adults on various tasks to examine if a ‘genuine HAROLD effect’ would be produced, that is, a reduction in the regional functional lateralisation due to a bilateral activation. The methodology used Statistical Lateralization Maps (SLMs) which can help create an anatomical map representing brain regions that are significantly lateralised at a certain statistical threshold (Jansen et al., 2006). Following a voxel-by-voxel statistical evaluation of activation, their findings did not confirm the HAROLD phenomenon as a general aging phenomenon applicable for cognitive tasks in general, but more as a special manifestation of age-related compensatory processes triggered by specific task demands (Berlingeri et al., 2013).

An additional pattern of neurofunctional reorganization focusing on lateralization has been reported to occur within only one hemisphere, or else, intrahemispherically. The PASA (Posterior Anterior Shift in Aging) phenomenon provides a picture of such type of reorganization (Dennis & Cabeza, 2008), describing an age-related shifting of activation from the occipitotemporal to the frontal cortex (Davis, Dennis, Daselaar, Fleck, & Cabeza, 2008; Grady et al., 1994). PASA, originally reported in a PET study (Grady et al., 1994), was confirmed for numerous studies and cognitive tasks including perception, visual attention, verbal working memory, problem solving and verbal episodic retrieval (Davis et al., 2008; Dennis & Cabeza, 2008). In a static functional connectivity of the resting brain study using an episodic memory task, the opposite effect was found, meaning an anterior to posterior shift, confirming the PASA phenomenon (Zhang, Lee, & Qiu, 2017). Other functional connectivity studies on working memory have also confirmed findings that are in line with the PASA phenomenon (Madden et al., 2010; Nagel et al., 2011). PASA is considered to reflect a general age-related compensation of sensory processing deficits by decreasing activation in occipitotemporal regions and increasing activation in frontal regions, rather than reflect task difficulty (Davis et al., 2008), often associated with increased PFC activations regardless of age (Braver et al., 2001; Grady et al., 1998; Konishi, Jimura, Asari, & Miyashita, 2003). The PASA phenomenon could thus indicate the adoption of alternative cognitive strategies to cope with aging-related neural deficiencies.

An alternative, probably more general and complementary explanation was proposed as an alternative to describe neurofunctional reorganization during aging. The CRUNCH (Compensation Related Utilization of Neural Circuits Hypothesis) proposal considers age-related neurofunctional reorganization as a positive evolution, a continuous variable that concerns both younger and older adults; the defining element for neurofunctional reorganization is not age but task complexity and demands, resulting in increased or reduced activation of brain regions (Reuter-Lorenz & Cappell, 2008). If the CRUNCH hypothesis is true, then it is expected that if the task is equally difficult for younger and older adults, then their brain activations should also be equal (Schneider-Garces et al., 2010). Several authors have referred to the two-pole of age vs. task difficulty to account for functional reorganization (Davis et al., 2008). CRUNCH suggests that older adults would demonstrate increased neural recruitment of regions that would require lower brain activity in younger adults, as seen in the PFC and the parietal cortex in episodic memory (Spaniol & Grady, 2012) and in working memory tasks (Mattay et al., 2006; Reuter-Lorenz & Cappell, 2008). Overactivation is proposed to be observed in areas where additional resources are required to meet task demands, whereas underactivation would be seen in areas of ‘redundant’ tasks from where resources migrate towards other more urgent task requirements (e.g., for the default network, discussed below) (Reuter-Lorenz & Cappell, 2008). Both younger and older adults would benefit from increased bilateral neural recruitment because it would improve the brain’s ability to meet complex processing demands. The difference is that older adults would use this advantage at lower levels of task complexity (Reuter-Lorenz, Stanczak, & Miller, 1999), gradually and continuously recruiting additional resources until a resource threshold is reached and processing becomes insufficient (Reuter-Lorenz & Cappell, 2008). The CRUNCH hypothesis emphasizes the flexibility and adaptability of the brain, notably the aging brain, to resolve cognitive complexity. It is not clear however if the observed increased activation is really compensatory or if it reflects inter-individual differences in responding to cognitive loads (Grady, 2012).

The neurofunctional reorganization proposals discussed above seem to be exclusive of another; their tendency to focus and attribute meaningfulness in increased or decreased activation in isolated brain regions makes it difficult to select a model that could fully describe and explain age-related neurofunctional reorganization (Sala-Llonch, Bartrés-Faz, & Junqué, 2015). They could however not be necessarily exclusive but complementary to each other. Recent studies tend to combine data on functional, structural and lifetime environmental factors to explain reorganization in a more integrative manner. In this direction, the STAC (Scaffolding Theory on Aging and Cognition) hypothesis aims to be more comprehensive and proposes that aging is no longer characterized by uncontrollable decline of cognitive abilities because the brain inherently develops its own resilience, repairs its deficiencies and protects its functions (Park & Reuter-Lorenz, 2009; Reuter-Lorenz & Cappell, 2008). Accordingly, reorganisation is a normal function, observed not only in aging population but also in brain-damaged patients (Cabeza et al., 1997). Such a neurofunctional reorganization in engaging additional neural resources would provide a means to preserve cognitive abilities, despite age-related structural and functional decline (Park & Reuter-Lorenz, 2009). A study on functional connectivity and hubs- brain areas densely connected with other ones provided evidence for a compensatory reorganization in aging supporting the STAC model (Zhang et al., 2017). Although both inter- and intra-hemispheric activation patterns are observed in older adults, it is believed that interhemispheric reorganization is more successful than the intrahemispheric one because it involves the recruitment of alternative networks (Cabeza et al., 2002).

Whether reorganisation is intra or inter-hemispheric or whether it increases or decreases, the brain appears to be flexible and unpredictable in adopting multiple reorganization pattern depending on required processing demands (Ansado, Marsolais, Methqal, Alary, & Joanette, 2013; Zhang et al., 2017). Functional reorganization could therefore take the form of both inter- and intra-hemispheric changes in activation and manifest as both increased and decreased activation of specific regions, both of functional significance (Grady et al., 2006; Persson, Lustig, Nelson, & Reuter-Lorenz, 2007). More recently, the STAC-r proposition extended the STAC hypothesis to include even more life-course parameters that could enhance, maintain or compromise brain capabilities, its capacity to compensate for its own decline as well as cognitive functions throughout lifetime (Reuter-Lorenz & Park, 2014). It appears that the more adaptable and the more dynamic the brain is in adapting its own activation to the required task and given its own condition, the better it would maintain its cognitive abilities (Turner & Spreng, 2015).

Possible explanations for neurofunctional reorganization in aging

Several efforts are being made to understand why brain activation changes with age. A most positive explanation is the compensatory hypothesis, in line with the resources (Craik, 1986) and speed views (Salthouse, Hancock, Meinz, & Hambrick, 1996) and applicable to several of the neurofunctional reorganization propositions discussed above (Reuter-Lorenz & Lustig, 2005). Accordingly, the aging brain resources are no longer sufficient to maintain performance and therefore the brain needs to recruit additional resources from the same or the contralateral hemisphere to compensate for its own neural decline, demonstrated as increased activation or overactivation (Cabeza et al., 2002). To make a strong case for its compensatory role, overactivation would need to be present only in older but not in younger adults and would need to be accompanied with improved or maintained performance only in the older but not in the younger adults (Grady, 2008). Evidence for a compensatory re-organization to age-related decline was provided from an 8-year longitudinal study where performance was stable but was accompanied by both increased and decreased activation (Beason-Held, Kraut, & Resnick, 2008). Compensatory increased activation can also be observed following unilateral brain damage through the engagement of the unaffected hemisphere (Cabeza et al., 2002). Despite the potential cost of selecting, recruiting, reallocating and integrating additional neural circuits to execute the task, the compensation benefits are thought to be bigger, making neuronal reorganization cost-efficient for performance (Banich, 1998). Younger adults could also benefit from overactivation when a task is cognitively demanding, however, to economize on resources, it would normally not be required (Cabeza, 2002).

The same phenomenon of age-related neurofunctional reorganization could also be viewed from a more negative side: according to the de-differentiation hypothesis, neurons age and lose their specialization they had acquired during childhood for optimal functioning, manifested as increased activation (Baltes & Lindenberger, 1997; Jiang, Petok, Howard, & Howard, 2017). Bilateral overactivation would thus be the result of random and non-selective recruitment of neurons in an attempt to meet processing demands (Cabeza, 2002). According to CRUNCH, overactivation would reflect a nonselective recruitment of disinhibited regions that the brain fails to control (Reuter-Lorenz & Lustig, 2005). In a recent study aiming to explain whether de-differentiation is a consequence of or compensation to cognitive decline, a novel technique was used to assess the sparseness of neuronal activations as an indirect measure of neuronal selectivity, but did not however confirm its compensatory function (Jiang et al., 2017). In either case, if the de-differentiation hypothesis is true, one would expect to see performance deteriorating. On the contrary however, it appears that the larger the re-organization, the better the performance (Reuter-Lorenz & Lustig, 2005). Overactivation could be the result of a combination of optimal and non-optimal brain restructuring, making the compensation and the de-differentiation hypotheses simultaneously possible and reflecting both age-related and age-unrelated factors (Koen & Rugg, 2019).

An additional explanation for age-related neurofunctional reorganisation is that aging selectively affects the default mode network. The default mode network is thought to be normally activated during a non-task state of monitoring the internal and external environment (Grady et al., 2006) and deactivated during cognitive activity so as to reallocate attention and resources towards such activities (Persson et al., 2007). When a cognitive task is demanding, deactivations would be smaller and slower for older adults, thus demonstrating less inhibition (Nyberg et al., 1996; Persson et al., 2007; Reuter-Lorenz & Cappell, 2008) and more distraction by task-irrelevant information, in line with the inhibitory control view (Zacks, 1989) and the cognitive theory of aging (Grady et al., 2006). Paradoxically, the PFC which is responsible for filtering out irrelevant information (Cabeza, 2002) presents also the largest overactivations (Grady et al., 2006; Reuter-Lorenz & Lustig, 2005). An age-related reduced efficiency of transferring attention away from resting areas towards task requirements is probably affecting the thin balance between default-mode and task-related activation, resulting in age-related reduced cognitive performance (Grady et al., 2006).

An alternative explanation for neurofunctional reorganization phenomena is the ‘cognitive reserve’ hypothesis, which attributes successful cognitive processing in aging to complex interactions between genetics, environmental influences on brain reserve and pathology, and the ability to actively compensate for the effects of pathology (Stern, 2009). Cognitive reserve depends on both neural reserve and neural compensation, a distinction reflecting inter-individual variability to use resources efficiently, flexibly or differently to perform a cognitive task and also, to deploy alternative strategies during a disruptive brain pathology (Cabeza et al., 2018). Accordingly, to cope with increased task complexity, the older adults could recruit the same regions as the younger ones (neural reserve) or could recruit alternative regions (neural compensation), and sometimes they could adopt both strategies in a flexible and adaptive manner (Ansado, Monchi, et al., 2013). Training, exercise (Stern et al., 2005), good cardiovascular health and low-calorie diet (Bruce-Keller, Umberger, McFall, & Mattson, 1999) are believed to protect cognitive reserve whereas conversely, sleep deprivation, neurological damage or genetic vulnerabilities may lower the cognitive reserve compromising performance (Reuter-Lorenz & Cappell, 2008).

Neurofunctional reorganization, manifested as both increased and decreased activation in different brain areas and during various cognitive tasks, is a complex phenomenon to interpret and predict, leading to antagonistic or complementary aging propositions (Ansado, Marsolais, et al., 2013). Several researchers have attempted to identify the 'common factor' (Salthouse, Atkinson, & Berish, 2003) in age-related brain activation patterns to explain reorganization phenomena. Cabeza (2002) considers that neurofunctional reorganization is more likely to be non-intentional and neuron-originated rather than a planned change of cognitive strategies, since it is manifested in simple tasks or following unilateral brain damage, over which one has little control. On the contrary, Reuter-Lorenz and Cappell (2008) consider unlikely that such a huge variability in brain activation stems from one 'common factor' or is due to age-related structural changes in the brain, because then it would be consistent across all tasks. Instead, aging seems to selectively affect specific regions, mainly default-mode regions and the dorsolateral PFC (Grady et al., 2006).

In summary, some inconsistencies are found in the interpretation of results, with both increased and decreased activation reported as the result of aging (Grady et al., 2006; Stern et al., 2005). Neurofunctional reorganization can take the form of both inter- and intra-hemispheric changes in activation and manifest as both increased and decreased activation of specific regions (Grady et al., 2006). When performance is non-optimal, decreased activation is interpreted as a manifestation of cognitive impairment, attributed to neural decline, deficient inhibitory control or de-differentiation (Reuter-Lorenz & Cappell, 2008); on the other hand, when performance is good, it is claimed to be compensatory. Most studies seem to agree on overactivation, interpreting it as compensatory and positive, whether it is understood as increased attention or as suppression of distracting elements (Raichle et al., 2001). Increased activation however is also found in Alzheimer's disease (AD) and mild cognitive impairment (MCI) patients, demonstrating either a potentially compensatory role or a progressive pathology predicting further decline (Persson et al., 2007; Reuter-Lorenz & Lustig, 2005). It has also been proposed that increased activation could simply reflect additional cognitive effort and not necessarily compensatory mechanisms (Berlingeri et al., 2013). It seems that neurofunctional reorganisation of the aging brain is more complex and further research is still required to be able to 'draw' a pattern of activation that integrates the existing findings in a comprehensive model.

Anatomy of neurofunctional reorganization phenomena

The neurofunctional reorganization phenomena discussed above refer to specific regions of the brain where activation patterns shift as a result of aging. One of the areas most often discussed in the aging neurofunctional reorganization literature refers to the PFC where activation is found to increase e.g. as a result of task difficulty (Braver et al., 2001; Grady et al., 1998; Konishi et al., 2003). The PFC is found to be of prime importance in neurofunctional reorganization studies because of its engagement in numerous higher-level cognitive operations (Cabeza, 2002) including memory function (Grady et al., 2006; Nyberg et al., 2003), semantic memory retrieval and semantic processing (various studies in (Cabeza et al., 1997) and inhibitory control (Cabeza, 2002). A thorough review on PFC functions is provided by (Cabeza & Nyberg, 2000). A the same time paradoxically, the PFC is where both age-related overactivation but also atrophy are more pronounced in the older adults (Ansado, Monchi, et al., 2013; Cabeza, 2004; Reuter-Lorenz &

Cappell, 2008). Increased activation in the PFC is sometimes accompanied by medial temporal lobe underactivation, interpreted as the PFC compensating for age-related medial temporal lobe function decline to maintain memory (Reuter-Lorenz & Cappell, 2008; Reuter-Lorenz & Lustig, 2005).

Age-related neurofunctional reorganization is found to concerns numerous parts of the brain whether it is manifested as increased or decreased activation in older adults in comparison with younger ones. Increased activation in older adults is found in the parietal and temporal cortex for example, that could suggest a generalization of the HAROLD phenomenon beyond the PFC (Cabeza, 2002; Grady, McIntosh, Horwitz, & Rapoport, 2000). Age-related overactivation has been reported in the cuneus and precuneus during a recognition task, an area often associated with memory retrieval (Cabeza et al., 1997). Increased age-related activation is also found in the default-mode regions (medial frontal, cingulate and the precuneus) which could be attributed to progressive reduction in inhibitory control (Grady et al., 2006; Raichle et al., 2001). On the contrary, reduced medial parietal and frontal deactivations in older adults were found during a verb generation task, which could suggest a relation between disruption of the default-mode network and cognitive impairment (Persson et al., 2007). Age-related decreased activation is also reported in the occipital fusiform during memory tasks (Cabeza, 2004) which could be linked to reduced sensory processing (Grady et al., 2006). Age-related reduced activation has also been reported in the caudate, which is associated with habit and probabilistic learning (Grady et al., 2006). The corpus callosum involved in inhibitory functions is similarly found to be affected by aging (Reuter-Lorenz et al., 1999). Overall, it seems that neurofunctional reorganization concerns many areas of the brain, but not necessarily following a specific pattern. It is possible that neurofunctional reorganization would depend largely on the individual, the task undertaken, the nature of the cognitive processes used to perform the task and the perceived task complexity, among others (Ansado, Marsolais, et al., 2013).

Factors affecting aging and neurofunctional reorganization

A diversity of methodologies has been adopted to study age-related neurofunctional reorganization. Thus, comparing findings from studies that have used various neuroimaging methods and various cognitive tasks to measure performance and activation can challenge the delivery of conclusions in terms of defining a more generalizable pattern. Neurofunctional reorganization findings are reported in various tasks and studies, from simple motor processes to higher cognitive processes including attention, episodic memory, working memory, perception and inhibitory control (Cabeza, 2002; Reuter-Lorenz & Cappell, 2008; Schneider-Garces et al., 2010). A variety of tasks have been used to study this area, including for example verb generation following visually presented nouns, naming tasks, recognition memory tasks, autobiographical, encoding and recall memory tasks, word stem completion and word recognition tasks, among others. The processing of semantic relations in words considering aging theories seems to have not however been sufficiently studied yet. In terms of study participants, most studies on neurofunctional reorganization have compared groups of younger versus older adults, without history of neurological disease or other, and with normal scoring on intelligence and other cognitive tests. The mean age for younger adults recruited was found to be 25 years old and for older adults 70 years old. Grady (2006) addressed the question of age graduality when studying brain differences and recruited middle-aged (mean age 50 years old) in addition to younger and older adults, reporting findings that age-related differences in brain activity occur gradually from young to middle to older age.

Individual cognitive reserve differences are found to play an important role when it comes to neurofunctional reorganization and performance (Cabeza et al., 2018; Stern, 2009). Education has been largely reported to play a protective role for cognitive performance during aging (Paolieri, Marful, Morales, & Bajo, 2018; Springer, McIntosh, Winocur, & Grady, 2005; Stern, Alexander, Prohovnik, & Mayew, 1992; Yaffe et al., 2009). For instance, higher level of education is associated with better performance in semantic processing tasks (van Hooren et al., 2007) whereas lower levels of education are associated with higher risk of developing Alzheimer's Disease (D. A. Evans et al., 1997). In most studies of the neurofunctional reorganization literature discussed above, the education level of participants has been controlled between younger and older within the same study, but has varied however from one study to another, depending also on the country's educational system. In line with the cognitive reserve hypothesis, higher education level is important probably because it creates a reserve capacity which compensates for behavioral performance despite neural decline (Alexander et al., 1997; Cabeza, 2002; Grady et al., 2006; Satz, 1993; Springer et al., 2005; Stern et al., 1992). Any strategy increasing the cognitive reserve (Stern et al., 2005), such as practicing cognitive skills throughout life (Erickson et al., 2007; Persson & Reuter-Lorenz, 2008) and bilingualism (Bialystok, Craik, Klein, & Viswanathan, 2004) could contribute against cognitive decline and thus impact neurofunctional reorganization and performance (Barulli & Stern, 2013).

Semantic Processing

Semantic memory

Language and its relation with other types of cognitive processing has been the object of a plethora of studies with language often considered to be the window to the brain (for example the works of Lev Vygotskij (Vygotski, 1986) and Noam Chomsky (Chomsky, 1972)). Since birth we are 'programmed' to acquire language, useful for communication and survival, well-preserved and sometimes even improved during aging, despite otherwise deterioration of cognitive skills and structural changes taking place in the brain. Language deficits following brain damage have provided a means to study and map various language functions in the brain, allocating specific brain areas to language comprehension, production, reading and writing among others. Nevertheless, a full portrait of how language and its various components is organized in the brain is still under research with both linguistic and neurofunctional theories aiming to explain with the help of available neuroimaging techniques the relation between neural networks and linguistic abilities, including semantic processing, which is the object of interest of this study.

‘Semantic processing refers to the cognitive act of accessing stored knowledge about the world’ (Binder, Desai, Graves, & Conant, 2009). To understand and create language, semantic memory is required, or else common knowledge with members of our culture about the meaning of words, general knowledge about objects, facts and people, without specific connection to time or space (Cabeza & Nyberg, 2003; Graham, Simons, Pratt, Patterson, & Hodges, 2000; Hagoort, 1998; Patterson, Nestor, & Rogers, 2007; Raymer & Gonzalez Rothi, 2008; Tulving, 1972). Some early theories on semantic memory have suggested that semantic representations are anatomically compartmentalized in the brain, either segregated by category or by modality (e.g. visual, auditory, tactile, olfactory…), reflecting the origin of information (Hagoort, 1998; Thompson-Schill, Aguirre, D’Esposito, & Farah, 1999). More contemporary theories share findings that there is only one single, widely distributed semantic representation system (Patterson et al., 2007). This system is thought to give meaning to internal and external stimuli regardless of their modality (e.g. objects, pictures, sounds, words, tastes etc.) and is thought to be coded in distinct neuroanatomical sensory, motor and linguistic subsystems (Dilkina & Lambon Ralph, 2012; Fuggetta, Rizzo, Pobric, Lavidor, & Walsh, 2009; Patterson et al., 2007; Thompson-Schill et al., 1999). In addition to the distinct subsystems, a single semantic hub is claimed to exist in the anterior temporal lobes (ATLs) bilaterally, acting as a convergence zone to support the interactive activation of representations in all modalities and for all semantic categories (Patterson et al., 2007). Semantic memory could thus rely on a distributed neural architecture and its independent convergence zone or semantic hub.

An individual semantic representation is thought to exist in the brain for every item separately (Martin & Chao, 2001). As seen previously, semantic representations would form a distributed network structure, organized together in superordinate, subordinate, coordinate and associated relations, regardless of their form or modality (Raymer & Gonzalez Rothi, 2008). Semantic representations functionalities are distinguished in terms of storage and access (Hagoort, 1998) while corresponding regions would exist in the semantic neural network for both operations (Grossman et al., 2013). Through this network structure, words are thought to be partially interlinked with each other (Fuggetta et al., 2009; Landis & Regard, 1988; Wende et al., 2012). When a word is recognized, words directly linked with it in the semantic network are also activated, creating an automatic semantic activation process called semantic priming (Bonner, Peelle, Cook, & Grossman, 2013; Landis & Regard, 1988) which is thought to be independent of memory-related processes (Cabeza & Nyberg, 2003). That would be the case for example with the word *cat* which would likely activate, among others, the word *dog*. If one of these 'second-level' activated words shows up (e.g. dog), its recognition and processing is facilitated (Cabeza & Nyberg, 2003; Dilkina & Lambon Ralph, 2012). Words are therefore not processed independently from each other, but when a word is recognized, multiple networks are also activated in a flexible manner, facilitating the processing of word pairs or larger groups of words to efficiently retrieve and manipulate semantic representations.

Hemispheric asymmetries in the semantic processing of words

Mapping brain areas responsible for language processing dates since findings on Broca's and Wernicke's patients, when brain lesions was the only way to map language processing areas (Bookheimer, 2002). Today, thanks to modern neuroimaging methods like fMRI and despite challenges in distinguishing semantic from other cognitive processes, high-resolution brain (Amunts et al., 2013) and language mappings are able to define core, mainly left-lateralized semantic regions in great detail (Binder et al., 2009; Demonet, Thierry, & Cardebat, 2005; Maya Visser, Jefferies, Embleton, & Lambon Ralph, 2012; Zacà, Jarso, & Pillai, 2013). The PFC is found once again to be involved in numerous semantic processes such as encoding, semantic memory retrieval and word generation (Cabeza et al., 1997), and tasks such as written word recognition, verbal working memory and conceptual priming (Nyberg et al., 2003). The posterior brain regions such as the ventral temporal cortex are found to be involved in organizing conceptual knowledge, largely modulated by word imageability (Sabsevitz, Medler, Seidenberg, & Binder, 2005). The anterior temporal lobes are believed to serve as a semantic hub converging multimodal information (Patterson et al., 2007; M. A. Wilson et al., 2012) while the angular gyrus is proposed to integrate sensory–motor with abstract features of words and objects (Bonner et al., 2013). The 'translation' of any-modality input into coherent semantic representations is mapped into specific brain regions as well (Maya Visser et al., 2012).

Language is asymmetrically distributed in the hemispheres, with the left hemisphere generally more involved, and the right hemisphere complementing it (Beeman & Chiarello, 1998; Chiarello, 1988; Demonet et al., 2005; Joanette, Goulet, & Hannequin, 1990; Landis & Regard, 1988). The semantic contributions of the right hemisphere-based networks varies from a subject to another but is generally thought to be less performant than the left hemisphere, having especially difficulty in understanding subtleties of language or metaphorical meaning in clinical populations (Beeman, 1993; Joanette et al., 1990). The left hemisphere was thought to supposedly dominates by controlling and preventing the right hemisphere to deal with the same information for semantic processing (Joanette et al., 1990; Landis & Regard, 1988). The part of the semantic system which is found in the left hemisphere is thought to be organized based on a hierarchy of logical semantic relations (Abernethy & Coney, 1990) and is proposed to process specific meanings while inhibiting irrelevant ones (Chiarello, 1988). The part of the semantic system found in the right hemisphere on the contrary is considered to be organized based on simple associations between concepts (Abernethy & Coney, 1990) and is suggested to process semantic relations without focus for a single interpretation but with widespread non-selective meanings (Beeman & Chiarello, 1998; Chiarello, 1988).

Although the left hemisphere appears to be sufficient for semantic processing of words, there is evidence that an interhemispheric contribution is necessary for optimal lexico-semantic processing (Joanette et al., 1990). Such 'redundant' semantic processing by the two hemispheres is believed to favor accurate responding and minimize errors (Hoptman & Davidson, 1994). The two hemispheres process semantics in a complementary, parallel and mutually supportive manner (Beeman & Chiarello, 1998), manifesting the duality of brain functioning when it comes to semantic processing. Although there is a left hemisphere preference for semantic processing, some attributes of words, including their concreteness, imageability, frequency and their emotional component have been shown to be associated with the right hemisphere's processing capacities (Nocentini, Goulet, Roberts, & Joanette, 2001). Overall, interhemispheric processing runs in parallel (Beeman et al., 1994) and has been found to be "greater than the sum of its parts," suggesting that both hemispheres cooperatively contribute and interact, demonstrating a high degree of interdependence (Banich & Karol, 1992; Bookheimer, 2002). The current availability of modern neuroimaging methods continues to shed light on where semantic regions are distributed in the brain and how they are organized.

Factors influencing the semantic processing of words

Semantic processing and related neural activation can be influenced by various semantic features (Pexman, Lupke, & Hino, 2002). Processing concrete versus abstract words for example provokes hemispheric asymmetries (Demonet et al., 2005; Sabsevitz et al., 2005), probably because concrete words activate both a verbal and a nonverbal code and have more semantic features as opposed to abstract words which are processed mainly verbally (Hagoort, 1998). The 'hedonic valence' base (degree of positive or negative affective association) has been reported to have an impact on semantic processing (Vigliocco et al., 2013). Highly imageable words engage the right hemisphere more (Nocentini et al., 2001), as they have richer semantic representations and activate more semantic features (G. a. L. Evans, Lambon Ralph, & Woollams, 2012; G. L. Murphy, 1990; Pexman et al., 2002; Sabsevitz et al., 2005). Different activation patterns can be found for words representing natural versus man-made artifacts (Dilkina & Lambon Ralph, 2012; Fuggetta et al., 2009; Hagoort, 1998) and action versus non-action words (Papeo, Pascual-Leone, & Caramazza, 2013) among other word features. Words differing by age of acquisition have been found to produce different behavioral results (Cortese & Khanna, 2007; M. A. Wilson, Cuetos, Davies, & Burani, 2013). Similarly, various visual word processing experiments have yielded differences in task performance in semantic processing (Balota, Cortese, Sergent-Marshall, Spieler, & Yap, 2004; Raymer & Gonzalez Rothi, 2008).

Apart from individual words, several studies have used semantic relations, or else word-word relations to demonstrate the qualitatively different organization of lexical knowledge in the brain (Nocentini et al., 2001). Taxonomic (or categorical) versus thematic (or functional or associative or locative) semantic relations are such an example. Taxonomic relations such as dog and fox are members of the same category (e.g. animals), share some features in common (e.g. four legs) (de Zubicaray, Hansen, & McMahon, 2013) and are accessed actively (Klix, 1978). Thematic relations on the other hand are concrete, based on personal experience and co-occurrence in space and time (e.g. dog-bone) (de Zubicaray et al., 2013; Dilkina & Lambon Ralph, 2012; Schmidt et al., 2012) and are directly stored in semantic memory (Klix, 1978). It is reported that taxonomic relations demonstrate a more extensive activation bilaterally, probably because they are weaker and more difficult to process as they are learned later in childhood (Scott, Greenfield, & Urbano, 1985; Scott, Serchuk, & Mundy, 1982), being based on knowledge of sharing common features (Noppeney & Price, 2004; Paivio, 1991). Semantic associations are believed to depend on the inferior temporal fusiform gyrus (Ishai, Ungerleider, Martin, Schouten, & Haxby, 1999; Wierenga et al., 2008).

Semantic distance is defined as the distance between the nodes corresponding to these terms in an ontology hierarchy, or else, the shorter the distance, the higher the similarity (Gan, Dou, & Jiang, 2013). Processing semantic relations that are close (easier e.g. cheetah-tiger) or distant (more difficult e.g. bike-boat), is found to influence performance and neural activation. When processing a distant semantic relation pair, the right hemisphere is more likely to be engaged (Beeman & Chiarello, 1998; Joanette et al., 1990). Higher N400 event-related potential effects have been observed in an EEG (electro-encephalogram) study, typically seen in semantic incongruence (Ortu, Allan, & Donaldson, 2013). In the more difficult trials of a semantic similarity judgment task, where participants had to decide which of the two words presented was closer to meaning to a third word, they made more errors, had longer response times and produced greater bilateral activation in regions associated with attention, working memory and response monitoring, probably reflecting the longer period of time in which information was held in working memory (Sabsevitz et al., 2005). It could be possible that the brain demonstrates ‘preferences’ over specific word features with different brain regions of the two hemispheres being engaged differentially in semantic processing of words.

Language abilities and aging

Semantic processing in aging

Language processing in aging is probably the best preserved cognitive function despite changes in underlying neural structures (Prinz et al., 2004) and general cognitive decline (Kemper & Anagnopoulos, 1989; Wingfield & Grossman, 2006). Performance in language tasks is overall well preserved during aging, and sometimes even improves in terms of vocabulary and semantic processing (Kavé, Samuel-Enoch, & Adiv, 2009; Verhaegen & Poncelet, 2013). Semantic memory measured by vocabulary tasks and visual word processing is an area where older adults perform the best, probably because older adults have more years of experience practicing with words (Balota et al., 2004; Kahlaoui et al., 2012; Laver, 2009). Several factors seem to be involved in regards to preservation of semantic processing abilities in aging. Age of acquisition was found to be one of the most important variables for word recognition (Cortese & Khanna, 2007). Other studies using single-word comprehension task showed little age-related change (Lustig & Buckner, 2004; Madden et al., 1996, 2002). One study showed that word frequency has more predictive power for older than for younger adults (Spieler & Balota, 1997). Performance in a lexical decision of word/nonword discrimination task was found to be comparable between younger and older adults, while compensatory additional recruitment of prefrontal regions was not observed (Madden et al., 2002). Older adults are found to perform well when they try to generate words that have a lot of links within the semantic neural network, such as everyday items, which is not the case when they need to remember more distant items such as one’s name for example (Burke, MacKay, Worthley, & Wade, 1991). Semantic priming is found to remain unaffected during aging, probably because of its independence from memory functions (Allen, Madden, Weber, & Groth, 1993).

Some semantic tasks appear to be more demanding however and performance is reduced. In a study using a verb generation task where participants were presented with a noun and had to verbally generate an associate verb as quickly as possible, therefore to select among competing conceptual representations, the older adults had longer reaction times (Thompson-Schill, D'Esposito, Aguirre, & Farah, 1997). Verbal fluency is considered to deteriorate during aging (Brickman et al., 2005; Pasquier, Lebert, Grymonprez, & Petit, 1995). When older adults listen to rapid discourse, they are more likely to process information less fast, and as a result will need to 'rehearse' in their memory what they heard to be able to understand the sentence (Wingfield & Grossman, 2006). This could be because working memory limitations affect cognition in the older adults (Wingfield & Grossman, 2006) or because older adults may have difficulty constraining their thought to the same task (West, 1996).

Performance of older adults in semantic processing tasks is reduced when the task is more demanding for attention or working memory. Reduced performance in older adults may be due to impaired semantic representations (storage deficit) or to access and retrieval operations (access deficit) (Hagoort, 1998). A decline of linguistic performances has also been associated with a decline in general executive functions (Baciu et al., 2016). Indeed, age-related differences are most pronounced in conditions where demands for cognitive control are higher (Persson et al., 2007). For example, in a task of lexical decision and word naming, reaction times were higher for older than for younger adults (Balota et al., 2004), probably due to the interference effect (Kinsbourne & Byrd, 1985; Persson et al., 2007). A similar pattern was observed in a semantic similarity judgment task where increasing task difficulty modulated activation mainly in attention, working memory and response monitoring systems (Sabsevitz et al., 2005). It seems that longer input, output and decision processes can affect performance in older adults, it is nevertheless believed that the processes themselves remain the same across ages (Balota et al., 2004).

When studying the neurofunctional reorganization phenomena, most studies have used memory, executive and other cognitive tasks. Even among those who have used linguistic tasks, most have used tasks that are quite demanding for attention and working memory, thus blurring the distinction between pure semantic processing from other cognitive processes. To study the HAROLD phenomenon in semantic processing for example, various tasks have been used, including a semantic memory retrieval task (Stebbins et al., 2002), an auditory processing of syllables task using event-related potentials (ERPs) (Bellis, Nicol, & Kraus, 2000) and a word-stem cued recall task (e.g. rea_____=> reason) (Bäckman et al., 1997). Such tasks are quite demanding for general-domain cognitive resources, such as working memory and attention. Few studies have used deep semantic processing tasks to test performance while reducing other age-affected cognitive operations.

The focus of this study is age-related neurofunctional reorganization activation patterns during semantic processing. It will examine the taxonomic vs. thematic types of relations with high vs. low task demands, through a semantic similarity judgment task whereby participants need to decide which of two words presented on the screen is more related to a third word. Semantic similarity judgment tasks are thought to be ideal to explore deep semantic processing as they are thought to activate large semantic networks as in semantic priming and independently of working memory processes (Evans et al., 2012; Reilly & Peelle, 2008). When a word is recognized, semantic representations are automatically created, minimizing mental imagery demands (Bonner et al., 2013; Pulvermüller, Hauk, Nikulin, & Ilmoniemi, 2005), therefore the demands of this task for attention and memory, most affected by aging, would be reduced in comparison to other tasks. Semantic priming is found to remain unaffected during aging, probably because of its independence from memory functions (Allen et al., 1993). Additionally, this type of semantic relation processing –albeit with a different task- has been shown to provoke different activation patterns, indicating a qualitative difference of their processing (Nocentini et al., 2001). The semantic distance variable that is manipulated in this study adds the quantitative aspect, and helps differentiate one effect from the other in regards to performance and brain activation (Sabsevitz et al., 2005). These complex relations will be explored to help understand how the aging brain neuroneurofunctionally reorganizes to maintain optimal performance in a task that on its own activates large semantic networks, and explore their interplays.

Objectives and Hypotheses

General Objective

This research project aims to explore aging and neurofunctional reorganization during a semantic processing task of semantic similarity judgment by younger and older adults, an ability well-preserved in aging. More specifically, the aim of this study is to identify whether aging affects the brain activity subserving semantic memory in accordance with the CRUNCH predictions, through a semantic judgment task with two levels of demands (low and high). Task demands will be manipulated through semantic distance, which is found to influence both performance and brain activation levels. This objective is addressed in chapters 3 and 4 (second and third articles).

Also, we aim to understand how the type of semantic relation (taxonomic-thematic) will affect neurofunctional activation and performance in younger and older adults. More specifically, this study aims to bridge the gap in the literature on the existence and evolution of semantic hubs in aging, in light of the dual and single-hub theories. It will evaluate the effect of aging on the role of the Anterior Temporal Lobes (ATLs) and the Temporo-parietal junction (TPJ) as neural representations of the semantic hubs responsible for taxonomic and thematic processing, respectively. This objective is addressed in chapter 5 (fourth article).

Hypotheses

The specific hypotheses of this research project are:

Effect of semantic distance

We expect that brain activity and behavioral performance (dependent variables) will support the CRUNCH model predictions when demands on semantic memory are manipulated in younger and older adults (age and task demands: independent variables). More specifically, it is expected that :

1) the effects of semantic distance (low vs. high-demand relations) on neurofunctional activation and behavioral performance (accuracy and RTs) during the semantic judgment task will be significantly different between younger and older participant groups, with younger adults performing with higher accuracy and faster response times than older adults. Furthermore, we predict age group differences in brain activation in semantic control regions bilaterally which are sensitive to increasing task demands. This will be evident with a significant interaction effect between age group and task demands within regions of interest consisting of the core semantic control regions. This will support the idea of the brain's declining ability to respond to increasing task demands with advancing age. If the interaction above is not supported, the following are expected:

2) In the low-demand (LOW) condition, both younger and older participants will perform equally in terms of accuracy and with fewer errors than in the high-demand condition. However, it is anticipated that older adults will present longer RTs and significant increases in activation in left-lateralized semantic control regions compared to the younger participants.

3) In the high-demand (HIGH) condition, it is expected that younger adults will perform better (higher accuracy and lower RTs) and present significant activation in the left-hemisphere semantic control regions compared to older adults. Older adults are expected to exhibit reduced performance compared to younger adults (lower accuracy and higher RTs), reduced activation in left-lateralized semantic control regions, and increased activation in right-lateralized semantic control regions compared to the younger adults.

The above hypotheses are addressed in chapters three and four.

Effect of semantic relation type

This study will compare younger with older adults when processing taxonomic vs. thematic relations in a semantic judgment task and will study the respective roles of the ATLs and TPJ as neural hubs of the brain network underlying the semantic network, while manipulating for semantic control demands. Semantic relationships can be classified as taxonomic or thematic depending on whether they are members of the same category, the product of more formal learning or whether they co-occur in space and time, naturally learned from direct experience, respectively. The semantic distance variable that will be manipulated in this study will add the quantitative aspect, and will help differentiate one effect from the other in regards to performance and brain activation. The study's hypotheses are:

1. If the dual-hub theory is true, a) A double dissociation is expected across age groups such that processing of taxonomic relations will significantly activate the ATLs but not the TPJ, whereas processing of thematic relations will significantly activate the TPJ but not the ATLs. This will confirm that ATLs and TPJ act as semantic hubs in both younger and older adults.

2. If the single-hub theory is true, a) for both younger and older adults, we expect to find increased activation in ATL for both taxonomic and thematic semantic relations whereas activation in the TPJ will vary only as a function of task demands, given its role in semantic control. As such, differences in brain activation between taxonomic and thematic processing will depend on task demand levels but not on type of semantic relation processing.

The above hypotheses are addressed in chapter five.

Chapter 2 - First article. LANGAGE, CERVEAU ET VIEILLISSEMENT: UNE COMPLICITÉ TOUT AU LONG DE LA VIE

LANGUAGE, BRAIN AND AGING:

A LIFE-LONG COMPLIANCE

par

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Resumé

Les bases neurobiologiques du langage ne sont pas seulement dynamiques durant la période d'apprentissage. De plus en plus de preuves montrent que l'organisation neurofonctionnelle pour le langage évolue tout au long de la vie, contribuant à maintenir les habiletés de communication qui sont si importantes pour un vieillissement actif. Le maintien des habiletés de communication avec l'âge contraste avec les altérations observées sur le plan neurobiologique offrant ainsi une forme de paradoxe du couplage cognition-cerveau. L'imagerie cérébrale permet de mieux comprendre cette réorganisation. Ainsi, une réorganisation neurofonctionnelle permettant au cerveau de compenser le déclin lié au vieillissement, ou exprimant le recours à des stratégies caractérisant l'âge avancé, serait à la base du maintien de nombreuses habiletés cognitives, dont le langage. Plusieurs phénomènes comme la réserve cognitive, HAROLD, PASA, CRUNCH et STAC ont tenté de décrire complètement la réorganisation cérébrale, mais le cerveau reste plastique et utilise plusieurs stratégies pour s'adapter au vieillissement. Cette revue permet d'aborder cette question à partir du traitement sémantique des mots. Ce traitement représente une composante de choix du langage pour comparer un élément fort des habiletés de communication entre personnes jeunes et âgées, ainsi que d'observer les caractéristiques de la réorganisation neurofonctionnelle qui en permet le maintien.

Mots-clés vieillissement · langage · réorganisation · cerveau · cognitive

Abstract

The neurobiological bases of language remain activated long after the period of language acquisition. Growing evidence shows that the neurofunctional organization of language develops throughout the lifetime and thus contributes to the maintenance of communication abilities, an important element for active aging. However, the maintenance of communication abilities in older people is in contrast with the observed neurobiological changes taking place, therefore demonstrating that a paradox exists known as the brain-cognition mismatch. It has been hypothesized that neurofunctional reorganisation allows the brain to compensate for age-related neural decline and maintenance of various cognitive abilities, such as language. Several phenomena like the cognitive reserve, HAROLD, PASA, CRUNCH and STAC have attempted to explain the mechanisms of cerebral reorganisation. Yet no theory has fully explained this phenomenon yet, as the brain displays flexible strategies for adapting to aging. This review compares the semantic treatment of words, a language component usually well preserved in aging, between younger and older adults while observing the characteristics of the neurofunctional reorganisation.

Keywords: aging · language · reorganization · brain · cognitive

Introduction

La capacité à communiquer savoir, sentiments et opinions avec autrui constitue une caractéristique essentielle de l'être humain. Cette capacité à communiquer se maintiendra tout au long de notre vie et dépend de l'intégrité de notre cerveau. L'organisation du cerveau pour le langage a été l'une des premières fenêtres ouvertes permettant d'étudier et de comprendre le fonctionnement de la cognition humaine. À l'image des neurones cérébraux qui sont programmés et conc¸us pour se connecter les uns aux autres, c'est la communication par le langage qui permet à l'humain de se connecter les uns avec les autres. Au cours du vieillissement, nous voyons certaines fonctions, telles que la mobilité, diminuer tandis que les capacités de communication restent stables, cette capacité permettant aux humains de rester interconnectés. L'objectif de cet article est de résumer certains travaux issus à la fois de la littérature et des contributions de notre équipe quant à la manière dont le cerveau arrive à maintenir une surprenante efficience de ses habiletés de communication lors du vieillissement. Les habiletés de communication représentent donc un cas de résilience cognitive face aux impacts du vieillissement et mettent en jeu des phénomènes de réorganisation neurofonctionnelle tout au long du vieillissement.

Vieillissement, societés et communication

L'espérance de vie mondiale a augmenté de fac¸on spectaculaire depuis quelques milliers d'années en particulier grâce à la diminution de la mortalité infantile, au contrôle des infections et à l'amélioration générale de la qualité de vie. La proportion des personnes âgées de plus de 65 ans dans la population mondiale augmente continuellement et l'Organisation mondiale de la santé (OMS) estime que 2 milliards d'individus auront plus de 60 ans en 2050. Parallèlement, l'incidence des maladies liées au vieillissement et des maladies chroniques augmente aussi: on estime que 35,6 millions d'individus souffrent actuellement d'une démence et qu'un demi-million de Canadiens vivent avec une démence ou avec la maladie d'Alzheimer selon la Société Alzheimer de Canada. Les conséquences sociales et financières de ces démences pour les individus et leurs familles ont conduit l'OMS à les déclarer en 2012 priorité de santé publique. Nos sociétés s'intéressent de plus en plus aux solutions permettant un vieillissement actif, ainsi qu'à la prevention du déclin cognitif et à la préservation des habiletés cognitives. Elles cherchent à permettre aux populations de vieillir en restant actif et autonome, et ce physiquement, mentalement et socialement, selon un « processus consistant à optimiser les possibilités de bonne santé, de participation et de sécurité afin d'accroître la qualité de vie pendant la vieillesse », comme le propose l'OMS. Il est même considéré que se préparer à mieux vieillir commence dès la petite enfance, en évitant par exemple, les facteurs environnementaux connus comme pouvant accélérer ou induire des limites neurofonctionnelles, comme en témoigne les liens entre traumatismes crâniens précoces et accroissement des maladies neurodégénératives apparaissant tardivement dans la vie. Plusieurs modèles ont été développés concernant le vieillissement actif, dont celui du « mieux vieillir » introduit par Rowe et Kahn [1], qui souligne l'importance de l'absence de maladies et de facteurs de risque, le maintien d'une vie active et socialement significative ainsi que la préservation des fonctions physiques et cognitives. Toute stratégie qui peut potentiellement augmenter ce qui est concu comme une forme de réserve cognitive (voir Stern [2], ci-dessous) peut aider à contribuer à réduire le déclin cognitif. Parmi les stratégies, notons l'exercice physique [3], et la pratique régulière d'une activité intellectuelle [4]. Au contraire, la privation de sommeil ou les accidents cérébraux peuvent diminuer la réserve cognitive et compromettre ainsi la performance cognitive [5].

Le cerveau qui vieillit et qui s'adapte

Plusieurs études ont tenté de décrire l'impact duvieillissement sur le cerveau et la réorganisation neurofonctionnelle qui l'accompagne, ainsi que de caractériser le vieillissement normal par rapport au vieillissement en lien avec des maladies neurodégénératives. Lors du vieillissement, la substance blanche [6] et la masse cérébrale diminuent progressivement. Certaines régions, comme l'hippocampe, sont plus affectées que d'autres qui sont beaucoup moins affectées, comme c'est le cas pour le cortex visuel. L'influence de ces changements du substrat neurobiologique sur la cognition varie en fonction des habiletés cognitives et des individus.

Certaines habiletés cognitives comme la mémoire, les processus attentionnels, la vitesse de traitement de l'information et le processus d'inhibition (c'est-à-dire la capacité à « bloquer » l'information non utile) sont affectées [7, 8], tandis que la performance comportementale [9] et les habiletés de langage restent largement intactes ou même s'améliorent au cours du vieillissement [10]. Il existe donc un certain paradoxe pour le langage entre, d'une part, le maintien des habiletés de communication et, d'autre part, une atteinte progressive du substrat neurobiologique qui en est responsable : une forme de paradoxe du couplage cognition-cerveau. Ce paradoxe constitue l'élément le plus impressionnant d'un cerveau qui vieillit de façon optimale et qui, malgré les importants changements biologiques et structurels, arrive à maintenir certaines de ses fonctions cognitives. L'utilisation de techniques d'imagerie cérébrale (e.g. IRMf, TEP) permet de décrire l'éventuelle réorganisation neurofonctionnelle en fonction des tâches cognitives, des individus et de leur âge [11, 12]. Ainsi, l'activation cérébrale peut augmenter ou diminuer dans certaines régions en recrutant des circuits neuronaux distincts dans le même hémisphère ou dans l'hémisphère opposé, résultant en une réorganisation neurofonctionnelle qui démontre la plasticité du cerveau au cours du vieillissement [9, 13]. Stern [2] propose de rendre compte du paradoxe du couplage cognition-cerveau grâce à la théorie de la reserve cognitive. La réserve cognitive permettrait d'optimiser la performance liée à la cognition chez les personnes âgées en bonne santé. Deux processus sont impliqués dans cette optimisation du vieillissement : soit le recrutement des réseaux neuronaux existants est optimisé (réserve neurale), soit de nouveaux réseaux neuronaux alternatifs ou supplémentaires sont recrutés (compensation neurale). Ainsi, les personnes âgées démontrent une variabilité dans leur capacité à utiliser des ressources neuronales de façon efficace, flexible ou différente, parfois utilisant la réserve neurale en même temps que la compensation neurale. Cela démontre la nature adaptative du cerveau [14]. D'après cette idée, un traitement cognitif optimal pendant le vieillissement dépendrait entre autres des facteurs génétiques, des influences environnementales sur le cerveau et de la capacité indivi individuelle à compenser les effets pathologiques de maladies. Plusieurs études ont tenté de comprendre comment le cerveau se réorganise fonctionnellement avec l'âge, l'hypothèse de compensation étant la plus fréquemment évoquée. Selon cette hypothèse, les ressources du cerveau qui vieillit ne suffisent plus pour effectuer les tâches cognitives : des ressources supplémentaires doivent donc être recrutées dans le même hémisphère ou dans l'hémisphère controlatéral afin de compenser pour son propre déclin [12]. Ainsi, pour Grady et al. [12], dans certains conditions les personnes âgées vont donc utilizer leurs deux hémisphères pour certaines tâches cognitives alors que les jeunes adultes n'en utiliseront qu'un seul. Sans recrutement neuronal supplémentaire chez la personne âgée, la performance est diminuée. La compensation se manifeste donc par une sur-activation mais aussi une désactivation des certaines régions cérébrales. Une telle réorganisation est pareillement observée sur des sujets ayant subit des dommages cérébraux unilatéraux : les regions controlatérales sont alors recrutées pour maintenir les fonctions cognitives [15]. La réorganisation peut même survenir chez les jeunes adultes pendant des tâches cognitives difficiles [16] : la réorganisation du cerveau devient alors avantageuse [17] puisque la performance cognitive reste optimale. Toutefois, comme on le verra plus loin, le principe de compensation n'est pas le seul qui peut expliquer le paradoxe du couplage pour le langage puisque, dans certains cas, il se pourrait que ce soient des stratégies cognitives distinctes qui soient utilisées par les personnes âgées et qui fassent en sorte de rendre leur performance similaires à celles des plus jeunes. Plusieurs phénomènes de réorganisation neurofonctionnelle avec l'âge ont été décrits. HAROLD (Hemispheric Asymmetry Reduction in Older Adults) décrit une reorganization du cerveau à travers les deux hémisphères et notamment le cortex préfrontal pour des tâches de mémoire et exécutives, de sorte que l'asymétrie est diminuée chez les personnes âgées performantes, par rapport aux jeunes adultes ou par rapport aux personnes âgées dont la performance est moins bonne [16]. Le phénomène PASA (Posterior Anterior Shift in Aging) décrit quant à lui une réorganisation au sein du même hémisphère qui se caractérise par une diminution de l'activation dans les aires occipito-temporales concomitant d'un accroissement des activations dans les régions frontales [18]. La reorganization PASA serait plutôt liée au vieillissement qu'à la difficulté de la tâche [19]. Une autre proposition, le principe CRUNCH (Compensation Related Utilization of Neural Circuits Hypothesis), accentue le caractère positif de la reorganization neurofonctionnelle d'un cerveau plastique et adaptatif, où l'élément définitif n'est pas l'âge mais la complexité de la tâche cognitive [5]. Enfin, le phénomène STAC (Scaffolding Theory of Aging and Cognition) traite de la résilience du cerveau vieillissant et de sa capacité à réparer ses propres déficiences et à protéger ses fonctions [5, 20]. Qu'elle soit intra- ou inter-hémisphérique, qu'elle augmente ou qu'elle diminue, la réorganisation cérébrale reste flexible selon les besoins de traitement [21], démontrant ainsi la capacité du cerveau à s'adapter au vieillissement. La réorganisation cérébrale qui se manifeste par des accroissements ou des diminutions de l'activation cérébrale en neuro-imagerie fonctionnelle reste un phénomène complexe, difficile à décrire et à comprendre. Ces phénomènes de réorganisation seraient-ils mutuellement exclusifs ou bien complémentaires, influencés par la nature de l'habileté cognitive, la disponibilité des structures intègres ou bien les exigences de la tâche et la capacité à les atteindre ? Plusieurs études ont tenté de répondre à ces questions et d'identifier les facteurs communs aux mécanismes de réorganisation [22]. Cabeza [16] considère que la réorganisation est neurobiologique et non intentionnelle plutôt que le résultat d'un changement planifié de strategies cognitives, puisqu'elle se manifeste aussi lors des tâches qu'on ne contrôle que très peu. Reuter-Lorenz et Cappell [5], au contraire, doutent qu'une reorganization si variable soit due aux changements structurels du cerveau dus à l'âge car elle serait alors identique pour toutes les tâches cognitives. La réorganisation neurofonctionnelle est interprétée positivement ou négativement en function de la performance aux tâches cognitives [3, 9]. Une certaine ambiguïté existe à propos de la désactivation, alors que la plupart des études considèrent la sur-activation comme une conséquence positive [23]. Pourtant, une certaine sur-activation est aussi observée lors des maladies neurodégénératives comme la maladie d'Alzheimer et le trouble cognitif léger (mild cognitive impairment). Cette suractivation pourrait expliquer la fonction compensatoire du cerveau ou son déclin progressif [13, 24]. Plus de travaux sont requis pour développer un modèle complet permettant d'expliquer l'adaptation du cerveau au cours du vieillissement et son rôle dans le maintien des habiletés cognitives.

Langage, cerveau et vieillissement: une complicité pour un vieillissement actif

Le langage permet de communiquer y compris au cours du vieillissement, il est très bien préservé et peut meme s’améliorer. En dépit de leurs différences, les langues du monde reposent pratiquement toutes sur la présence d’un lexique partagé de même qu’une forme ou une autre de syntaxe, qui permet la combinatoire requise pour communiquer [10]. L’ensemble est en lien avec la mémoire sémantique qui est requise pour la compréhension et l’expression du langage. C’est une connaissance générale portant sur les objets, les évènements et les personnes, partagée avec les membres de notre communauté [25]. Dès lors, on peut étudier le traitement sémantique des mots, organisés en un unique réseau de représentations distribuées et interconnectées [26]. La communication par le langage dépend de plusieurs habiletés linguistiques et cognitives qui bénéficient du soutien de réseaux neurofonctionnels qui dependent eux-mêmes de régions cérébrales bien distinctes [27]. Par exemple, les aires de Broca et deWernicke, utilisées notamment lors de la lecture et de l’écriture, sont mises à profit lors de la compréhension et à la production du langage [28]. Les habiletés linguistiques dépendent ainsi de plusieurs réseaux neuronaux largement distribués à travers le cerveau. Bien que l’hémisphère gauche ait tendance à dominer les habiletés linguistiques et l’hémisphère droit à les compléter [29] ; ces deux hémisphères collaborent pour le traitement sémantique du langage [30]. Le cortex préfrontal est impliqué dans plusieurs processus sémantiques comme le codage, la récupération de la mémoire sémantique, la génération des mots [11], la reconnaissance des mots écrits, la mémoire de travail verbal et l’amorc¸age conceptuel [31]. Les régions postérieures organisent les connaissances conceptuelles [32] alors que les lobes antérieurs-temporaux agissent comme une « zone de convergence » et coordonnent l’information multimodale [26, 33]. Comme il a été évoqué précédemment, les habiletés linguistiques sont parmi les mieux préservées pendant le vieillissement normal [7]. PourWingfield et Grossman [10], ce maintien des habiletés résulte de la mise en jeu de phénomènes de réorganisation neurofonctionnelle. De toutes les composantes du langage, le traitement sémantique de mots est l’une de mieux préservée et de mieux distribuée entre les deux hémisphères [21]. Ainsi, les personnes âgées obtiennent généralement de bons résultats aux tests de mémoire sémantique impliquant des tâches de vocabulaire ou de traitement visuel des mots, et ce probablement en lien avec leur expérience du langage [34]. L’âge d’acquisition d’un mot est une variable importante pour sa reconnaissance [35] et la fréquence d'un mot a plus d'influence chez les personnes âgées que chez les personnes jeunes [36]. Les personnes âgées génèrent les mots d'autant plus facilement qu'ils sont bien connectés dans le réseau sémantique. Par exemple, les mots d'usage courant sont plus facilement générés que les mots plus rares [37]. Cependant, d'autres études ont conclu à une difference négligeable entre les personnes âgées et les personnes jeunes, notamment en étudiant la compréhension d'un mot unique [38], l'identification d'un mot par rapport à un pseudo-mot [39] et l'amorc¸age sémantique, probablement parce que ce dernier est indépendant de la fonction de mémoire [40]. Pendant une tâche de jugement sémantique consistant à décider si le mot présenté est un animal ou non, la performance des personnes âgées en temps de reaction était comparable à celle de jeunes [21]. Leur activation neuronale semble confirmer l'existence d'une reorganization neurofonctionnelle comme expliqué plus haut. En revanche, cette réorganisation ne correspondait pas aux phénomènes HAROLD, PASA et CRUNCH déjà présentés. En effet, entre autres phénomènes, une augmentation de l'activation dans les lobes temporaux chez les personnes âgées a été observée. Cette sur-activation dans ces régions, responsables de la mémoire sémantique, suggère que les personnes âgées utiliseraient la mémoire sémantique pour accomplir la tâche alors que les jeunes utiliseraient plutôt les fonctions exécutives [21]. Dans le cas d'une étude de fluence verbale et notamment de production de mots, le modèle HAROLD n'est pas toujours observé. Marsolais et al. [41] ont récemment utilize une tâche qui consistait à produire le plus de mots possibles d'une catégorie donnée, par exemple les animaux, afin d'étudier la récupération qui devient de plus en plus difficile au cours de la tâche. Globalement, ils remarquent peu de différences significatives entre les deux groupes, que ce soit pour la performance ou les indicateurs en neuroimagerie fonctionnelle. L'activation neurofonctionnelle a été plus affectée par la durée de l'expérience que par l'âge des participants [41]. Dans une autre étude utilisant une tâche de fluence verbale considérant à la fois le maintien et changement de thème, les résultats ont montré une activation augmentée des régions temporales et frontales chez les personnes âgées par rapport aux jeunes [42]. Malgré la bonne préservation du traitement sémantique des mots chez les personnes âgées, certaines tâches verbales, comme celles nécessitant attention ou mémoire de travail, leur sont plus difficiles. Par exemple, les personnes âgées sont plus lentes que les personnes jeunes pour générer un verbe suite à l'exposition à un nom [43] ou pour juger de la similarité sémantique [44]. Ces différences s'expliquent probablement par le fait que les processus de décision sont plus longs [34]. En conclusion, le type de voies neuronales recrutées pour maintenir la performance dans le traitement sémantique de mots dépend plutôt de la nature de la tâche que de l'âge de participants. Pour maintenir sa performance, le cerveau reste flexible à utiliser de nombreuses stratégies, qu'elles soient de réserve ou de compensation cognitive, ou encore de recours à une stratégie cognitive distincte [21].

Conclusion

Les travaux sur les phénomènes de reorganization fonctionnelle qui permettent le maintien des habiletés de communication avec l'âge démontrent clairement que le vieillissement est tout sauf statique. En effet, pour assurer ce maintien si important pour la préservation des contacts sociaux à un âge avancé, tout porte à croire que le cerveau s'adapte progressivement, tout au cours de la vie. Maintenir un vieillissement actif eu égard à la communication, c'est progressivement s'adapter. Une telle évolution de la nature de l'organisation neurofonctionnelle pour une même habileté et un même niveau de performance est probablement le reflet d'une évolution dans la manière et la stratégie utilisée par la personne âgée qui est distincte de celle mise en jeu par les plus jeunes. Le savoir accumulé, une attitude distincte face à la realization de tâches, et des manières différentes d'être contribuent probablement à la mise en jeu de manières distinctes de résoudre les tâches proposées. Si tel est le cas, vieillir est donc évoluer. Et la complicité entre le cerveau et le langage permettent cette évolution au profit du maintien des contacts sociaux à un âge où ces derniers sont encore plus importants, à la fois en soutien à la personne âgée et permettant le passage du savoir avec la génération plus jeune.

Lien d'intérêts

Les auteurs déclarent ne pas avoir de lien d'intérêt en rapport avec cet article.

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Chapter 3 – Second article. Registered report protocol: Age-preserved semantic memory and the CRUNCH effect manifested as differential semantic control networks: an fMRI study

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Abstract

Semantic memory representations are overall well-maintained in aging whereas semantic control is thought to be more affected. To explain this phenomenon, this study aims to test the predictions of the Compensation Related Utilization of Neural Circuits Hypothesis (CRUNCH) focusing on task demands in aging as a possible framework. The CRUNCH effect would manifest itself in semantic tasks through a compensatory increase in neural activation in semantic control network regions but only up to a certain threshold of task demands. This study will compare 40 younger (20-35 years old) with 40 older participants (60-75 years old) in a triad-based semantic judgment task performed in an fMRI scanner while manipulating levels of task demands (low vs. high) through semantic distance. In line with the CRUNCH predictions, differences in neurofunctional activation and behavioral performance (accuracy and response times) are expected in younger vs. older participants in the low- vs. high-demand conditions manifested in semantic control Regions of Interest.

Introduction

Language overall is well preserved in aging [1] and semantic memory may even improve across the lifespan [2]–[6], despite numerous neurophysiological declines in other cognitive domains that occur in the aging brain[6]–[8]. When compared with attention or memory, the relative preservation of language throughout lifetime [9] could be justified by the necessity to maintain successful communication, resulting in compensatory, flexible or atypical recruitment of neural resources [6]. Performance in terms of accuracy in semantic tasks is generally well maintained in older adults considering their more extensive experience with word use and a larger vocabulary than younger adults [2], [5], [6], [10]–[13]. Response times (RTs) however are often longer compared to younger adults [10], possibly because older adults are slower in accessing and retrieving conceptual representations from their semantic store [14]–[16], engaging the required executive function resources [17], and necessary motor responses [18]. Aside from behavioral performance, findings reported in the literature about the neural correlates sustaining semantic memory of older adults when compared with younger ones, are often conflicting, depending on the task utilized, inter-individual variability and the specific age group. Though several age-focused neurofunctional reorganization phenomena (e.g. Hemispheric Asymmetry Reduction in Older Adults-HAROLD [19] and Posterior-Anterior Shift in Aging-PASA [20] aim to explain how aging affects cognitive skills in general, it is still not clear how aging impacts the underlying pattern of activation sustaining semantic memory, given its relative life-course preservation. The relative preservation of semantic memory performance in older adults when compared with other cognitive fields [9], [21], [22] could be partly justified by the proposed dual nature of the semantic memory system, as expressed within the controlled semantic cognition framework [23]–[26]. The present study focuses on the question of preservation of semantic memory in aging, defined as the 'cognitive act of accessing stored knowledge about the world' [27] using a semantic judgment task manipulating semantic control with two demand levels (low and high).

To account for conflicting findings in terms of brain activation during semantic memory tasks and the relative preservation of semantic memory in normal aging, a possible explanation is to consider it the result of adaptive mechanisms captured within the CRUNCH model (Compensation Related Utilization of Neural Circuits Hypothesis) [28]. This theory states that it is the level of task difficulty that impacts performance and neurofunctional activation in both younger and older individuals, whereas aging could be thought of as the expression of increasing task demands earlier than in younger adults. Accordingly, additional neural resources are recruited to attempt compensation when faced with elevated task requirements, echoing an aspect of the aging process manifestation [29], [30]. Compensation is thus defined as 'the cognition-enhancing recruitment of neural resources in response to relatively high cognitive demand' [29]. Alternatively, age-related reorganization phenomena refer to reduced neural efficiency, also known as dedifferentiation, resulting in reduced performance in the older [31]–[34].

At the same time and as part of the age-related neurofunctional reorganization, neural resources may migrate from the default mode network (DMN) towards more urgent task requirements, which can be expressed as underactivation in such areas subserving 'redundant' tasks [28].

Indeed, the more task demands increase, the more DMN activation is expected to decrease, however this ability to 'silence' the DMN reduces in older adults [35]. Both over- and underactivation are relevant terms referring to comparisons with optimal patterns of activation as seen in younger adults [28]. Although the CRUNCH model describes compensatory neural mechanisms, it is not without its limits. For older adults, the overactivation benefit is thought to reach a threshold beyond which additional neural resources do not suffice, after which activation declines and performance deteriorates [28]. The relationship between task demands and fMRI activation has been described as an inverted U-shaped one, with the curve of older adults being to the left of the curve of younger ones. In other words, older adults would recruit additional neural resources at lower levels of task demands, reach a maximum and decrease in activity as task demands continue to increase earlier than younger ones (see figure 3a in [29], [30]).

The CRUNCH hypothesis was conceived on evidence from a working memory study. Activation increased in the dorsolateral prefrontal cortex when accuracy was maintained and decreased when accuracy was compromised, depending on task load, or else, the number of items successfully retained [36], [37]. Congruent results were found in another working memory study, claiming that older adults may achieve the same outcomes using different neural circuits or strategies to achieve age-matched performance [38]. However, the CRUNCH predictions were not confirmed in recent working memory studies. In a working memory study with 3 load conditions using functional near-infrared spectroscopy (fNIRS), activation in the younger progressively increased in the PFC as difficulty increased and performance was maintained [39]. fNIRS is a brain imaging methodology measuring hoxygenation, dehoxygenation, and total hemoglobin, and advantageous in comparison to fMRI as it is noise-free, portable, non-invasive, less sensitive to movement, thus allowing participants to naturally execute tasks (e.g. narration), however, with less imaging capabilities going beyond the cortical surface (Schecklmann et al., 2008). However in the older adults, when performance was compromised during the most difficult condition, activation in the PFC bilaterally remained high. Similarly, in a visuospatial working memory task with 4 levels of task demands, the CRUNCH predictions were not found [40]. Instead, an increase in activation was found in a large network (premotor, prefrontal, subcortical and visual regions) however, no ‘crunch’ point after which activation decreases was found for the older group. Though older adults showed increased activation across regions at the higher task loads when compared with the younger ones, at the group level this difference was not significant, thus challenging the CRUNCH prediction of interaction between difficulty and fMRI activation.

Compatible with the CRUNCH expectations, increased activations with relatively maintained performance have been reported in frontoparietal regions in several language studies, however the results are not always consistent. More precisely, in a discourse comprehension study using fNIRS, increased activation was found in the left dorsolateral prefrontal cortex in older adults while performance was mostly equal to their younger counterparts [41]. In a sentence comprehension study, increased activation was observed in both younger and older adults during the more complex sentences in regions such as the bilateral ventral inferior frontal gyrus (IFG)/anterior insula, bilateral middle frontal gyrus (MFG), bilateral middle temporal gyrus (MTG), and left inferior parietal lobe [42]. Older adults showed increased activity compared with the younger in the IFG bilaterally and the anterior insula in the difficult condition, however their performance in terms of accuracy was not maintained. Partially compatible with CRUNCH, overactivations with maintained performance have also been observed in a picture naming study manipulating for task demands/inhibition [43]. When naming difficulty increased, both younger and older adults showed increased activation in bilateral regions such as the IFG, the anterior cingulate gyri, the pre-, post-central, supramarginal and angular gyri, together with maintained performance while response times (RTs) of older adults did not significantly increase [43]. Few studies exist on semantic memory in light of increasing task demands, which is the focus of the current study.

Given the large volume of concepts and processes involved, semantic memory relies on a widely distributed and interconnected mainly left-lateralized core semantic network [17], [27], [44]–[46] and bilaterally the anterior temporal lobes (ATL) proposed to act as semantic hubs [47], [48]. Semantic memory is suggested to be organized as a dual system composed of two distinctive but interacting systems, one specific to representations and one specific to cognitive-semantic control [25], [46], [49]–[53]. In other words, it is thought to include processes related to stored concept representations with their modality-specific features which would interact with control processes in charge of selecting, retrieving, manipulating and monitoring them for relevance and the specific context, while at the same time suppressing irrelevant information [24]–[26], [54]–[57]. Within the controlled semantic cognition framework [26], the semantic control network would be significantly recruited during more complex tasks underpinned by left-hemisphere regions such as the prefrontal cortex (PFC), inferior frontal gyrus (IFG), posterior middle temporal gyrus (pMTG), dorsal angular gyrus (dAG), dorsal anterior cingulate (dACC), and dorsal inferior parietal cortex (dIPC) [25], [26], [45], [46], [51], [53], [58], [59], potentially extending towards the right IFG and PFC when demands further intensify [46]. One of the most up-to-date and extensive meta-analysis of 925 peaks over 126 contrasts from 87 studies on semantic control and 257 on semantic memory, found further evidence for the regions involved in semantic control, concluding them to the left-lateralized IFG, pMTG, pITG (posterior inferior temporal gyrus), and dmPFC (dorsomedial prefrontal cortex) regions [24]. Regions related to semantic control are thought to be largely overlapped by the neural correlates of the semantic network [24] but also thought to largely overlap with regions related to the ‘multiple-demand’ frontoparietal cognitive control network involved in planning and regulating cognitive processes [26], [60].

Differential recruitment has been found for easy and harder semantic tasks in younger adults including recruitment of semantic control regions for the latter. In a study using transcranial magnetic stimulation (TMS) on the roles of the angular gyrus (AG) and the pMTG, participants were required to perform identity or thematic matchings that were either strongly or weakly associated, based on ratings previously collected and where RTs were used as a function of association strength. Stimulation to the AG and the pMTG confirmed their roles in more automatic and more controlled retrieval respectively [58]. An fMRI study used a triad-based semantic similarity judgment task to compare between concrete and abstract nouns (imageability) while manipulating additionally for difficulty. Difficulty was based on semantic similarity scores based on ratings of words, and for every triad, a semantic similarity score was computed to classify them as easy or hard. Increased activations were found during the hard triads and regardless of word imageability, in regions modulating attention and response monitoring such as bilaterally in the cingulate sulcus, the medial superior frontal gyrus and left dorsal inferior frontal gyrus [61]. In a triad-based synonym judgment task comparing concrete vs. abstract words, where triads were categorized as easy or difficult based on the respective response time in relation to the group mean, a main effect of difficulty was confirmed, with increased activations reported in the left temporal pole, left IFG and left MTG [62]. In a triad-based task where participants were requested to match words for colour and semantic relation to probe more automatic or controlled semantic processing respectively, greater activation was found in the IFG and IPS during the more difficult triads that were based on colour-matching. Accuracy was overall maintained equally across conditions but there were more errors and longer RTs in the 'difficult' colour condition, lending support to the controlled semantic cognition idea [50]. There is therefore evidence to support an increase in activation in semantic control regions when semantic processing demands increase, which could be attributed to 'matching' task requirements with available neural resources, in line with CRUNCH predictions. When it comes to aging, though the system related to representations is thought to be well-maintained, the system related to cognitive-semantic control is thought to be more affected [23]. This study focuses on how the relation between semantic control network activation and increasing task demands is affected by aging.

The neural correlates sustaining semantic memory are thought to be largely age-invariant, with only small differences existing in neural recruitment as a function of age [16], [22], [63]–[66]. In a recently conducted meta-analysis of 47 neuroimaging studies comparing younger and older people, increases in activation in semantic control regions in older adults were reported when compared with younger ones, while accuracy was found to be equal between the two groups [22]. Though this increase in activation could be attributed to compensatory accounts, it could also reflect age-related loss of neuronal specificity or efficiency [22]. Several studies report activation and performance results in line with the compensatory overactivation account. In a semantic judgment task, participants had to decide whether two words share a common feature (shape or color) with their performance being categorized as better or worse based on a split from behavioral data [56]. In better performing older adults, activation was increased relative to younger adults in control regions such as the inferior parietal and bilateral premotor cortex, regions important for executive functions and object visual processing as well as relative to poorer performing older adults, in the premotor, inferior parietal and lateral occipital cortex. A further analysis for gray matter found that increased gray matter in the right precentral gyrus was associated with maintained performance [56]. In a semantic categorization study, older participants performed as accurately as the younger ones but had slower RTs. Their maintained performance was correlated with activation in a larger network than the one of younger ones, including parts of the semantic control network (such as left frontal and superior parietal cortex, left anterior cingulate, right angular gyrus and right superior temporal cortex), which was reportedly atypical and excluded the PFC [44].

Specifically to left IFG recruitment, believed to be in charge of top-down semantic control [45], [49], [51], [67], its association with the ‘difficult’ condition has been reported in several studies. In a triad-based semantic judgment task evaluating for rhyme, semantic and perceptual similarity, interaction and conjunction analyses revealed a significant interaction between age and the high-load semantic condition. Older adults overrecruited the control-related regions of the left IFG, left fusiform gyrus and posterior cingulate bilaterally, when competition demands increased while their accuracy was even better than their younger counterparts [66]. In a picture-naming task, older adults recruited overall larger frontal areas than younger ones in both hemispheres. Though the bilateral -and not the solely-left- recruitment of the IFG was beneficial to performance of older participants, the recruitment of other right-hemisphere regions was negatively correlated with accuracy [16]. The authors provided support to the finding that the neural substrates for semantic memory representations are intact in older adults whereas it is the executive aspect of language functions, including accessing and manipulating verbal information, that are most affected by aging [16]. In another study with younger adults only, aiming to dissociate the role of the IFG in phonologically vs. semantically cued word retrieval, the recruitment of anterior-dorsal parts of the LIFG was associated with the high task demands condition in the semantic fluency condition, while performance was maintained [68].

Evidence therefore exists for a correlation between an increase in activation of semantic control regions when faced with increased task demands, which could be indicative of the compensation account to favor semantic memory performance in both younger and older adults, and potentially reflecting the ascending part of the U-shaped relation between fMRI activation and task demands. Attributing however a causal relation between increased activation in the semantic control network and compensation is not straightforward. Distinguishing between the compensation and de-differentiation accounts can be challenging, as merely correlating brain activation with behavioral outcomes to claim compensation is methodologically incomplete [69], [70]. Many studies do not manipulate or cannot be compared for task demands and thus interpreting results that correlate neural activation with behavior can be confusing [53]. For example, in a study where task demands are lower, reorganization may be interpreted as compensatory when performance is maintained whereas when performance is more affected, it can be attributed to dedifferentiation. Numerous methodological caveats exist when attempting to allocate meaning a posteriori to age-related reorganization, given the observational nature of neuroscience, but also the need for more robust methodological designs, including longitudinal studies that measure in-person changes, between regions comparison and better analytic approaches (for a review see [70]). Correlating increased activation with improved performance at a single point in time and attributing it to compensation would require additional measures, also given that compensation may be attempted or only partly successful [30], [71].

According to the CRUNCH theory, the compensatory increase in activation of semantic control regions is thought to reach a plateau beyond which additional resources no longer benefit performance [28]. As such, reduced activation in cognitive control regions when semantic processing demands increase has also been reported. According to CRUNCH, this reduced activation could be interpreted as neural resources having already reached their maximum capacity and no longer being sufficient to successfully sustain compensation for the task [28]. Indeed, the meta-analysis of 47 neuroimaging studies comparing activation in younger and older adults (mean age of younger participants: 26 years (SD=4.1) and mean age of older participants: 69.1 (SD=4.7) during semantic processing tasks, also reported decreased activation in the older adults in typical semantic control regions in the left hemisphere (IFG, pMTG, ventral occipitotemporal regions and dIPC) together with increased activation in 'multiple-demand network' regions in the right hemisphere (IFG, right superior frontal and parietal cortex including the middle frontal gyrus, dIPC and dACC) especially when performance was sub-optimal [22]. In a semantic judgment task (living vs. non-living judgement of words) study with two levels of difficulty and four across-the-lifespan age groups, activation outside the core semantic network increased with age linearly and contralaterally towards the right hemisphere (right parietal cortex and middle frontal gyrus) in the easy condition, while accuracy was maintained [64]. In the difficult condition however, RTs were slower and reduced activation was observed in older participants in semantic control regions, namely the frontal, parietal and cingulate cortex regions, suggesting a declining ability of brain to respond to increasing task demands by mobilizing semantic control network resources as age increases [64].

Similarly, increased activation in right-lateralized semantic control regions was detrimental to performance in both younger and older participants in a word generation study manipulating for task difficulty [72]. Indeed, activation in the ventral IFG bilaterally was correlated with difficult items as opposed to easier ones and reduced performance irrespective of age. In a verbal fluency study by the same group using correlation analysis, a strong negative correlation was found between performance and activation in the right inferior and middle frontal gyrus ROIs [73]. Older adults demonstrated a more bilateral activation than younger ones especially in the right inferior and middle frontal regions whereas their performance during the semantic task was negatively impacted. However, this right-lateralized semantic control network increase in activation together with a drop in performance has not been consistently documented. For example, in a semantic judgment task on word concreteness using magnetic encephalography (MEG), older participants overactivated the right posterior middle temporal gyrus, inferior parietal lobule, angular gyrus and the left ATL and underactivated the control-related left IPC as a result of increased task demands while their performance was equivalent to the younger, thus lending support to compensatory accounts [65]. According to CRUNCH, the above findings could be interpreted within the descending part of the inverted U-shaped relation between semantic processing demands and fMRI activation [29], whereby after a certain difficulty threshold, available neural resources from the semantic or multiple-demand control network have reached their maximum capacity and further lead to reduced activations and a decline in performance [30].

In summary, it seems that depending on the semantic task used and its perceived or actual difficulty, both increased and decreased activations have been reported in the semantic control network along with variations in consequent performances. The relationship between neural activation, task difficulty and behavioral performance is not straightforward. It is possible that the neural correlates of semantic memory remain relatively invariant throughout aging when the task is perceived as easy. On the other hand, when task difficulty or the perception of it increases, activation and behavioral performance may increase or reduce depending on the nature of the task and its level of perceived or actual difficulty, in line with CRUNCH. Accordingly, maintained performance could depend on the additional recruitment of semantic control network resources but only between certain thresholds of difficulty, before which increasing activation would be unnecessary or beneficial and after which performance would decline.

Age-related reorganization phenomena alternative to CRUNCH

A number of alternative neurofunctional reorganization phenomena have been reported to account for the evolution of general cognitive skills in aging (for reviews, see ([30], [74], [75]). Such phenomena often refer to the engagement of compensatory mechanisms and redistribution of resources through overactivation or deactivation often including in the PFC [28], [30]. For example, the HAROLD neurofunctional reorganization phenomenon refers to a hemispheric asymmetry reduction in older adults with the objective of maintaining high performance [19]. To reduce the asymmetry, brain activation can increase and/or decrease in certain brain areas by recruiting additional and alternative neuronal circuits from the contralateral hemisphere. The resulting asymmetry reduction optimizes performance, whereas elderly adults who maintain a unilateral or asymmetrical activation pattern similar to the younger, do not perform as well [19]. Several studies have recently challenged the accuracy of the HAROLD model [76], [77]. An alternative pattern of neurofunctional reorganization has been reported to occur intrahemispherically. The PASA (Posterior Anterior Shift in Aging) phenomenon provides a picture of such type of reorganization [78], describing an age-related shifting of activation from the occipitotemporal to the frontal cortex [20], [79]. PASA is considered to reflect a general age-related compensation phenomenon for processing sensory deficits by decreasing activation in occipitotemporal regions and increasing activation in frontal regions rather than reflect task difficulty [20]. A recent metaanalysis [80] on healthy aging provided support for the findings of the PASA phenomenon, however, others have challenged its compensatory claim [81]. Additionnally to the above intra- and inter-hemispheric reorganization phenomena is the 'cognitive reserve' hypothesis, which attributes successful cognitive processing in aging to complex interactions between genetic and environmental factors that influence brain reserve and the brain's ability to compensate for age-related pathologies [82]. Cognitive reserve is proposed to depend on both neural reserve and neural compensation, a distinction reflecting inter-individual variability to use resources efficiently, flexibly or differently while performing cognitive tasks but also using alternative strategies in pathological situations. Accordingly, older adults can adapt to aging and cope with increased task demands in a flexible manner by activating regions similarly to the younger or alternative ones or both.

Alternatively, neurofunctional reorganization phenomena are attributed to reduced neural efficiency, also known as dedifferentiation, resulting in reduced performance in the older [31], [32], [34], [83], [84]. According to the dedifferentiation hypothesis, aging reduces the specialization of neurons which is critical for their optimal functioning [31]. Accordingly, increased activations could be the result of randomly recruiting neurons in an attempt to meet processing demands [19], or could reflect the brain's failure to selectively recruit specific regions [34] whereas increasing task demands may aggravate the non-specificity of neural responses [85]. Evidence exists to support the idea that neural responses are less specific in older adults when compared with younger ones, as demonstrated in the ventral visual cortex during a viewing of pictures task [83], [86], during a working memory task [87] (for a review, see [88] and in motor evoked potentials [89]). It is not clear however whether this loss of neural specificity would be the result of aging or could be attributed to larger experience of older adults in recognizing objects [83]. At the same time, it is thought that both compensation and dedifferentiation phenomena may take place in the same person simultaneously in different regions [87]. The dedifferentiation account would predict a reduction in performance together with an increase in activation, thus resembling the descending part of the inverted-U shape relation between task demands and fMRI activation, as per CRUNCH.

An additional explanation for age-related functional reorganisation is that aging selectively affects the default mode network (DMN). This network is normally activated during a situation when one is not involved in any task but instead monitors their internal and external environment [7] and deactivated when performing cognitive tasks so as to reallocate attentional resources towards them [35]. It is thought that the semantic network is largely activated at rest, as individuals would be engaged in language-supported thinking when not performing specific tasks [90]. It has been found that when the task is cognitively demanding, DMN deactivations are smaller and slower for older adults, implying that they are more easily distracted whereas their capacity to inhibit irrelevant information is compromised [28], [35], [91], in line with the inhibitory control view [92] and the cognitive theory of aging [7]. In difficult semantic tasks, maintained performance was associated with increased segregation between DMN and semantic control regions at rest, whereas reduced performance was associated with increased verbal thinking at rest [93]. It is possible that aging reduces the efficiency of transferring attention away from resting areas towards task requirements, thus probably affecting the balance between DMN and task-related activity and resulting in reduced cognitive performance [7].

The neurofunctional reorganization proposals discussed above seem to be exclusive of another as they tend to focus and attribute meaningfulness in increased or decreased activation in isolated brain regions, whereas none seems to fully capture and explain age-related reorganization [94]. Several researchers have attempted to identify the 'common factor' [95] in age-related brain activation patterns to explain reorganization. Cabeza (2002) [19] considers that functional reorganization is more likely to be non-intentional and neuron-originated rather than a planned change of cognitive strategies, since it is manifested in simple tasks or following unilateral brain damage, over which one has little control. On the contrary, Reuter-Lorenz and Cappell (2008) [28] consider unlikely that such a huge variability in brain activation stems from the same 'common factor' or is due to age-related structural changes in the brain, because then it would be consistent across all tasks. Instead, aging seems to selectively affect specific regions, mainly default-mode regions and the dorsolateral PFC [7]. At the same time, inter-individual variabilities need to be emphasized when accounting for age-affected cognitive domains as some individual show faster than average decline whereas others very little [96].

Recent studies tend to combine data on functional, structural and lifetime environmental factors to explain reorganization in a more integrative manner. In this direction, the more comprehensive Scaffolding Theory on Aging and Cognition- STAC hypothesis proposes that aging is no longer characterized by uncontrollable decline of cognitive abilities because the brain develops its own resilience, repairs its deficiencies and protects its functions [28], [97]. This idea is reflected in the aging models that emphasize the plasticity of the brain due among other factors to training interventions and their impact on neural structure, as well as functional and behavioral outcomes [98]–[100]. The impact of short-term practice as well as long-life training would impact younger and older adults differently [69]. Accordingly, engaging in intellectually challenging activities and new learnings throughout the course of a lifetime but also on a shorter-term course could stimulate plasticity of the brain. The capacity of the brain to resolve the mismatch between intellectual demands and available neurofunctional resources and its capacity to trigger behavioral adaptive strategies, would define its plasticity and affect its brain knowledge systems and processing efficiency [69]. Plasticity would demonstrate itself as increased functional activation especially in regions that are most structurally affected by aging because of atrophy, loss of grey and white matter density and cortical thinning, such as in the fronto-parietal network [99]. Aging could thus be characterized by structural loss but also neural and functional adaptation to this loss, including through the utilization of new strategies [99]. Indeed, age-related overactivations seem to be a reliable and consistent pattern observed in multiple domains regardless of whether they are more localized, contralateral or seen in the fronto-parietal multiple-demand network [101]. In summary, the more adaptable and the more dynamic the brain is, the better it would maintain its cognitive abilities [102].

Specifically to semantic memory preservation in aging, it is not clear what mechanisms are in place to account for the preservation of semantic memory in aging, supported by the intersection of both domain-general and linguistic abilities [66]. Findings in the literature about the adoption of neurofunctional activation pattern during semantic processing in aging, vary. Two additional compensatory hypotheses have been proposed: the executive hypothesis refers to the recruitment of domain-general executive processes seen as overactivation in prefrontal, inferior frontal and inferior parietal brain regions to compensate for age-related cognitive decline [6], [103], as seen for example in a semantic judgment task [56]. Indeed, the metaanalysis of semantic memory studies performing activation likelihood estimation (ALE) between younger and older participants [22], found a shift in activation from semantic-specific regions to more domain-general ones, in line with the executive hypothesis. The semantic hypothesis on the other hand, also known as left anterior-posterior aging effect (LAPA), refers to the recruitment of additional semantic processes in older adults, seen as overactivation in 'language' regions in the left posterior temporo-parietal cortex [104], [105]. Given the larger decline in older adults of executive over language functions could justify this latter hypothesis considering that language is better maintained over executive processes [106]. Evidence for the semantic hypothesis was found in a study using semantic judgment task where participants had to decide if a word is an animal or not. Older participants had more bilateral parietal, temporal and left fusiform activations than younger ones who presented more dorsolateral activations, which the authors interpreted as older participants relying more on semantic processes whereas younger ones relying more on executive strategies [107]. However, language and executive functions are overall intertwined given that regions such as the left inferior frontal gyrus and the PFC are proposed to serve both executive and language functions, thus blurring the intersection between the semantic and executive hypothesis [53].

An alternative approach can be seen within the good-enough theory, which claims that participants tend to construct semantic representations which are 'good-enough' or shallow rather than more complete or detailed ones, with the aim to perform the task at hand with the least effort and save on processing resources [108]–[110]. This theory refers to overall language processing, but it could also be applied to the semantic representation of words as inferred by the semantic judgment task used for the current study. Accordingly, participants and especially older adults at increased task demands, may resort to a more 'shallow' or superficial interpretation of the semantic judgment task they are required to perform and instead of analyzing thoroughly all semantic aspects of the words they are presented with (e.g. semantic features of the apple in comparison with the grape or cherry), may bypass some aspects of the task and thus resort to a quick decision. Such a shallow processing could be manifested with decreased activation overall, as well as in the semantic control network which would be in charge of selectively controlling for semantic features while ignoring others [56]. This alternative explanation is in line with the idea that at peak levels of demand, participants may become frustrated with frequent errors or difficulty to resolve competing representations, and may deploy inefficient strategies [111].

In summary, some inconsistencies have been found in the interpretation of results, with both increased and decreased activation reported as the result of aging [7], [112]. Neurofunctional reorganization can take the form of both inter- and intra-hemispheric changes in activation and manifests as both increased and decreased activation of specific regions [7]. When performance is compromised, reduced activation is interpreted as impairment, attributed to neural decline, inefficient inhibitory control or de-differentiation [28] whereas when performance is maintained, it is claimed to be compensatory. Most studies seem to agree on increased activation, interpreting it as compensatory and positive, whether it is understood as increased attention or as suppression of distracting elements [113]. Overactivation is also found in Alzheimer’s disease (AD) and mild cognitive impairment (MCI) patients demonstrating either its compensatory role or a progressive pathology predicting further decline [34], [35]. It seems that neurofunctional reorganisation of the aging brain is more complex and further research is still required to be able to ‘draw’ a pattern of activation that integrates the existing findings in a comprehensive model and one that can be applied to semantic memory, one of the best preserved cognitive fields in aging.

Current study

The aim of this study is to identify whether aging affects the brain activity subserving semantic memory in accordance with the CRUNCH predictions, through a semantic judgment task with two levels of demands (low and high). Task demands will be manipulated through semantic distance, which is found to influence both performance and brain activation levels [49], [61], [67], [114]–[117]. We hypothesize that brain activity and behavioral performance (dependent variables) will support the CRUNCH model predictions when demands on semantic memory are manipulated in younger and older adults (age and task demands: independent variables). More specifically, it is expected that 1) the effects of semantic distance (low vs. high-demand relations) on neurofunctional activation and behavioral performance (accuracy and RTs) during the semantic judgment task will be significantly different between younger and older participant groups, with younger adults performing with higher accuracy and faster response times than older adults. Furthermore, we predict age group differences in brain activation in semantic control regions bilaterally which are sensitive to increasing task demands [24]. This will be evident with a significant interaction effect between age group and task demands within regions of interest consisting of the core semantic control regions: IFG, pMTG, pITG and dmPFC. This will support the idea of the brain’s declining ability to respond to increasing task demands with advancing age. If this interaction is not found between task demands and age, the following are expected 2) In the low-demand (LOW) condition, both younger and older participants will perform equally in terms of accuracy and with less errors than in the high-demand condition. However, it is anticipated that older adults will present longer RTs and significant increases in activation in left-lateralized semantic control regions compared to the younger participants. 3) In the high-demand (HIGH) condition, it is expected that younger adults will perform better (higher accuracy and lower RTs) and present significant activation in the left-hemisphere semantic control regions compared to older adults. Older adults are expected to exhibit reduced performance compared to younger adults (lower accuracy and higher RTs), reduced activation in left-lateralized semantic control regions, and increased activation in right-lateralized semantic control regions compared to the younger adults. To illustrate the hypothesized relations between task demands and accuracy, RTs and activation in younger and older adults, see figures 1, 2 and 3 below. The theoretical relations between task demands and activation are represented in the decrease in activation in the left hemisphere (cross-over interaction, figure 3) and the increase in activation in the right hemisphere (difference in slopes interaction, figure 4), confirming the hypothesized CRUNCH predictions. These portray the main effects of age and task demands as well as their interaction highlighted by thick lines.

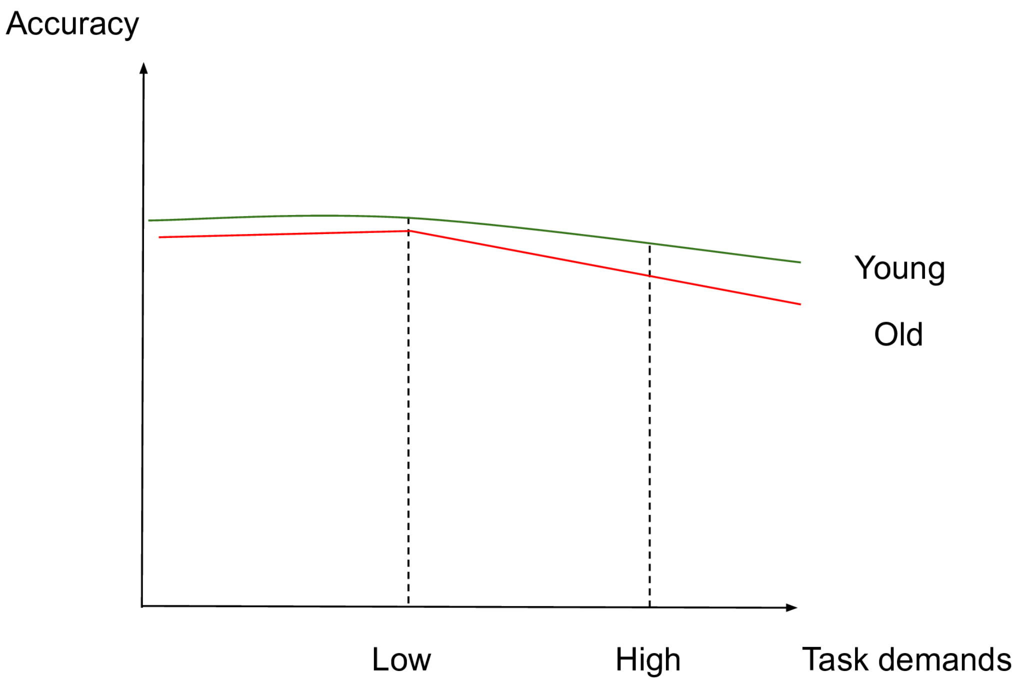

Figure 1. – Figure 1. Accuracy and task demands in younger and older adults

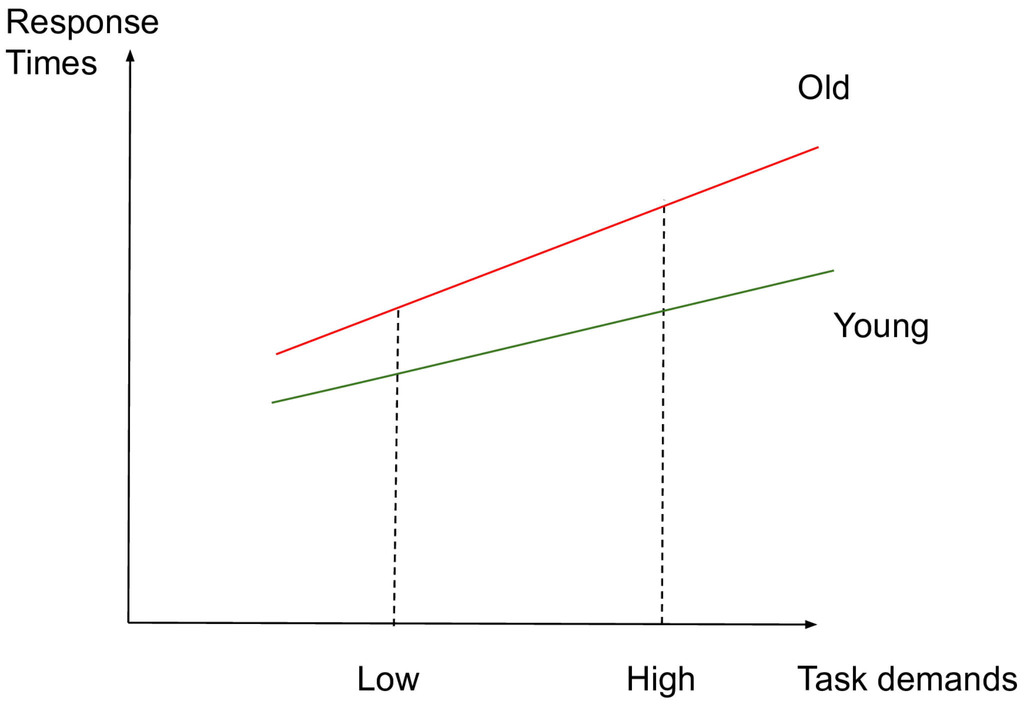

Figure 2. – Figure 2. RTs and task demands in younger and older adults

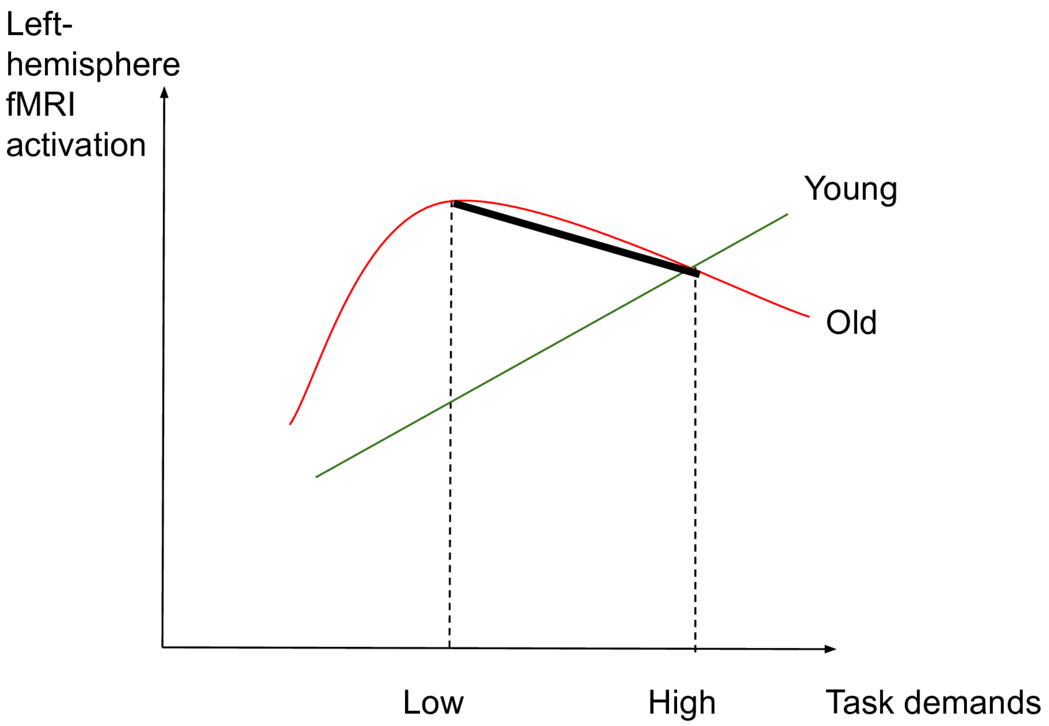

Figure 3. – Figure 3. Left-hemisphere activation and task demands in younger and older adults

Figure 4. – Figure 4. Right-hemisphere and task demands in younger and older adults

These analyses are looking for age and task demands on task performance and on brain activation in separate analyses. Follow-up exploratory analyses within the ROIs will explicitly test how differential brain activation is related to task performance. It is hypothesized that older adults who have high levels of brain activation in left-lateralized semantic control regions during the high-demand condition, similar to the younger adults, will have higher levels of task performance (reduced errors and RTs) than their counterparts whose brain activation is lower in these regions, as per the CRUNCH model, indicating that they have not yet reached their crunch point after which performance and activation decline. To accept the above hypotheses, at least one ROI from the ones mentioned is expected to be activated.

A control condition is part of the task and was designed to maximize perceptual processing requirements and minimize semantic processing ones [118], [119]. As a test of positive control, within group comparisons with the control condition are expected to show activation in the primary visual and motor cortices, which are involved with viewing of the stimuli, response preparedness and motor responses [64], [120], [121]. No CRUNCH effects are expected in the control condition. Task effects within each age group will also be tested and activation is expected to be of greater amplitude in the high vs. low condition in both younger and older age groups.

This task design utilizes explicit definitions of low and high levels of task demand. However, each individual participant will experience their own subjective level of task difficulty. Perceived difficulty of triads will be measured on a difficulty 1-7 likert-scale (e.g. 1: very easy, 7: very difficult. Subsequent analyses will explore this question with heterogeneous slopes models using individualized rescaled levels of task difficulty and will compare brain activation with performance, brain activation with perceived difficulty and performance with perceived difficulty. This approach will determine how the relationship between individual task difficulty and brain activity is affected by age group.

Proposed experiment: Materials and methods

The authors comply with the Centre de Recherche Institut Universitaire de Gériatrie de Montréal (CRIUGM) Ethics Committee and the Centre intégré universitaire de santé et de services sociaux du Centre-Sud-de-l'Île-de-Montréal requirements (CÉR-VN: Comité d'Éthique de la Recherche-Vieillissement et Neuroimagerie), in line with the principles expressed in the Declaration of Helsinki. The ethics committee of CRIUGM and CÉR-VN approved this study with number CER VN 16-17-09. The approval letter is available in the OSF repository (DOI: 10.17605/OSF.IO/F2XW9).

For all methodology aspects of this current study, compliance with the OHBM COBIDAS report/checklist [122] and guidelines [123] will be aimed for as much as possible. We will share the preprocessed functional datasets in MNI space publicly in Open Science Framework (https://osf.io/) with a digital object identifier (DOI: 10.17605/OSF.IO/F2XW9) to permanently identify the dataset [122], and we will index it at the Canadian Open Neuroscience Platform (https://conp.ca/) to increase findability. In addition, once these become available, we will upload our unthresholded statistical maps to neurovault (https://neurovault.org/), an online platform sharing activation data. Permanent links to the unthresholded statistical maps to be uploaded at Neurovault will be provided as part of the dataset deposited on the OSF, under the same DOI (DOI: 10.17605/OSF.IO/F2XW9). Data will be organized following the Brain Imaging Data Structure (BIDS) to maximize shareability. Supporting documentation for this study is available at DOI: 10.17605/OSF.IO/F2XW9.

Participants

A sample of 80 participants will be tested for this study: 40 in each group, Younger: 20-35 years old and Older: 60-75 years old (male=female). We will recruit 86 participants assuming that some will be excluded in the process due to low task performance, excessive motion or technical issues. Participants will be recruited through the Centre de Recherche Institut Universitaire de Gériatrie de Montréal (CRIUGM) ‘Banque de Participants’, but also through poster announcements posted in Montreal and in social media. Participants will be bilingual (French and English-speaking) with French as their dominant language used on a daily basis. Multilingual participants will be excluded, as speaking many languages may influence semantic performance [124]. Participants will be matched for education level with college studies (CEGEP) as a minimum level of education, since education is a measure of cognitive reserve [82]. Participants will undergo a series of neuropsychological and health tests to determine their eligibility for the study as inclusion/exclusion criteria:

- A health questionnaire (pre-screening to take place on the phone) to exclude participants with a history of dementia, drug addiction, major depression, stroke, aphasia, cardiovascular disease, diabetes, arterial hypertension or any drugs that could affect results. The pre-screening includes questions for bilingualism and use of French language, which needs to be the dominant one (inclusion criteria) (the complete questionnaire is available on osf.io, DOI: 10.17605/OSF.IO/F2XW9).

- The Edinburgh Handedness Inventory scale: participants will be right-handed with minimum score for right-handedness of 80 [125].

- The MoCA (Montreal Cognitive Assessment) test with a minimum cutoff score of 26 [126], [127].

- The MRI-compatibility checklist (Unité Neuroimagerie Fonctionnelle/UNF) test (available at https://unf-montreal.ca/forms-documents/).

The following tests will also be performed with participants:

- The Similarities (Similitudes) part of the Weschler Adult Intelligence Scale (WAIS-III) test [128], [129]

- The Pyramids and Palm Trees Test (PPTT) (version images) [130] will be used as a measure of semantic performance.

- The questionnaire Habitudes de Lecture (Reading Habits) (based on [131] as a measure of cognitive reserve [82].

Participants will provide written informed consent and will be financially compensated for their participation according to the CRIUGM and Ethics Committee policies.

Power Analysis

This sample size is based on power calculation results from an age group comparison on a similar semantic task [132]. This dataset used a Boston naming semantic task and compared healthy younger and older age groups. From this dataset effect size estimates were calculated from the contrasts for high versus low task demands within and between age groups. Effect sizes were extracted from the primary regions of interest for this study as defined by a recent meta-analysis of semantic control [24]. From the identified locations, a 10 mm cube was defined to identify the effect size at the published location, mean effect size and the robust maximum effect size in the ROI. Statistical power was then estimated using the G*Power tool [133]. Within group measures had robust effect sizes and demonstrated that sufficient power (alpha = 0.05, beta = 0.90) was achieved with a sample size of 40 participants in each group. The between group comparison of differential activation had sufficient power within bilateral temporal gyri and medial PFC. In addition, the proposed study will use more than twice the number of trials used in the data used for power estimations. This will decrease the within participant variation and will increase the power above that provided by the [132] study. The table of effect sizes used for the power analyses for within and between group comparisons are included as supplementary material at OSF.

Materials

Participants will be administered a task of semantic similarity judgment in French and that is suitable for the Quebec context developed for the current study, similar to the Pyramids and Palm Trees test (PPTT) [130]. The task proposed here involves triads of words resembling a pyramid where participants will need to judge within a time limit of 4 seconds which of the two words below (target or distractor) is more related to the word above (stimulus). Both target and distractor words are associated in a semantic relation with the stimulus word. Participants will thus be required to select which of the two competing words has a stronger semantic relationship to the stimulus word as measured by semantic distance between the stimulus and the distractor. Two types of triads exist: a) low-demand (distant) relations: the more distant the semantic relation between stimulus and distractor, the less demanding will be to select the correct target and b) high-demand (close) relations: the closer the semantic relation between stimulus and distractor, the more demanding will be to select the correct target as competition between the target and distractor words will be higher [61].

The task (150 triads in total) has two experimental conditions (120 triads: 60 low-demand (LOW) and 60 high-demand (HIGH) semantic relations) and one control condition (30 triads). For the control condition, the task will be to indicate which of the two consonant strings, which will be presented pseudo-randomly, are in the same case as the target strings (e.g. DKVP: RBNT-kgfc). The stimuli will look like Figure 5 below:

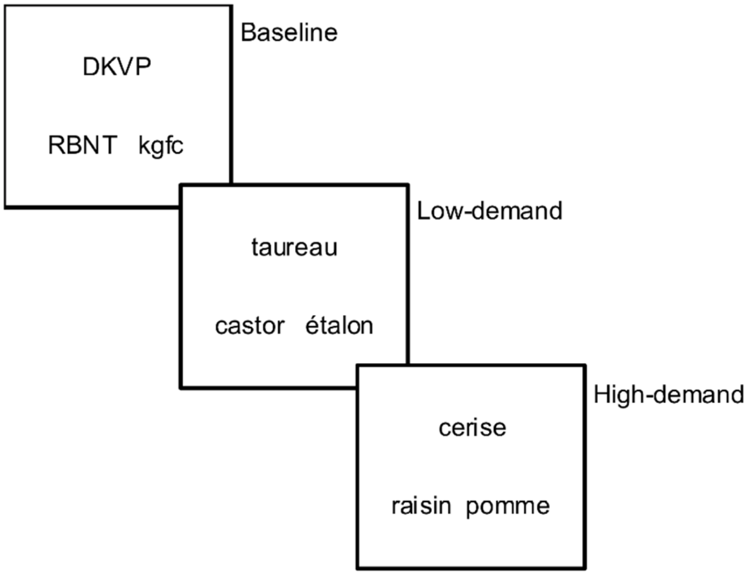

Figure 5. – Figure 5. Examples of triads

Stimuli description

The stimuli were developed for the current study. In every condition, the targets and distractors were matched for: a) Type of semantic relation: taxonomic and thematic. For thematic relations, the semantic distance was calculated with the help of a dictionary: ‘Dictionnaire des associations verbales (sémantiques) du français’ (http://dictaverf.nsu.ru/dict, version accessed on 2014), as a function of the number of respondents that associated two words together (i.e., the larger the number of respondents, the more closely associated the two words are, and vice versa). As such, a score of 1 means that only one person provided this answer (distant thematic relation) whereas a score of 100 means that 100 people provided this answer (close thematic relation). The database was open for additional contributions online as more people provided feedback on the task, as such, it is possible that today’s most frequently cited responses may be different than the ones provided when the stimuli was developed. b) Frequency, based on the Lexique 3 database referring to films [134] c) Imageability, based on the Desrochers 3600 database [135]. Additional imageability ratings were collected from 30 participants for items without ratings in the above database. A Pearson’s correlation was performed with 30 test words from the Desrochers database to confirm that the ratings given for the new words were relevant compared to the ones that already exist. Participants rating items with a correlation value less than 0.6 were excluded, as it was deemed that they were not concentrated on the task. The final imageability rating of an item was the mean of the scores given by all included participants. ANOVA and Bonferroni corrected Tukey tests were performed to ensure the matching of a target and distractor for every condition. Finally, targets and distractors were matched on d) Word length.

The stimuli were created in a gradual process, continuously testing and evaluating its adequacy and aiming for a less than 40% error rate with pilots to test it, measure response times and gather comments. Every time, the four conditions were matched and passed an ANOVA test for mean frequency, imageability and length. Also, pilot participants were asked questions about the duration of the task and the sufficiency of time to respond. To evaluate the validity of the stimuli pertaining to low vs. high demands and younger vs. older adults, a pilot evaluation of stimuli was conducted by 28 participants (14 were older adults, age range: 67-79 years old, female = 9 and 14 were younger, age range: 21-35 years old, female=10) for 60 triads (30 low-demand and 30 high-demand) using E-Prime. Repeated measures analysis of variance (ANOVA) was applied to the mean accuracy and median response data within each level of task demand (control, low, high) across the two age groups. The results are described below:

Accuracy

The Greenhouse-Geisser estimate for the departure from sphericity was $\varepsilon = 0.63$. There was not a significant interaction between age group and task demand, $F(1.27, 32.94) = 0.065$. $p = 0.85$, $\eta2 = 0.0025$. The main effect of task demand was significant, $F(1.27, 32.94) = 10.36$, $p = 0.0015$, $\eta2 = 0.28$. The estimated marginal means were: Control = 0.84, Low = 0.80 and High = 0.72. The main effect of age group was not significant, $F(1, 26) = 0.34$, $p = 0.57$, $\eta2 = 0.013$.

Response Times

The Greenhouse-Geisser estimate for the departure from sphericity was $\varepsilon = 0.54$. There was not a significant interaction between age group and task demand, $F(1.08, 28.14) = 1.14$. $p = 0.30$, $\eta2 = 0.042$. The main effect of task demand was significant, $F(1.08, 28.14) = 49.38$, $p < 0.0001$, $\eta2 = 0.66$. The estimated marginal means were: Control = 1390ms, Low = 2230ms and High = 2292ms. The main effect of age group was significant, $F(1, 26) = 4.78$, $p = 0.038$, $\eta2= 0.15$.

Based on the above pilot data, we confirm that our task includes task demands effect that impacts task performance (accuracy and RTs) differently between younger and older adults, in the expected directions.

The following definitions were used:

Low-demand (distant) triads:

- For taxonomic relations:

All items (stimulus, target, distractor) belong in the same semantic category (e.g., animals). Stimulus and target words belong in the same semantic sub-category (e.g. birds). For example, taureau: ÉTALON-castor (bull: STALLION-beaver).

- For thematic relations:

Both the target and distractor words are thematically related to the stimulus and belong in the list of answers referred by dictaverf. To ensure the largest distance possible, the target was the first adequate answer mentioned in dictaverf, whereas the distractor was the last or closest to the last answer, meaning that it had a score close to 1. For example, sorcier: village-BAGUETTE (wizard: village-WAND).

Alternatively, to ensure the largest distance possible, the following criteria were used: when the distractor word is 1 (which means only 1 person provided this answer), when the distractor word is between 2-5 and the target word is above 10, and when the difference between the target and distractor words is bigger than 100.

High-demand (close) triads:

- For taxonomic relations:

All items in the triad come from the same semantic sub-category (e.g. birds). The stimulus and target items share a visual or structural feature whereas the distractor word does not. For example, 'cerise: RAISIN-pomme' (cherry: GRAPE-apple) where cherries and grapes have a similar size and bunch structure.

- For thematic relations:

Both the target and distractor words are thematically related to the stimulus. The target was the first adequate answer mentioned in dictaverf whereas the distractor had a score smaller or equal to half of the score of the target and was bigger or equal to 4. This criterion was used to ensure that the distractor was a more frequently mentioned answer but distant enough from the target (e.g. half of the people mentioned the distractor as opposed to mentioning the target). For example, ‘enfant: JOUET-sourire’ (child: TOY-smile).

Experimental Design

Session 1: Neuropsychological tests

Participants will be recruited through the CRIUGM pool of participants and public announcements, with initial eligibility assessed through a phone interview (health questionnaire and MRI compatibility form). If eligible, the participant will partake in the first experimental session (approximately 90 minutes), during which they will sign the informed consent and MRI-compatibility forms, complete neuropsychological tests (see Participants section above) and practice with 15 practice triads (5 for every condition). Participants who qualify (meet the inclusion criteria from health questionnaire, MRI-compatibility questionnaire, MOCA and Edinburgh Handedness Inventory scale) for the fMRI scanning session following tests will proceed with the second session one week later (maximum 2 weeks later).

Session 2: fMRI scanning

For the second experimental session, the time commitment from the participant: is 90 minutes to allow for practice with triads, getting ready and leaving, following COVID-19 requirements. During this session, participants will listen to task instructions, and practice with 3 triads (1 per condition). Participants’ vision will be corrected, if necessary, with MRI-175 compatible lenses according to their prescription shared from the previous session. Additionally, pregnancy tests will be carried out when relevant, earplugs will be given to reduce machine noise and instructions will be given to remain still in the scanner while foam rubber pads in the head coil will restrict movement. Participants will then proceed with the actual task in the scanner. Stimuli will be presented with E-Prime 2.0.10.356 software run on Microsoft Windows 10 through an LCD projector projecting to a mirror over the participant’s head. Participants will select their responses using the index fingers of both hands on the MRI-compatible response box. A response on the right will be with their right hand and a response on the left with their left hand. Response data and response times (RTs) will be recorded via E-Prime for further analysis. No feedback will be shared with participants. Participant testing will alternate between younger and older adults to minimize any bias due to scanner changes/upgrades.

The semantic task will be event-related. Triads will be presented for 4 seconds, during which participants will need to make their choice by pressing on the left or the right button to select the word on the left or right respectively. A black screen will follow for approximately 2.2s (this interstimulus interval (ISI) will vary randomly between 0.67s and 3.8s to minimize possible correlations with the BOLD signal). A fixation point will appear for 1.3s to prepare the participant for the next trial. The whole trial will last between 5.97s and 9.10s, with an average of 7.5s. See below for a description of the methods used to determine the ISIs. Black screens were included at the beginning and the end of the two Runs. Information on the scanning flow is available in Figure 6 below:

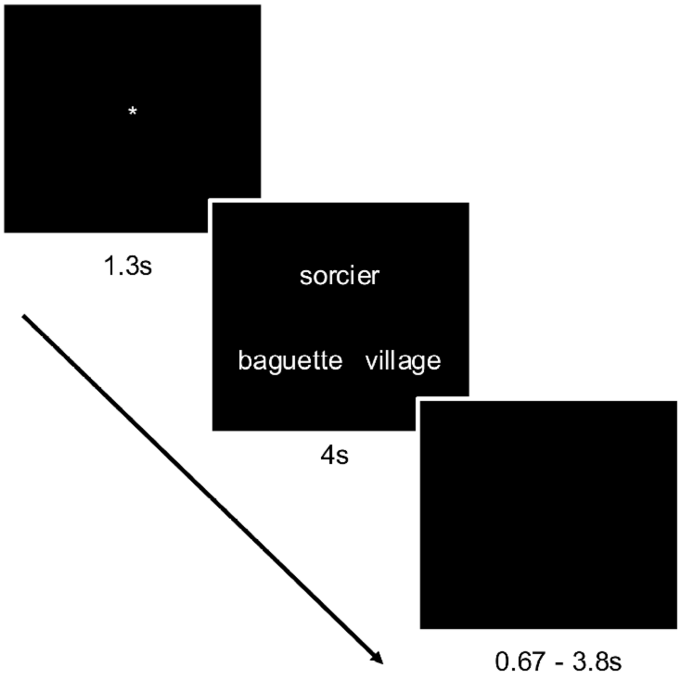

Figure 6. – Figure 6. Example of trial

The task will be split in two Runs with 75 triads per Run (30 low-demand (LOW), 30 high-demand (HIGH) and 15 control triads), interleaved in a pseudo-random fashion. The duration for every Run will be 9:45 minutes. The whole session is expected to last 45 minutes, including a 5-min break between Runs 1 and 2.

Session 3

In regards to perceived task difficulty, an additional session with participants one week following the fMRI acquisitions will take place, whereby they will rate each triad on a difficulty 1-7 Likert scale (eg. 1: very easy, 7: very difficult). We will further assess whether perceived difficulty correlates with actual performance scores (accuracy rates and RTs) and whether perceived difficulty correlates with levels of activation in the younger and older adults (e.g. whether increased levels of perceived difficulty correlate with increased RTs and reduced accuracy, as well as levels of activation in semantic control regions).

Stimuli order and ISIs

To design the experiment in a way that maximizes design efficiency, optimal trial ordering and interstimulus intervals (ISIs) were chosen [136]. The methodology used simulated designs of random ordering of the three conditions. In addition, the ISIs were randomly drawn from Gamma distributions across a range of parameter values (shape: 0.1 to 10, scale: 0.1 to 5). This approach included expected error rates produced during the stimuli pilots to maximize design efficiency in the face of errors. A total of 800,000 simulations were performed. The ISI distribution and specific list as well as the condition order in which there was the smallest decrease in required BOLD signal response for detection as errors increased were chosen. The related ISIs are uploaded to the OSF platform.

fMRI data acquisition

Functional scans will be performed on a 3Tesla Syngo MR E11 Prisma_fit Siemens MRI machine with 32 channels at UNF (Unité de Neuroimagérie Fonctionnelle), CRIUGM. The start of the stimulus presentation software will be triggered by a pulse sent from the MRI to the stimulus laptop. To detect effects between conditions and to ensure a good fMRI signal in the brain, pilot data collected using the scanning protocol described here suggested a minimum temporal signal to noise ratio (TSNR) of 20 throughout the brain [137]. Participant data will be excluded if TSNR, assessed from every participant’s time series, is below 20. We will acquire T1-weighted MRI images for co-registration with fMRI data and atlases and to identify ROIs to be used as masks in the functional data analysis. An meMPRAGE (multi-echo MPRAGE) sequence (704 total MRI files) will be acquired with 1x1x1mm resolution, 2.2s repetition time, 256x256 acquisition matrix, a

Field of View (FOV) of 256mm covering the whole head and echo times of 1.87ms, 4.11ms, 6.35ms, 8.59ms, 13ms and 15ms. The phase encoding orientation will be sagittal with a flip angle of 8 degrees.

For the functional scans (Run 1 and 2), T2-weighted BOLD data will be acquired on the entire brain (including the cerebellum) using an Echo Planar Imaging (EPI) sequence with 50 slices, resolution 2.5x2.5x3mm, echo time of 20ms, repetition time of 3s and a flip angle of 90 degrees. Field of view will be 220x220mm and the acquisition matrix will be 88x88, in AC-PC direction covering 150mm in the z-direction. Slice order will be ascending-interleaved. For each Run, 195 scans will be collected. The SIEMENS default double-echo FLASH sequence for field map distortion correction with the same parameters will be acquired after each sequence for inhomogeneity correction. Functional images will be reconstructed to the collected matrix size with no prospective motion correction. Two initial dummy scans will be collected and discarded by the MRI allowing for T1 saturation.

Proposed analyses

Behavioral data analysis

Response times and accuracy rates will be collected for every participant. Sex will be used as a covariate in all analyses. To account for performance, brain imaging analysis will focus on correct trials only ensuring that we are looking at brain activation related to accurate performance. Behavioral data (RT and accuracy) will be analyzed using mixed- design ANCOVA with age as a between-subjects factor and condition (high vs. low demands) as within-subject factor. Accuracy rates will be transformed using Fisher logit approximation to avoid ceiling effects. Group analyses of the imaging data will be performed including behavioral covariates to investigate age group differences in the relationships between brain activity and task performance. Multiple comparisons across the 40 ROIs will be made using false discovery rate adjustments. Analyses will explicitly focus on the relationships between brain activation and task performance. These analyses will identify brain regions where age group differences in activation are dependent or independent of task performance. Time-outs (delayed responses) will be modeled and analyzed separately. Any missing or incomplete data will be excluded (the whole participant).

Imaging data analysis

Preprocessing

Preprocessing image analysis will be performed with SPM12 software (141). Images will be corrected for slice timing (differences in slice acquisition time), with ascending-interleaved slice order and using the acquisition time for the middle slice as the reference. We will use field map correction to correct EPI images for distortion using the Calculate VDM toolbox and the first EPI image as reference. The gradient field map images will be pre-subtracted by the scanner to provide phase and magnitude data separately. Motion correction will be applied for within-subject registration and unwarping. Motion parameters will be used later as confound variables. Data will be visually inspected for excessive motion. Participants with estimated acute motion parameters of more than 2mm, or 1-degree rotation, between scans in any direction, will be excluded. EPI functional volumes will be registered to the average anatomical volume calculated by the machine over the 4 echoes of meMPRAGE T1-weighted anatomical scan. The mean anatomical image will be used as the reference image and as quality control. Anatomical variations between participants will be reduced by aligning the structural images to the standard space MNI template, followed by visual inspection of their overlay. An 8mm full width at half maximum (FWHM) Gaussian blur will be then applied to smooth images within each Run. The final voxel size after preprocessing will be 3x3x3 mm.

fMRI data analysis

fMRI data analysis was performed with SPM12 focusing on the ATLs bilaterally and the left TPJ as primary regions of interest (ROIs). Using files created by E-Prime during stimulus presentation, stimulus onset files will be created and regressors will be defined. For the 1st level (intrasubject) analysis, a General Linear Model (GLM) employing the canonical Hemodynamic Response Function (HRF) and its derivative both convolved with a model of the trials will be used to estimate BOLD activation for every subject as a function of condition for the fMRI task. The inclusion of the derivative term accounts for inter-individual variations in the shape of the hemodynamic response. Correct trials will be modeled separately for low demand and high demand conditions. Incorrect trials for low and high demands will be modelled together in their own regressor and not investigated further. Each participant's fMRI time series (2 Runs) will be analyzed in separate design matrices using a voxel-wise GLM (first-level models). Movement parameters obtained during preprocessing, and their first and second derivatives, will be included as covariates (regressors) of no interest to reduce the residual variance and the probability of movement-related artifacts. A high-pass filter with a temporal cut-off of 200s and a first-order autoregressive function correcting for serial autocorrelations will be applied to the data before assessing the models. Two contrasts of interest will be calculated collapsing across the two Runs. These contrasts will be low-demand, correct trials > control and high-demand, correct trials > control. These contrasts will be used for second level group analyses to compare age group and effects of task demand.

The analysis will first test for an interaction between age group and task demands. A significant finding will support hypothesis one. It is expected that a significant interaction will be driven by significant post-hoc t-tests of age group within the low-demand condition, where the older age group will have significantly greater activation than the younger age group in left semantic control regions. This finding will support hypothesis two. It is also expected that there will be a significant post-hoc t-test of age group within the high demand condition where the younger age group will have significantly greater activation than the older in the left semantic control regions. It is also expected that the older age group will have significantly greater activation in the right semantic control regions. This finding will support hypothesis three.

To account for differences in HDR between younger and older adults, the event-related first-level statistical model of the fMRI data will include the event-chain convolved with the double-Gamma hemodynamic response function and its first derivative. The inclusion of this extra regressor will capture variance in the data due to any inter-participant or inter-group variations in the shape of the hemodynamic responses.

Defining the anatomical/functional ROIs

This study's hypotheses depend on ROIs that include semantic control regions associated with low and high-demand conditions. To identify ROIs of the semantic control network demonstrating demand related differences in brain activation, the results of a recent meta-analysis will be used [24]. This analysis utilized data from 126 comparisons and 925 activation peaks and is the most comprehensive and up to date meta-analysis of semantic control networks. The results identified twenty highly significant peak locations throughout the inferior frontal gyrus, insula, orbitofrontal cortex, precentral gyrus, middle and inferior temporal gyri and the fusiform gyrus, see Table 1 [24] for specific x, y, z locations. Spheres of diameter of 10mm will be created at each of these locations and the corresponding contralateral locations, by flipping the sign of the x-coordinate. Participant level parameter estimates (contrast values) will be extracted using MarsBar [138]. This approach uses the methods presented in a recent analysis of the CRUNCH effect in a similar population [40]. Correction for multiple comparisons will use the false discovery rate across the forty ROIs [139]. Secondary, exploratory analyses of the more general semantic control network will use the maps of semantic control for domain general control as identified in the [24] metaanalysis.

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Chapter 4 – Third article. Registered report: Age-preserved semantic memory and the CRUNCH effect manifested as differential semantic control networks: an fMRI study

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Abstract

Semantic memory representations are overall well-maintained in aging whereas semantic control is thought to be more affected. To explain this phenomenon, this study aims to test the predictions of the Compensation Related Utilization of Neural Circuits Hypothesis (CRUNCH) focusing on task demands in aging as a possible framework. The CRUNCH effect would manifest itself in semantic tasks through a compensatory increase in neural activation in semantic control network regions but only up to a certain threshold of task demands. This study compares 39 younger (20-35 years old) with 39 older participants (60-75 years old) in a triad-based semantic judgment task performed in an fMRI scanner while manipulating levels of task demands (low versus high) through semantic distance. In line with the CRUNCH predictions, differences in neurofunctional activation and behavioral performance (accuracy and response times) were expected in younger versus older participants in the low- versus high-demand condition manifested in semantic control Regions of Interest. Our older participants had intact behavioral performance as proposed in the literature for semantic memory tasks (maintained accuracy and slower RTs). Age-invariant behavioral performance in the older as compared to the younger group is necessary to test the CRUNCH predictions. Our older adults were also characterized by high cognitive reserve, as shown in our neuropsychological tests. Our behavioral results confirmed our study design that the task was successful in manipulating task demands, with error rates and RTs increasing with increasing task demands in both the age groups. We did not find an interaction between age group and task demands conditions, nor a statistically significant difference in activation between the low and the high-demand conditions for either RTs or accuracy. In regards to brain activation, we did not find the expected age group by task demand interaction, nor a significant main effect of task demands condition. We found results that overall are compatible with neural activation in the semantic network and the semantic control network, largely in fronto-temporo-parietal regions. ROI analyses demonstrated significant effects (but not interaction) of task demands in the left and right inferior frontal gyrus, the left posterior middle temporal gyrus, the posterior inferior temporal gyrus and the pre-frontal gyrus. Overall, our test did not confirm the CRUNCH predictions.

Introduction

Language overall is well preserved in aging [1] and semantic memory may even improve across the lifespan [2]–[6], despite numerous neurophysiological declines in other cognitive domains that occur in the aging brain [6]–[8]. When compared with attention or memory, the relative preservation of language throughout lifetime [9] could be justified by the necessity to maintain successful communication, resulting in compensatory, flexible or atypical recruitment of neural resources [6]. Performance in terms of accuracy in semantic tasks is generally well maintained in older adults considering their more extensive experience with word use and a larger vocabulary than younger adults [2], [5], [6], [10]–[13]. Response times (RTs) however are often longer compared to younger adults [10], possibly because older adults are slower in accessing and retrieving conceptual representations from their semantic store [14]–[16], engaging the required executive function resources [17], and necessary motor responses [18]. Aside from behavioral performance, findings reported in the literature about the neural correlates sustaining semantic memory of older adults when compared with younger ones are often conflicting, depending on the task utilized, inter-individual variability and the specific age group. Though several age-focused neurofunctional reorganization phenomena (e.g. Hemispheric Asymmetry Reduction in Older Adults-HAROLD [19] and Posterior-Anterior Shift in Aging-PASA [20] aim to explain how aging affects cognitive skills in general, it is still not clear how aging impacts the underlying pattern of activation sustaining semantic memory, given its relative life-course preservation. The relative preservation of semantic memory performance in older adults when compared with other cognitive fields [9], [21], [22] could be partly justified by the proposed dual nature of the semantic memory system, as expressed within the controlled semantic cognition framework [23]–[26]. The present study focuses on the question of preservation of semantic memory in aging, defined as the 'cognitive act of accessing stored knowledge about the world' [27] using a semantic judgment task manipulating semantic control with two demand levels (low and high).

To account for conflicting findings in terms of brain activation during semantic memory tasks and the relative preservation of semantic memory in normal aging, a possible explanation is to consider it the result of adaptive mechanisms captured within the CRUNCH model (Compensation Related Utilization of Neural Circuits Hypothesis) [28]. This theory states that it is the level of task demands that impacts performance and neurofunctional activation in both younger and older individuals, whereby aging could be thought of as the expression of increasing task demands earlier than in younger adults. Accordingly, additional neural resources are recruited to attempt compensation when faced with elevated task requirements, echoing an aspect of the aging process manifestation [29], [30]. Compensation is thus defined as 'the cognition-enhancing recruitment of neural resources in response to relatively high cognitive demand' [29]. Alternatively, age-related reorganization phenomena refer to reduced neural efficiency, also known as dedifferentiation, resulting in reduced performance in older adults [31]–[34].

At the same time and as part of the age-related neurofunctional reorganization, neural resources may migrate from the default mode network (DMN) towards more urgent task requirements, which can be expressed as underactivation in such areas subserving 'redundant' tasks [28]. Indeed, the more task demands increase, the more DMN activation is expected to decrease, however this ability to 'silence' the DMN is reduced in older adults [35]. Both over- and underactivation are relevant terms referring to comparisons with optimal patterns of activation as seen in younger adults [28]. Although the CRUNCH model describes compensatory neural mechanisms, it is not without its limits. For older adults, the overactivation benefit is thought to reach a threshold beyond which additional neural resources do not suffice, after which activation declines and performance deteriorates [28]. The relationship between task demands and fMRI activation has been described as an inverted U-shaped one, with the curve of older adults being to the left of the curve of younger ones. In other words, older adults would recruit additional neural resources at lower levels of task demands, reach a maximum and decrease in activity as task demands continue to increase earlier than younger ones (see figure 3a in [29], [30]).

The CRUNCH hypothesis was conceived on evidence from a working memory study. Activation increased in the dorsolateral prefrontal cortex when accuracy was maintained and decreased when accuracy was compromised, depending on task demands, or else, the number of items successfully retained [36], [37]. Congruent results were found in another working memory study, claiming that older adults may achieve the same outcomes using different neural circuits or strategies to achieve age-matched performance [38]. However, the CRUNCH predictions were not confirmed in recent working memory studies. In a working memory study with 3 load conditions using functional near-infrared spectroscopy (fNIRS), activation in the younger progressively increased in the PFC as demands increased and performance was maintained [39]. However, in the older adults, when performance was compromised during the most difficult condition, activation in the PFC bilaterally remained high. Similarly, in a visuospatial working memory task with 4 levels of task demands, the CRUNCH predictions were not supported [40]. Instead, an increase in activation was found in a large network (premotor, prefrontal, subcortical and visual regions) however, no 'crunch' point after which activation decreases was found for the older group. Though older adults showed increased activation across regions at the higher task demands when compared with the younger ones, at the group level this difference was not significant, thus challenging the CRUNCH prediction of interaction between demands and fMRI activation.

Compatible with the CRUNCH expectations, increased activations with relatively maintained performance have been reported in frontoparietal regions in several language studies, however the results are not always consistent. More precisely, in a discourse comprehension study using fNIRS, increased activation was found in the left dorsolateral prefrontal cortex in older adults while performance was mostly equal to their younger counterparts [41]. In a sentence comprehension study, increased activation was observed in both younger and older adults during the more complex sentences in regions such as the bilateral ventral inferior frontal gyrus (IFG)/anterior insula, bilateral middle frontal gyrus (MFG), bilateral middle temporal gyrus (MTG), and left inferior parietal lobe [42]. Older adults showed increased activity compared with the younger in the IFG bilaterally and the anterior insula in the difficult condition, however their performance in terms of accuracy was not maintained. Partially compatible with CRUNCH, overactivations with maintained performance have also been observed in a picture naming study manipulating for task demands/inhibition [43]. When naming difficulty increased, both younger and older adults showed increased activation in bilateral regions such as the IFG, the anterior cingulate gyri, the pre-, post-central, supramarginal and angular gyri, together with maintained performance while response times (RTs) of older adults did not significantly increase [43]. Fewer studies exist on semantic memory in light of increasing task demands, which is the focus of the current study.

Given the large volume of concepts and processes involved, semantic memory relies on a widely distributed and interconnected mainly left-lateralized core semantic network [17], [27], [44]–[46] and bilaterally the anterior temporal lobes (ATL) proposed to act as semantic hubs [47], [48]. Semantic memory is suggested to be organized as a dual system composed of two distinctive but interacting systems, one specific to representations and one specific to cognitive-semantic control [25], [46], [49]–[53]. In other words, it is thought to include processes related to stored concept representations with their modality-specific features which would interact with control processes in charge of selecting, retrieving, manipulating and monitoring them for relevance and the specific context, while at the same time suppressing irrelevant information [24]–[26], [54]–[57]. Within the controlled semantic cognition framework [26], the semantic control network would be significantly recruited during more complex tasks underpinned by left-hemisphere regions such as the prefrontal cortex (PFC), inferior frontal gyrus (IFG), posterior middle temporal gyrus (pMTG), dorsal angular gyrus (dAG), dorsal anterior cingulate (dACC), and dorsal inferior parietal cortex (dIPC) [25], [26], [45], [46], [51], [53], [58], [59], potentially extending towards the right IFG and PFC when demands further intensify [46]. One of the most up-to-date and extensive meta-analysis of 925 peaks over 126 contrasts from 87 studies on semantic control and 257 on semantic memory, found further evidence for the regions involved in semantic control, concluding them to the left-lateralized IFG, pMTG, pITG (posterior inferior temporal gyrus), and dmPFC (dorsomedial prefrontal cortex) regions [24]. Regions related to semantic control are thought to be largely overlapped by the neural correlates of the semantic network [24] but also thought to largely overlap with regions related to the ‘multiple-demand’ frontoparietal cognitive control network involved in planning and regulating cognitive processes [26], [60].

Differential recruitment has been found for easy and harder semantic tasks in younger adults including recruitment of semantic control regions for the latter. In a study using transcranial magnetic stimulation (TMS) on the roles of the angular gyrus (AG) and the pMTG, participants were required to perform identity or thematic matchings that were either strongly or weakly associated, based on ratings previously collected and where RTs were used as a function of association strength. Stimulation to the AG and the pMTG confirmed their roles in more automatic and more controlled retrieval respectively [58]. An fMRI study used a triad-based semantic similarity judgment task to compare between concrete and abstract nouns (imageability) while manipulating additionally for difficulty. Difficulty was based on semantic similarity scores based on ratings of words, and for every triad, a semantic similarity score was computed to classify them as easy or hard. Increased activations were found during the hard triads and regardless of word imageability, in regions modulating attention and response monitoring such as bilaterally in the cingulate sulcus, the medial superior frontal gyrus and left dorsal inferior frontal gyrus [61]. In a triad-based synonym judgment task comparing concrete versus abstract words, where triads were categorized as easy or difficult based on the respective response time in relation to the group mean, a main effect of difficulty was confirmed, with increased activations reported in the left temporal pole, left IFG and left MTG [62]. In a triad-based task where participants were requested to match words for colour and semantic relation to probe more automatic or controlled semantic processing respectively, greater activation was found in the IFG and IPS during the more difficult triads that were based on colour-matching. Accuracy was overall maintained equally across conditions but there were more errors and longer RTs in the ‘difficult’ colour condition, lending support to the controlled semantic cognition idea [50]. There is therefore evidence to support an increase in activation in semantic control regions when semantic processing demands increase, which could be attributed to ‘matching’ task requirements with available neural resources, in line with CRUNCH predictions. When it comes to aging, though the system related to representations is thought to be well-maintained, the system related to cognitive-semantic control is thought to be more affected [23]. This study focuses on how the relation between semantic control network activation and increasing task demands is affected by aging.

The neural correlates sustaining semantic memory are thought to be largely age-invariant, with only small differences existing in neural recruitment as a function of age [16], [22], [63]–[66]. In a recently conducted meta-analysis of 47 neuroimaging studies comparing younger and older people, increases in activation in semantic control regions in older adults were reported when compared with younger ones, while accuracy was found to be equal between the two groups [22]. Though this increase in activation could be attributed to compensatory accounts, it could also reflect age-related loss of neuronal specificity or efficiency [22]. Several studies report activation and performance results in line with the compensatory overactivation account. In a semantic judgment task, participants had to decide whether two words share a common feature (shape or color) with their performance being categorized as better or worse based on a split from behavioral data [56]. In better performing older adults, activation was increased relative to younger adults in control regions such as the inferior parietal and bilateral premotor cortex, regions important for executive functions and object visual processing as well as relative to poorer performing older adults, in the premotor, inferior parietal and lateral occipital cortex. A further analysis for gray matter found that increased gray matter in the right precentral gyrus was associated with maintained performance [56]. In a semantic categorization study, older participants performed as accurately as the younger ones but had slower RTs. Their maintained performance was correlated with activation in a larger network than the one of younger ones, including parts of the semantic control network (such as left frontal and superior parietal cortex, left anterior cingulate, right angular gyrus and right superior temporal cortex), which was reportedly atypical and excluded the PFC [44].

Specifically to left IFG recruitment, believed to be in charge of top-down semantic control [45], [49], [51], [67], its association with the ‘difficult’ condition has been reported in several studies. In a triad-based semantic judgment task evaluating for rhyme, semantic and perceptual similarity, interaction and conjunction analyses revealed a significant interaction between age and the high-load semantic condition. Older adults overrecruited the control-related regions of the left IFG, left fusiform gyrus and posterior cingulate bilaterally, when competition demands increased while their accuracy was even better than their younger counterparts [66]. In a picture-naming task, older adults recruited overall larger frontal areas than younger ones in both hemispheres. Though the bilateral -and not the solely-left- recruitment of the IFG was beneficial to performance of older participants, the recruitment of other right-hemisphere regions was negatively correlated with accuracy [16]. The authors provided support to the finding that the neural substrates for semantic memory representations are intact in older adults whereas it is the executive aspect of language functions, including accessing and manipulating verbal information, that are most affected by aging [16]. In another study with younger adults only, aiming to dissociate the role of the IFG in phonologically versus semantically cued word retrieval, the recruitment of anterior-dorsal parts of the LIFG was associated with the high task demands condition in the semantic fluency condition, while performance was maintained [68].

Evidence therefore exists for a correlation between an increase in activation of semantic control regions when faced with increased task demands, which could be indicative of the compensation account to favor semantic memory performance in both younger and older adults, and potentially reflecting the ascending part of the U-shaped relation between fMRI activation and task demands. Attributing however a causal relation between increased activation in the semantic control network and compensation is not straightforward. Distinguishing between the compensation and de-differentiation accounts can be challenging, as merely correlating brain activation with behavioral outcomes to claim compensation is methodologically incomplete [69], [70]. Many studies do not manipulate or cannot be compared for task demands and thus interpreting results that correlate neural activation with behavior can be confusing [53]. For example, in a study where task demands are lower, reorganization may be interpreted as compensatory when performance is maintained whereas when performance is more affected, it can be attributed to dedifferentiation. Numerous methodological caveats exist when attempting to allocate meaning a posteriori to age-related reorganization, given the observational nature of neuroscience, but also the need for more robust methodological designs, including longitudinal studies that measure in-person changes, between regions comparison and better analytic approaches (for a review see

[70]). Correlating increased activation with improved performance at a single point in time and attributing it to compensation would require additional measures, also given that compensation may be attempted or only partly successful [30], [71].

According to the CRUNCH theory, the compensatory increase in activation of semantic control regions is thought to reach a plateau beyond which additional resources no longer benefit performance [28]. As such, reduced activation in cognitive control regions when semantic processing demands increase has also been reported. According to CRUNCH, this reduced activation could be interpreted as neural resources having already reached their maximum capacity and no longer being sufficient to successfully sustain compensation for the task [28]. Indeed, the meta-analysis of 47 neuroimaging studies comparing activation in younger and older adults (mean age of younger participants: 26 years (SD=4.1) and mean age of older participants: 69.1 (SD=4.7) during semantic processing tasks, also reported decreased activation in the older adults in typical semantic control regions in the left hemisphere (IFG, pMTG, ventral occipitotemporal regions and dIPC) together with increased activation in 'multiple-demand network' regions in the right hemisphere (IFG, right superior frontal and parietal cortex including the middle frontal gyrus, dIPC and dACC) especially when performance was sub-optimal [22]. In a semantic judgment task (living versus non-living judgement of words) study with two levels of difficulty and four across-the-lifespan age groups, activation outside the core semantic network increased with age linearly and contralaterally towards the right hemisphere (right parietal cortex and middle frontal gyrus) in the easy condition, while accuracy was maintained [64]. In the difficult condition however, RTs were slower and reduced activation was observed in older participants in semantic control regions, namely the frontal, parietal and cingulate cortex regions, suggesting a declining ability of brain to respond to increasing task demands by mobilizing semantic control network resources as age increases [64].

Similarly, increased activation in right-lateralized semantic control regions was detrimental to performance in both younger and older participants in a word generation study manipulating for task difficulty [72]. Indeed, activation in the ventral IFG bilaterally was correlated with difficult items as opposed to easier ones and reduced performance irrespective of age. In a verbal fluency study by the same group using correlation analysis, a strong negative correlation was found between performance and activation in the right inferior and middle frontal gyrus ROIs [73]. Older adults demonstrated a more bilateral activation than younger ones especially in the right inferior and middle frontal regions whereas their performance during the semantic task was negatively impacted. However, this right-lateralized semantic control network increase in activation together with a drop in performance has not been consistently documented. For example, in a semantic judgment task on word concreteness using magnetic encephalography (MEG), older participants overactivated the right posterior middle temporal gyrus, inferior parietal lobule, angular gyrus and the left ATL and underactivated the control-related left IPC as a result of increased task demands while their performance was equivalent to the younger, thus lending support to compensatory accounts [65]. According to CRUNCH, the above findings could be interpreted within the descending part of the inverted U-shaped relation between semantic processing demands and fMRI activation [29], whereby after a certain difficulty threshold, available neural resources from the semantic or multiple-demand control network have reached their maximum capacity and further lead to reduced activations and a decline in performance [30].

In summary, it seems that depending on the semantic task used and its perceived or actual difficulty, both increased and decreased activations have been reported in the semantic control network along with variations in consequent performances. The relationship between neural activation, task difficulty and behavioral performance is not straightforward. It is possible that the neural correlates of semantic memory remain relatively invariant throughout aging when the task is perceived as easy. On the other hand, when task difficulty or the perception of it increases, activation and behavioral performance may increase or reduce depending on the nature of the task and its level of perceived or actual difficulty, in line with CRUNCH. Accordingly, maintained performance could depend on the additional recruitment of semantic control network resources but only between certain thresholds of difficulty, before which increasing activation would be unnecessary or beneficial and after which performance would decline.

Age-related reorganization phenomena alternative to CRUNCH

A number of alternative neurofunctional reorganization phenomena have been reported to account for the evolution of general cognitive skills in aging (for reviews, see ([30], [74], [75]). Such phenomena often refer to the engagement of compensatory mechanisms and redistribution of resources through overactivation or deactivation often including in the PFC [28], [30]. For example, the HAROLD neurofunctional reorganization phenomenon refers to a hemispheric asymmetry reduction in older adults with the objective of maintaining high performance [19]. To reduce the asymmetry, brain activation can increase and/or decrease in certain brain areas by recruiting additional and alternative neuronal circuits from the contralateral hemisphere. The resulting asymmetry reduction optimizes performance, whereas elderly adults who maintain a unilateral or asymmetrical activation pattern similar to the younger, do not perform as well [19]. Several studies have recently challenged the accuracy of the HAROLD model [76], [77]. An alternative pattern of neurofunctional reorganization has been reported to occur intrahemispherically. The PASA (Posterior Anterior Shift in Aging) phenomenon provides a picture of such type of reorganization [78], describing an age-related shifting of activation from the occipitotemporal to the frontal cortex [20], [79]. PASA is considered to reflect a general age-related compensation phenomenon for processing sensory deficits by decreasing activation in occipitotemporal regions and increasing activation in frontal regions rather than reflect task difficulty [20]. A recent metaanalysis [80] on healthy aging provided support for the findings of the PASA phenomenon, however, others have challenged its compensatory claim [81]. Additionnally to the above intra- and inter-hemispheric reorganization phenomena is the ‘cognitive reserve’ hypothesis, which attributes successful cognitive processing in aging to complex interactions between genetic and environmental factors that influence brain reserve and the brain’s ability to compensate for age-related pathologies [82]. Cognitive reserve is proposed to depend on both neural reserve and neural compensation, a distinction reflecting inter-individual variability to use resources efficiently, flexibly or differently while performing cognitive tasks but also using alternative strategies in pathological situations.

Accordingly, older adults can adapt to aging and cope with increased task demands in a flexible manner by activating regions similarly to the younger or alternative ones or both.

Alternatively, neurofunctional reorganization phenomena are attributed to reduced neural efficiency, also known as dedifferentiation, resulting in reduced performance in the old [31], [32], [34], [83], [84]. According to the dedifferentiation hypothesis, aging reduces the specialization of neurons which is critical for their optimal functioning [31]. Accordingly, increased activations could be the result of randomly recruiting neurons in an attempt to meet processing demands [19], or could reflect the brain's failure to selectively recruit specific regions [34] whereas increasing task demands may aggravate the non-specificity of neural responses [85]. Evidence exists to support the idea that neural responses are less specific in older adults when compared with younger ones, as demonstrated in the ventral visual cortex during a viewing of pictures task [83], [86], during a working memory task [87] (for a review, see [88] and in motor evoked potentials [89]). It is not clear however whether this loss of neural specificity would be the result of aging or could be attributed to larger experience of older adults in recognizing objects [83]. The authors however consider the latter explanation unlikely, as longer experience is expected to enhance rather than compromise the selectivity of neural responses. At the same time, it is thought that both compensation and dedifferentiation phenomena may take place in the same person simultaneously in different regions [87]. The dedifferentiation account would predict a reduction in performance together with an increase in activation, thus resembling the descending part of the inverted-U shape relation between task demands and fMRI activation, as per CRUNCH.

An additional explanation for age-related functional reorganisation is that aging selectively affects the default mode network (DMN). This network is normally activated during a situation when one is not involved in any task but instead monitors their internal and external environment [7] and deactivated when performing cognitive tasks so as to reallocate attentional resources towards them [35]. It is thought that the semantic network is largely activated at rest, as individuals would be engaged in language-supported thinking when not performing specific tasks [90]. It has been found that when the task is cognitively demanding, DMN deactivations are smaller and slower for older adults, implying that they are more easily distracted whereas their capacity to inhibit irrelevant information is compromised [28], [35], [91], in line with the inhibitory control view [92] and the cognitive theory of aging [7]. In difficult semantic tasks, maintained performance was associated with increased segregation between DMN and semantic control regions at rest, whereas reduced performance was associated with increased verbal thinking at rest [93]. It is possible that aging reduces the efficiency of transferring attention away from resting areas towards task requirements, thus probably affecting the balance between DMN and task-related activity and resulting in reduced cognitive performance [7].

The neurofunctional reorganization proposals discussed above seem to be exclusive of one another as they tend to focus and attribute meaningfulness in increased or decreased activation in isolated brain regions, whereas none seems to fully capture and explain age-related reorganization [94]. Several researchers have attempted to identify the 'common factor' [95] in age-related brain activation patterns to explain reorganization. Cabeza (2002) [19] considers that functional reorganization is more likely to be non-intentional and neuron-originated rather than a planned change of cognitive strategies, since it is manifested in simple tasks or following unilateral brain damage, over which one has little control. On the contrary, Reuter-Lorenz and Cappell (2008) [28] consider unlikely that such a huge variability in brain activation stems from the same 'common factor' or is due to age-related structural changes in the brain, because then it would be consistent across all tasks. Instead, aging seems to selectively affect specific regions, mainly default-mode regions and the dorsolateral PFC [7] whereas inter-individual variabilities need to be emphasized when accounting for age-affected cognitive domains [96].

Recent studies tend to combine data on functional, structural and lifetime environmental factors to explain reorganization in a more integrative manner. In this direction, the more comprehensive Scaffolding Theory on Aging and Cognition- STAC hypothesis proposes that aging is no longer characterized by uncontrollable decline of cognitive abilities because the brain develops its own resilience, repairs its deficiencies and protects its functions [28], [97]. This idea is reflected in the aging models that emphasize the plasticity of the brain due among other factors to training interventions and their impact on neural structure, as well as functional and behavioral outcomes [98]– [100]. The impact of short-term practice as well as long-life training would impact younger and older adults differently [69]. Accordingly, engaging in intellectually challenging activities and new learnings throughout the course of a lifetime but also on a shorter-term course could stimulate plasticity of the brain. The capacity of the brain to resolve the mismatch between intellectual demands and available neurofunctional resources and its capacity to trigger behavioral adaptive strategies, would define its plasticity and affect its brain knowledge systems and processing efficiency [69]. Plasticity would demonstrate itself as increased functional activation especially in regions that are most structurally affected by aging because of atrophy, loss of grey and white matter density and cortical thinning, such as in the fronto-parietal network [99]. Aging could thus be characterized by structural loss but also neural and functional adaptation to this loss, including through the utilization of new strategies [99]. Indeed, age-related overactivations seem to be a reliable and consistent pattern observed in multiple domains regardless of whether they are more localized, contralateral or seen in the fronto-parietal multiple-demand network [101]. In summary, the more adaptable and the more dynamic the brain is, the better it would maintain its cognitive abilities [102].

Specifically to semantic memory preservation in aging, it is not clear what mechanisms are in place to account for the preservation of semantic memory in aging, supported by the intersection of both domain-general and linguistic abilities [66]. Findings in the literature about the adoption of neurofunctional activation pattern during semantic processing in aging, vary. Two additional compensatory hypotheses have been proposed: the executive hypothesis refers to the recruitment of domain-general executive processes seen as overactivation in prefrontal, inferior frontal and inferior parietal brain regions to compensate for age-related cognitive decline [6], [103], as seen for example in a semantic judgment task [56]. Indeed, the meta-analysis of semantic memory studies performing activation likelihood estimation (ALE) between younger and older participants [22], found a shift in activation from semantic-specific regions to more domain-general ones, in line with the executive hypothesis. The semantic hypothesis on the other hand, also known as left anterior-posterior aging effect (LAPA), refers to the recruitment of additional semantic processes in older adults, seen as overactivation in 'language' regions in the left posterior temporo-parietal cortex [104], [105]. Given the larger decline in older adults of executive over language functions could justify this latter hypothesis considering that language is better maintained over executive processes [106]. Evidence for the semantic hypothesis was found in a study using semantic judgment task where participants had to decide if a word is an animal or not. Older participants had more bilateral parietal, temporal and left fusiform activations than younger ones who presented more dorsolateral activations, which the authors interpreted as older participants relying more on semantic processes whereas younger ones relying more on executive strategies [107]. However, language and executive functions are overall intertwined given that regions such as the left inferior frontal gyrus and the PFC are proposed to serve both executive and language functions, thus blurring the intersection between the semantic and executive hypothesis [53].

An alternative approach can be seen within the good-enough theory, which claims that participants tend to construct semantic representations which are 'good-enough' or shallow rather than more complete or detailed ones, with the aim to perform the task at hand with the least effort and save on processing resources [108]– [110]. This theory refers to overall language processing, but it could also be applied to the semantic representation of words as inferred by the semantic judgment task used for the current study. Accordingly, participants and especially older adults at increased task demands, may resort to a more 'shallow' or superficial interpretation of the semantic judgment task they are required to perform and instead of analyzing thoroughly all semantic aspects of the words they are presented with (e.g., semantic features of the apple in comparison with the grape or cherry), may bypass some aspects of the task and thus resort to a quick decision. Such a shallow processing could be manifested with decreased activation overall, as well as in the semantic control network which would be in charge of selectively controlling for semantic features while ignoring others [56]. This alternative explanation is in line with the idea that at peak levels of demand, participants may become frustrated with frequent errors or difficulty to resolve competing representations, and may deploy inefficient strategies [111].

In summary, some inconsistencies are found in interpretation of results, with both increased and decreased activation reported as the result of aging [7], [112]. Neurofunctional reorganization can take the form of both inter- and intra-hemispheric changes in activation and manifests as both increased and decreased activation of specific regions [7]. When performance is compromised, reduced activation is interpreted as impairment, attributed to neural decline, inefficient inhibitory control or de-differentiation [28] whereas when performance is maintained, it is claimed to be compensatory. Most studies seem to agree on increased activation, interpreting it as compensatory and positive, whether it is understood as increased attention or as suppression of distracting elements [113]. Overactivation is also found in Alzheimer’s disease (AD) and mild cognitive impairment (MCI) patients demonstrating either its compensatory role or a progressive pathology predicting further decline [34], [35]. It seems that neurofunctional reorganisation of the aging brain is more complex and further research is still required to be able to ‘draw’ a pattern of activation that integrates the existing findings in a comprehensive model and one that can be applied to semantic memory, one of the best-preserved cognitive fields in aging.

Current study

The aim of this study is to identify whether aging affects the brain activity subserving semantic memory in accordance with the CRUNCH predictions, through a semantic judgment task with two levels of demands (low and high). Task demands will be manipulated through semantic distance, which is found to influence both performance and brain activation levels [49], [61], [67], [114]–[117]. We hypothesize that brain activity and behavioral performance (dependent variables) will support the CRUNCH model predictions when demands on semantic memory are manipulated in younger and older adults (age and task demands: independent variables). More specifically, it is expected that 1) the effects of semantic distance (low versus high-demand relations) on neurofunctional activation and behavioral performance (accuracy and RTs) during the semantic judgment task will be significantly different between younger and older participant groups, with younger adults performing with higher accuracy and faster response times than older adults. Furthermore, we predict age group differences in brain activation in semantic control regions bilaterally which are sensitive to increasing task demands [24]. This will be evident with a significant interaction effect between age group and task demands within regions of interest consisting of the core semantic control regions: IFG, pMTG, pITG and dmPFC. This will support the idea of the brain's declining ability to respond to increasing task demands with advancing age. If this interaction is not found between task demands and age, the following are expected 2) In the low-demand (LOW) condition, both younger and older participants will perform equally in terms of accuracy and with less errors than in the high-demand condition. However, it is anticipated that older adults will present longer RTs and significant increases in activation in left-lateralized semantic control regions compared to the younger participants. 3) In the high-demand (HIGH) condition, it is expected that younger adults will perform better (higher accuracy and lower RTs) and present significant activation in the left-hemisphere semantic control regions compared to older adults. Older adults are expected to exhibit reduced performance compared to younger adults (lower accuracy and higher RTs), reduced activation in left-lateralized semantic control regions, and increased activation in right-lateralized semantic control regions compared to the younger adults. To illustrate the hypothesized relations between task demands and accuracy, RTs and activation in younger and older adults, see figures 1, 2 and 3 below. The proposed theoretical relations between task demands and activation are represented in the decrease in activation in the left hemisphere (cross-over interaction, figure 3) and the increase in activation in the right hemisphere (difference in slopes interaction, figure 4), supporting the hypothesized CRUNCH predictions. These portray the main effects of age and task demands as well as their interaction highlighted by thick lines.

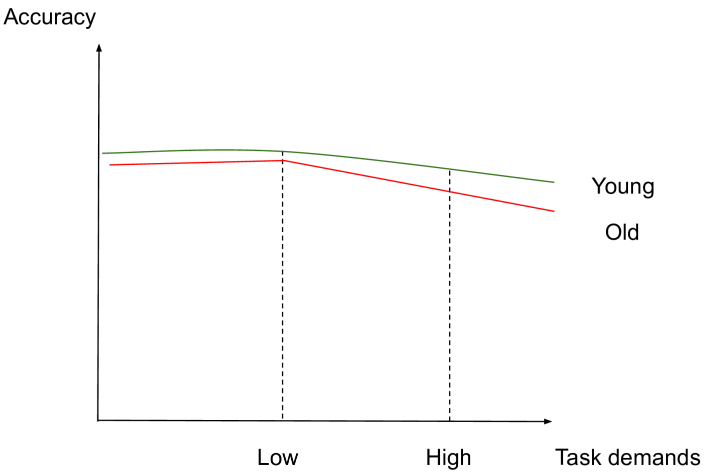

Figure 7. – Figure 1: Accuracy and task demands in younger and older adults

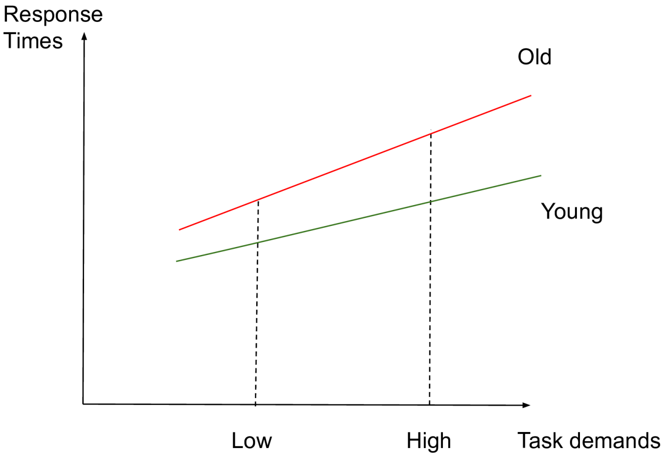

Figure 8. – Figure 2: RTs and task demands in younger and older adults

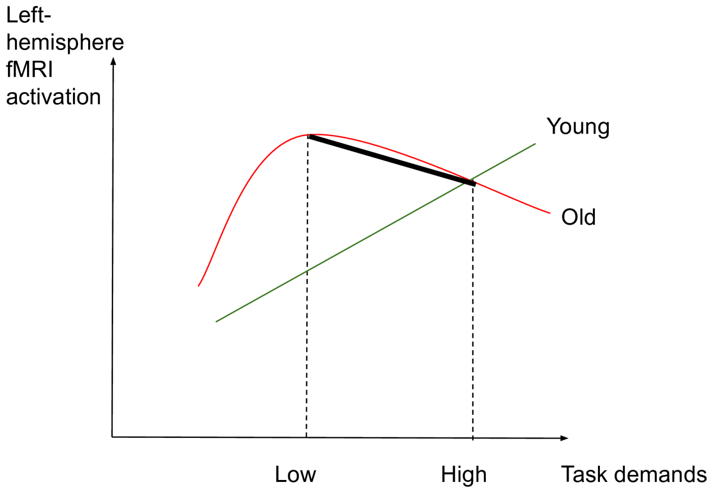

Figure 9. – Figure 3: Left-hemisphere activation and task demands in younger and older adults

Figure 10. – Figure 4: Right-hemisphere and task demands in younger and older adults

These analyses are looking for age and task demands effects on task performance and on brain activation in separate analyses. Follow-up exploratory analyses within the ROIs will explicitly test how differential brain activation is related to task performance. It is hypothesized that older adults who have high levels of brain activation in left-lateralized semantic control regions during the high-demand condition, similar to the younger adults, will have higher levels of task performance (reduced errors and RTs) than their counterparts whose brain activation is lower in these regions, as per the CRUNCH model, indicating that they have not yet reached their “crunch” point after which performance and activation decline. To support the above hypotheses, at least one ROI from the ones mentioned is expected to be activated.

A control condition is part of the task and was designed to maximize perceptual processing requirements and minimize semantic processing ones [118], [119]. As a test of positive control, within group comparisons with the control condition participants are expected to show activation in the primary visual and motor cortices, which are involved with viewing of the stimuli, response preparedness and motor responses [64], [120], [121]. No CRUNCH effects are expected in the control condition. Task effects within each age group will also be tested and activation is expected to be of greater amplitude in the high versus low condition in both younger and older age groups.

This task design utilizes explicit definitions of low and high levels of task demand. However, each individual participant will experience their own subjective level of task difficulty. Perceived difficulty of triads will be measured on a difficulty 1-7 likert-scale (e.g. 1: very easy, 7: very difficult). Subsequent analyses will explore this question with heterogeneous slopes models using individualized rescaled levels of task difficulty and will compare brain activation with performance, brain activation with perceived difficulty and performance with perceived difficulty. This approach will determine how the relationship between individual task difficulty and brain activity is affected by age group.

Materials and methods

The authors comply with the Centre de Recherche Institut Universitaire de Gériatrie de Montréal (CRIUGM) Ethics Committee and the Centre intégré universitaire de santé et de services sociaux du Centre-Sud-de-l'Île-de-Montréal requirements (CÉR-VN: Comité d'Éthique de la Recherche-Vieillissement et Neuroimagerie), in line with the principles expressed in the Declaration of Helsinki. The ethics committee of CRIUGM and CÉR-VN approved this study with number CER VN 16-17-09. The approval letter is available in the OSF repository (DOI: 10.17605/OSF.IO/F2XW9).

For all methodology aspects of this current study, compliance with the OHBM COBIDAS report/checklist [122] and guidelines [123] was aimed for as much as possible (full adherence, especially to the non-mandatory components, would require extensive additional procedures e.g., collecting IQ from participants). We share the preprocessed functional datasets in MNI space publicly in Open Science Framework (https://osf.io/) with a digital object identifier (DOI: 10.17605/OSF.IO/F2XW9) to permanently identify the dataset [122], and we index it at the Canadian Open Neuroscience Platform (https://conp.ca/) to increase findability. In addition, once these become available, we upload our unthresholded statistical maps to neurovault (https://neurovault.org/), an online platform sharing activation data. Permanent links to the unthresholded statistical maps to be uploaded at Neurovault will be provided as part of the dataset deposited on the OSF, under the same DOI (DOI: 10.17605/OSF.IO/F2XW9). Data are organized following the Brain Imaging Data Structure (BIDS) to maximize shareability. Supporting documentation for this study is available at DOI: 10.17605/OSF.IO/F2XW9.

Participants

A sample of 80 participants was required to be tested for this study: 40 in each group, Younger: 20-35 years old and Older: 60-75 years old (male=female). We contacted 265 participants in total (194 younger and 71 older). We recruited 84 (instead of 86 initially planned) participants assuming that some would be excluded in the process due to low task performance, excessive motion or technical issues. Recruitment took place from 17th June to 25 December 2021. From the 84 participants, 3 participants (2 older male, 1 younger female) were excluded as data (either behavioural or imaging) were missing, and 4 participants (3 younger females and 1 older male) were excluded due to excessive motion. We ended up with 78 participants in total, 39 younger and 39 older adults).

Participants were recruited through the Centre de Recherche Institut Universitaire de Gériatrie de Montréal (CRIUGM) 'Banque de Participants', and also through poster announcements posted in Montreal and on social media. Participants were bilingual (French and English-speaking or another second language) with French as their dominant language used on a daily basis. Multilingual participants were excluded, as speaking many languages may influence semantic performance [124]. Participants were matched for education level with college studies (CEGEP) as a minimum level of education, since education is a measure of cognitive reserve [82].

The inclusion criterion 'Born in Quebec' was finally dropped, as exclusion criteria were deemed too strict for recruitment (the Born in Quebec' criterion had been initially adopted to account for linguistic differences between French in Quebec versus other francophone-speaking countries, including France). The COVID-19 situation deemed the overall recruitment and testing of participants particularly challenging, given the need to minimize exposure of older adults as well as the overbooking of the MRI marchine at UNF, which left few available slots for scanning, overall causing delays.

Participants underwent the following series of neuropsychological and health tests to determine their eligibility for the study as inclusion/exclusion criteria:

- A health questionnaire (pre-screening took place on the phone) to exclude participants with a history of dementia, drug addiction, major depression, stroke, aphasia, cardiovascular disease, diabetes, arterial hypertension or taking any drugs that could affect results. The pre-screening included questions for bilingualism and use of French language, which needed to be the dominant one (inclusion criteria) (the complete questionnaire is available on osf.io, DOI: 10.17605/OSF.IO/F2XW9).

- The Edinburgh Handedness Inventory scale: participants were right-handed with minimum score for right-handedness of 80 [125].
- The MoCA (Montreal Cognitive Assessment) test with a minimum cutoff score of 26 [126], [127].
- The MRI-compatibility checklist (Unité Neuroimagerie Fonctionnelle/UNF) test (available at https://unf-montreal.ca/forms-documents/).

The following tests were also performed with participants:

- The Similarities (Similitudes) part of the Weschler Adult Intelligence Scale (WAIS-III) test [128], [129]
- The Pyramids and Palm Trees Test (PPTT) (picture version) [130] was used as a measure of semantic performance.
- The questionnaire Habitudes de Lecture (Reading Habits) (based on [131] as a measure of cognitive reserve [82].

Participants provided written informed consent and were financially compensated for their participation according to the CRIUGM and Ethics Committee policies.

Due to practical circumstances resulting from COVID-19, minor adjustments took place in the original protocol in regards to the timing of sessions.

Tableau 1. – Table 1 : Participants' demographic and neuropsychological scores

	Younger	Older
Mean Age	23.9	66.7
Sex (M/F)	17/22	14/25

Mean Years of education	17.3	17.2
Mean frequency of use of French language	3.3	3.4
Mean frequency of use of English language	2.15	1.07
Mean WAIS-III (/33)	17	17.4
Mean PPTT (/52)	49.8	50.9
Reading habits at 6 yrs old*	4.1	3.1
Reading habits at 12 yrs old	3.3	3
Reading habits at 18 yrs old	3.3	3.5
Reading habits at 40 yrs old	N/A	3.4
Reading habits currently	3.1	3.5

* Reading habits: 0: never 1: once per year or less 2: some times per year 3: some times per month 4: once or twice per week 5: everyday

Power Analysis

This sample size was based on power calculation resulting from an age group comparison on a similar semantic task [132]. This dataset used a Boston naming semantic task and compared healthy younger and older age groups. From this dataset effect size estimates were calculated from the contrasts for high versus low task demands within and between age groups. Effect sizes were extracted from the primary regions of interest for this study as defined by a recent meta-analysis of semantic control [24]. From the identified locations, a 10 mm cube was defined to identify the effect size at the published location, mean effect size and the robust maximum effect size in the ROI. Statistical power was then estimated using the G*Power tool [133]. Within group measures had robust effect sizes and demonstrated that sufficient power (alpha = 0.05, beta = 0.90) was achieved with a sample size of 40 participants in each group. The between group comparison of differential activation had sufficient power within bilateral temporal gyri and medial PFC. In addition, the proposed study used more than twice the number of trials used in the data used for power estimations. This would decrease the within participant variation and would increase the power above that provided by the [132] study. The table of effect sizes used for the power analyses for within and between group comparisons are included as supplementary material at OSF.

Materials

Participants were administered a task of semantic similarity judgment in French and that is suitable for the Quebec context developed for the current study, similar to the Pyramids and Palm Trees test (PPTT) [130]. The task proposed involved triads of words resembling a pyramid where participants needed to judge within a time limit of 4 seconds which of the two words below (target or distractor) was more related to the word above (stimulus). Both target and distractor words were associated in a semantic relation with the stimulus word. Participants were thus required to select which of the two competing words had a stronger semantic relationship to the stimulus word as measured by semantic distance between the stimulus and the distractor. Two types of triads were used: a) low-demand (distant) relations: the more distant the semantic relation between stimulus and distractor, the less demanding it would be to select the correct target; and b) high-demand (close) relations: the closer the semantic relation between stimulus and distractor, the more demanding it would be to select the correct target as competition between the target and distractor words would be higher [61].

The task (150 triads in total) had two experimental conditions (120 triads: 60 low-demand (LOW) and 60 high-demand (HIGH) semantic relations) and one control condition (30 triads). For the control condition, the task was to indicate which of the two consonant strings, which were presented pseudo-randomly, were in the same case as the target strings (e.g. DKVP: RBNT-kgfc). E-Prime automatically randomizes the location of correct responses (e.g. on the left or the right), to ensure variation. Please see Figure 5 for examples of stimuli for each condition:

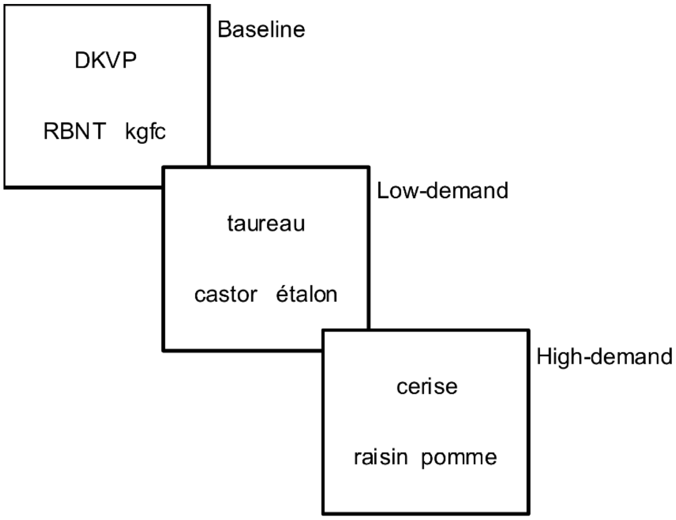

Figure 11. – Figure 5: Examples of triads

Stimuli development and pilot testing

Development of the stimuli proceeded as follows. In every condition, the targets and distractors were matched for: a) Type of semantic relation: taxonomic and thematic. Taxonomic relationships were developed as such: The creation of taxonomic triads was based on a) Definition of semantic categories (e.g. animals, birds, tools, clothes, jewellery, wild animals, musical instruments, trees, insects, fruits, vegetables, fish, transport means, cloth material, type of house, furniture…). b) Creation of triads based on definitions below. 3) Online testing of stimuli by 20 younger and 20 older pilot participants. Testing of triads entailed choosing the correct answer in the triad and scoring the triad for difficulty on a Likert scale of 1-5. 4) Removal of triads that was inconsistent with the responses and the scoring of pilot participants. 5) Selection of 'most successful' triads (30 par condition) e.g. pilot participants correctly responded to by 80% and scored triad as easy or difficult accordingly.

For thematic relations, the semantic distance was calculated with the help of a dictionary: 'Dictionnaire des associations verbales (sémantiques) du français' (http://dictaverf.nsu.ru/dict, version accessed on 2014), as a function of the number of respondents that associated two words together (i.e., the larger the number of respondents, the more closely associated the two words are, and vice versa). As such, a score of 1 means that only one person provided this answer (distant thematic relation) whereas a score of 100 means that 100 people provided this answer (close thematic relation); b) Frequency, based on the Lexique 3 database referring to films [134]; c) Imageability, based on the Desrochers 3600 database [135]. Additional imageability ratings were collected from 30 participants for items without ratings in the above database. A Pearson's correlation was performed between the scoring of this study's stimuli words with 30 test words scores from the Desrochers database to confirm that the ratings given for the new words were relevant compared to the ones that already exist in the database, by 30 Francophones from Quebec Participants' rating of items with a correlation value less than 0.6 were excluded, as it was deemed that they were not concentrated on the task. 0.6 was chosen as an extremely high power based on G*Power. The final imageability rating of an item was the mean of the scores given by all included participants. ANOVA and Bonferroni corrected Tukey tests were performed to ensure the matching of a target and distractor for every condition, meaning that for every condition, the target and the distractor were matched for imageability and frequency ratings. Finally, targets and distractors were matched on d) Word length.

The stimuli were created by a reiterative process, continuously testing and evaluating their adequacy and aiming for a less than 40% error rate with pilot participants to test it, measure response times and gather comments. Every time, the four conditions were matched and passed an ANOVA test for mean frequency, imageability and length.

Participants included both younger and older francophone Quebecers (new participants every time). Testing included the following steps: Participants selected if a triad was easy or difficult and rated it on a 1-5 scale. Triads that had had a score of 3 were removed, triads that had a score of (1 and 2) or (4 and 5) were collapsed. Participants' answer needed to correspond with the definition given (low- or high-demand). If it did not, the triad was removed. A score of 80% was defined as cutoff for participants rating the triad according to the initial definition. Pilot participants also shared feedback about the duration of the task and the sufficiency of time to respond.

After having created an initial set of triads, an evaluation by a team of linguists (Phaedra Royle) was performed to collect feedback and comments, which led to the replacement of 11 low-demand taxonomic triads, 10 high-demand taxonomic triads, 21 low-demand thematic triads, and 17 high-demand thematic triads. A first round of pilot testing took place with 6 younger participants and 5 older participants in January 2016. After correcting/replacing triads, a second round of testing pilot stimuli took place in February 2016 with 6 older participants and 3 younger participants. A new round of pilot testing with new stimuli took place in March 2016 with 6 new participants (3 younger and 3 older).

To evaluate the validity of the final stimuli pertaining to low versus high demands and younger versus older adults, a pilot evaluation of stimuli with new participants was conducted with 28 participants (14 older adults, age range: 67-79 years old, female = 9; and 14 younger adults, age range: 21-35 years old, female=10) for 60 triads (30 low-demand and 30 high-demand) using E-Prime. Repeated measures analysis of variance (ANOVA) was applied to the mean accuracy and median response data within each level of task demand (control, low, high) across the two age groups. The results are described below:

Accuracy

The Greenhouse-Geisser estimate for the departure from sphericity was ε = 0.63. There was not a significant interaction between age group and task demand, F (1.27, 32.94) = 0.065. p = 0.85, η2 =

0.0025. The main effect of task demand was significant, F (1.27, 32.94) = 10.36, p = 0.0015, η2 = 0.28. The estimated marginal means were: Control = 0.84, Low = 0.80 and High = 0.72. The main effect of age group was not significant, F (1, 26) = 0.34, p = 0.57, η2 = 0.013.

Response Times

The Greenhouse-Geisser estimate for the departure from sphericity was ε = 0.54. There was not a significant interaction between age group and task demand, F (1.08, 28.14) = 1.14. p = 0.30, η2 = 0.042. The main effect of task demand was significant, F (1.08, 28.14) = 49.38, p < 0.0001, η2 = 0.66. The estimated marginal means were: Control = 1390ms, Low = 2230ms and High = 2292ms. The main effect of age was significant, F (1, 26) = 4.78, p = 0.038, η2= 0.15.

Based on the above pilot data, we could confirm that our task includes an effect of task demands that impacts task performance (accuracy and RTs) differently between younger and older adults, in the expected directions.

The following definitions were used:

Low-demand (distant) triads:

- For taxonomic relations:

All items (stimulus, target, distractor) belong in the same semantic category (e.g., animals). Stimulus and target words belong in the same semantic sub-category (e.g., birds). For example, taureau: ÉTALON-castor (bull: STALLION-beaver).

- For thematic relations:

Both the target and distractor words are thematically related to the stimulus and belong in the list of answers referred by dictaverf. To ensure the largest distance possible, the target was the first adequate answer mentioned in dictaverf, whereas the distractor was the last or closest to the last answer, meaning that it had a score close to 1. For example, sorcier: village-BAGUETTE (wizard: village-WAND).

Alternatively, when the above criterion was not feasible, to ensure the largest distance possible, the following criteria were adopted: a) when the distractor word had a score of 1 (which means only 1 person provided this answer) the target could have any score, b) when the distractor word had a score between 2-5 then the target word had to have a score above 10, and c) when the difference between the target and distractor words was bigger than 100, then the actual scores did not matter.

High-demand (close) triads:

- For taxonomic relations:

All items in the triad come from the same semantic sub-category (e.g., birds). The stimulus and target items share a visual or structural feature whereas the distractor word does not. For example, ‘cerise: RAISIN-pomme’ (cherry: GRAPE-apple) where cherries and grapes have a similar size and bunch structure.

- For thematic relations:

Both the target and distractor words are thematically related to the stimulus. The target was the first adequate answer mentioned in dictaverf whereas the distractor had a score smaller or equal to half of the score of the target and was larger or equal to 4. The cutoff score was chosen empirically so that the score of the distractor was always larger for high-demand rather than low-demand triads. This criterion was used to ensure that the distractor was a more frequently mentioned answer but distant enough from the target (e.g. half of the people mentioned the distractor as opposed to mentioning the target). For example, ‘enfant: JOUET-sourire’ (child: TOY-smile).

Experimental Design

Session 1: Neuropsychological tests

Participants were recruited through the CRIUGM pool of participants and public announcements, with initial eligibility assessed through a phone interview (health questionnaire, French language, right-handedness and MRI compatibility). If eligible, the participant participated in the first experimental session (approximately 45 minutes), during which they signed the informed consent and MRI-compatibility forms, completed neuropsychological tests (see Participants section above) and practiced with 15 practice triads (5 for every condition). Participants who qualified (met the inclusion criteria from health questionnaire, MRI-compatibility questionnaire, MOCA and Edinburgh Handedness Inventory scale) for the fMRI scanning session following tests, proceeded with the second session one week later (maximum 2 weeks later).

Session 2: fMRI scanning

For the second experimental session, the time commitment from the participant was 90 minutes to allow for practice with the triads, getting ready and leaving, and following COVID-19 requirements. During this session, participants listened to task instructions, and practiced with 3 triads (1 per condition). Participants' vision was corrected, if necessary, with MRI-175 compatible lenses according to their prescription shared from the previous session. Additionally, pregnancy tests were carried out when relevant (as per the UNF requirements), earplugs were given to reduce machine noise and instructions were given to remain still in the scanner while foam rubber pads in the head coil restricted movement. Participants then proceeded with the actual task in the scanner. Stimuli were presented with E-Prime 2.0.10.356 software run on Microsoft Windows 10.

An LCD projector projected the stimuli to a mirror above the participant's head. [1]Participants selected their responses with a button press using the index fingers of both hands on the MRI-compatible response box. A response on the right was done with theright hand and a response on the left with the left hand. Response data and response times (RTs) were recorded via E-Prime for further analysis. No feedback was given to participants. Participant testing alternated between younger and older adults to minimize any bias due to scanner changes/upgrades.

The semantic task was event-related. Triads were presented for 4 seconds, during which participants responded. A black screen followed for approximately 2.2s (this interstimulus interval (ISI) varied randomly between 0.67s and 3.8s to maximize variance in the BOLD signal and ensure unpredictability). A fixation point appeared for 1.3s to prepare the participant for the next trial. The whole trial lasted between 5.97s and 9.10s, with an average of 7.5s. See below for a description of the methods used to determine the ISIs. Black screens were included at the beginning and the end of the Runs. Information on the scanning flow is available in Figure 6 below:

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[1] On 29 October 2021, after having recruited 13 participants, the laptop where E-Prime was installed crashed, resulting in using the UNF PC where E-Prime 3 was installed.

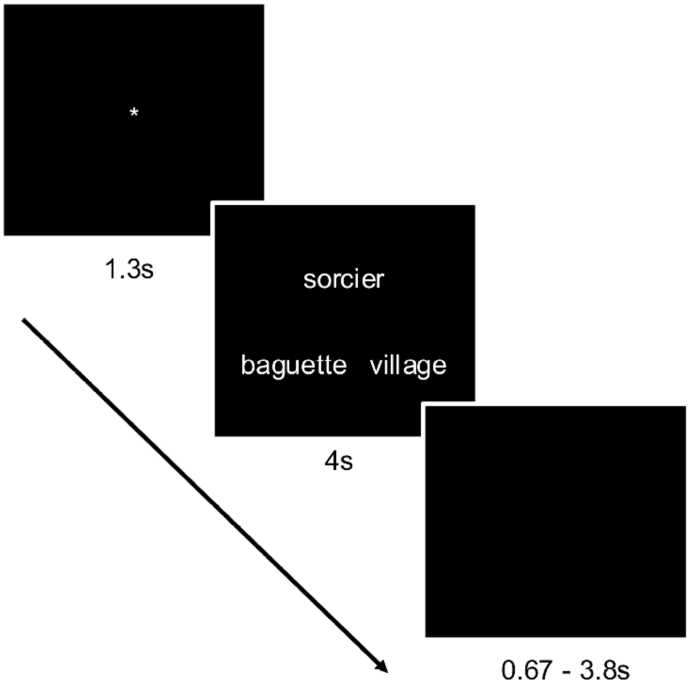

Figure 12. – Figure 6: Example of trial

The task was split in two Runs with 75 triads per Run (30 low-demand (LOW), 30 high-demand (HIGH) and 15 control triads), interspersed in a pseudo-random fashion, so that no more than four trials of the same condition or type are repeated in a row. The duration for every Run was 9:45 minutes. The whole session lasted approximately 45 minutes, including a 5-min break between Runs 1 and 2.

Session 3

To address perceived task difficulty, an additional session with participants immediately following the fMRI acquisitions took take place, whereby they rated each triad on difficulty level using a 1-7 Likert scale (eg. 1: very easy, 7: very difficult). The objective of this session was to further assess whether perceived difficulty correlated with actual performance scores (accuracy rates and RTs) and whether perceived difficulty correlated with levels of activation in the younger and older adults. In other words, we investigated whether increased levels of perceived difficulty correlated with increased RTs and reduced accuracy, as well as levels of activation in semantic control regions.

Stimuli order and ISIs

In order to maximize design efficiency, optimal trial ordering and interstimulus intervals (ISIs) were chosen [136]. The methodology used simulated designs of random ordering of the three conditions. In addition, the ISIs were randomly drawn from Gamma distributions across a range of parameter values (shape: 0.1 to 10, scale: 0.1 to 5). This approach included expected error rates produced during the stimuli pilot studies. A total of 800,000 simulations were performed. The ISI distribution and specific list as well as the condition order in which there was the smallest decrease in required BOLD signal response for detection as errors increased were chosen. The related ISIs are uploaded to the OSF platform.

fMRI data acquisition

Prior to data collection, minor deviations were performed on the fMRI acquisition parameters, also uploaded on the OSF platform and for which the journal editor was informed. These adjustments represent minor technical precisions motivated by recent technological improvements made to the MRI platform at our research institute and as recommended by the team of the technical platform at UNF.

Functional scans were performed on a 3Tesla Syngo MR E11 Prisma_fit Siemens MRI machine with 32 channel receive-coil at UNF (Unité de Neuroimagérie Fonctionnelle), CRIUGM. The start of the stimulus presentation software was triggered by a pulse sent from the MRI to the stimulus laptop.

To detect effects between conditions and to ensure a good fMRI signal in the brain, pilot data collected using the scanning protocol described here suggested a minimum temporal signal to noise ratio (TSNR) of 20 throughout the brain [137]. Participant data were excluded if TSNR, assessed from every participant's time series, was below 20. We acquired T1-weighted MRI images for co-registration with fMRI data and atlases and to identify ROIs to be used as masks in the functional data analysis. An meMPRAGE (multi-echo MPRAGE) sequence (704 total MRI files) was acquired with 1x1x1mm resolution, 2.2s repetition time, 256x256 acquisition matrix, a Field of View (FOV) of 256mm covering the whole head and echo times of 1.87ms, 4.11ms, 6.35ms, 8.59ms, for a total of 704 meMPRAGE slices (176 slices x 4 echoes= 704 slices). The phase encoding direction was A-P (anterior to posterior) and superior-inferior and slice orientation was sagittal with a flip angle of 8 degrees. Following scanning of the first participant and their comment about fatigue, we inversed the order so that task-based fMRI was before the resting state and ASL.

For the functional scans (Run 1 and 2), T2*-weighted BOLD data were acquired on the entire brain (including the cerebellum) using an Echo Planar Imaging (EPI) sequence with 50 slices, resolution 2.5x2.5x3mm, echo time of 20ms, repetition time of 3s and a flip angle of 90 degrees and parallel imaging (R=2). Field of view was 220x220mm and the acquisition matrix was 88x88, in AC-PC direction minus approximately 20 degrees covering 150mm in the z-direction. Slice order was ascending-interleaved. For each Run, 195 volumes were collected. Functional images will be reconstructed to the collected matrix size with no prospective motion correction. Two initial dummy scans will be collected and discarded by the MRI allowing for T1 saturation.

The SIEMENS default gradient field map sequence sequence for field map distortion correction was acquired after each sequence for inhomogeneity correction. 50 axial slices will be acquired, with resolution 2.5x2.5x3mm, repetition time of 520ms, and echo times of 4.92ms and 7.38ms. Phase-encode direction will be A-P (anterior-posterior) in the same axial orientation and same angulation as the EPI sequence.

Analyses' methodology

Behavioral analysis methods

Mixed-level modeling tested for age group and task demand-related effects in task accuracy and response time measures while controlling for sex. Mixed-level modeling is similar to repeated measures ANOVA except that it has the additional benefit of allowing each participant to have a random intercept and is superior at controlling type I errors [140], [143]. The intercept was a random effect across participants, while age group, task demands, and sex were fixed effects. Model estimation used restricted maximum likelihood, and degrees of freedom were estimated using the Satterthwaite method [145]. Testing for the significance of the random effect used the likelihood ratio test. A significant result demonstrates significant variability in intercept values across participants. The interclass correlation (ICC) value is reported, which is the proportion of the total variance in the dependent variable that is accounted for by the random intercept of each participant [144]. It is the proportion of variation in the data attributed to between-participant differences. In the context of identifying cross-participant similarities, i.e., group effects, the smaller the value, the better. A value of zero means that the simpler repeated-measures ANOVA would be as appropriate as the more complex mixed-level modeling. Analyses used Jamovi The Jamovi project (2021) (Version 1.6) [Computer Software], retrieved from https://www.jamovi.org. Any missing or incomplete data resulted in excluding the whole participant.

Image preprocessing methods

Preprocessing image analysis was performed with SPM12 software on the narval cluster of Calcul Québec at Compute Canada. Images were corrected for slice timing (differences in slice acquisition time), with ascending-interleaved slice order and using the acquisition time for the middle slice as the reference. We used field map correction to correct EPI images for distortion using the Calculate VDM toolbox and the first EPI image as reference. The gradient field map images were pre-subtracted by the scanner to provide phase and magnitude data separately. Motion correction was applied for within-subject registration and unwarping. Motion parameters were used later as confound variables. Three participants with acute motion parameters of more than 2mm, or 1-degree rotation, between scans in any direction, were excluded. Four additional participants were excluded as they had missing data (i.e., less volumes). EPI functional volumes were registered to the average anatomical volume calculated by the machine over the 4 echoes of meMPRAGE T1-weighted anatomical scan. The mean anatomical image was used as the reference image and as quality control. Anatomical variations between participants were reduced by aligning the structural images to the standard space MNI template, followed by visual inspection of their overlay. Data were visually inspected for excessive motion by inspecting with SPM's check reg tool that 5 landmarks across the EPI brain are well aligned with the standard space brain. Seven participants produced black images during this process. A problem was deemed to exist with their field map correction, thus field map correction was removed. An 8mm full width at half maximum (FWHM) Gaussian blur was then applied to smooth images within each Run. The final voxel size after preprocessing was 3x3x3 mm.

fMRI data analysis methods

fMRI data analysis was performed with SPM12 focusing on semantic control primary ROIs. Using files created by E-Prime during stimulus presentation, stimulus onset files were created and regressors were defined. For the 1st level (intrasubject) analysis, a General Linear Model (GLM) employing the canonical Hemodynamic Response Function (HRF) and its derivative both convolved with a model of the trials was used to estimate BOLD activation for every subject as a function of condition for the fMRI task. The inclusion of the derivative term accounted for inter-individual variations in the shape of the hemodynamic response. Correct trials were modeled separately for low demand and high demand conditions. Incorrect trials for low and high demands were modelled together in their own regressor and not investigated further. Each participant's fMRI time series (2 Runs) were analyzed in separate design matrices using a voxel-wise GLM (first-level models). Movement parameters obtained during preprocessing, and their first and second derivatives, were included as covariates (regressors) of no interest to reduce the residual variance and the probability of movement-related artifacts. A high-pass filter with a temporal cut-off of 200s and a first-order autoregressive function correcting for serial autocorrelations were applied to the data before assessing the models. Two contrasts of interest were calculated collapsing across the two Runs. These contrasts were low-demand, correct trials > control and high-demand, correct trials > control. These contrasts were used for second level group analyses to compare age group and effects of task demand.

The analysis first tested for an interaction between age group and task demands. A significant finding would support hypothesis one. If this interaction is not found, main effects would further be tested. Support for hypothesis 2 would demonstrate that the older age group would have significantly greater activation than the younger age group in left semantic control regions. Support for hypothesis 3 would be that within the high demand condition where the young age group will have significantly greater activation than the old in the left semantic control regions. It would also be expected that the older age group would have significant greater activation than the younger group in the right semantic control regions.

To account for differences in HDR between younger and older adults, the event-related first-level statistical model of the fMRI data included the event-chain convolved with the double-Gamma hemodynamic response function and its first derivative. The inclusion of this extra regressor would capture variance in the data due to any inter-participant or inter-group variations in the shape of the hemodynamic responses.

Defining the anatomical/functional ROIs methods

This study's hypotheses depend on ROIs that include semantic control regions associated with low and high-demand conditions. To identify ROIs of the semantic control network demonstrating demand related differences in brain activation, the results of a recent meta-analysis were used [24]. This analysis utilized data from 126 comparisons and 925 activation peaks and is the most comprehensive and up to date meta-analysis of semantic control networks. The results identified twenty highly significant peak locations throughout the inferior frontal gyrus, insula, orbitofrontal cortex, precentral gyrus, middle and inferior temporal gyri and the fusiform gyrus, see Table 1 [24] for specific x,y,z locations. Spheres of diameter of 10mm were created at each of these locations and the corresponding contralateral locations, by flipping the sign of the x-coordinate. Participant level parameter estimates (contrast values) were extracted using MarsBar [138]. This approach used the methods presented in a recent analysis of the CRUNCH effect in a similar population [40]. Correction for multiple comparisons used the false discovery rate across the forty ROIs [139]. Secondary, exploratory analyses of the more general semantic control network used the maps of semantic control for domain general control as identified in the [24] metaanalysis.

Region of interest analysis methods

Sphere of ten millimeters in radius were drawn around each of the twenty x,y,z coordinates provided in the Jackson’s 2021 semantic control meta-analysis paper [148]. For each participant, the average brain activity within each ROI for both task demand levels was calculated. This provided two numbers per person for each of the twenty ROIs. A linear mixed effects model, similar to that used for behavioral analyses, was fit to each ROI using the lme4 package in r (v1.1-28) [141].

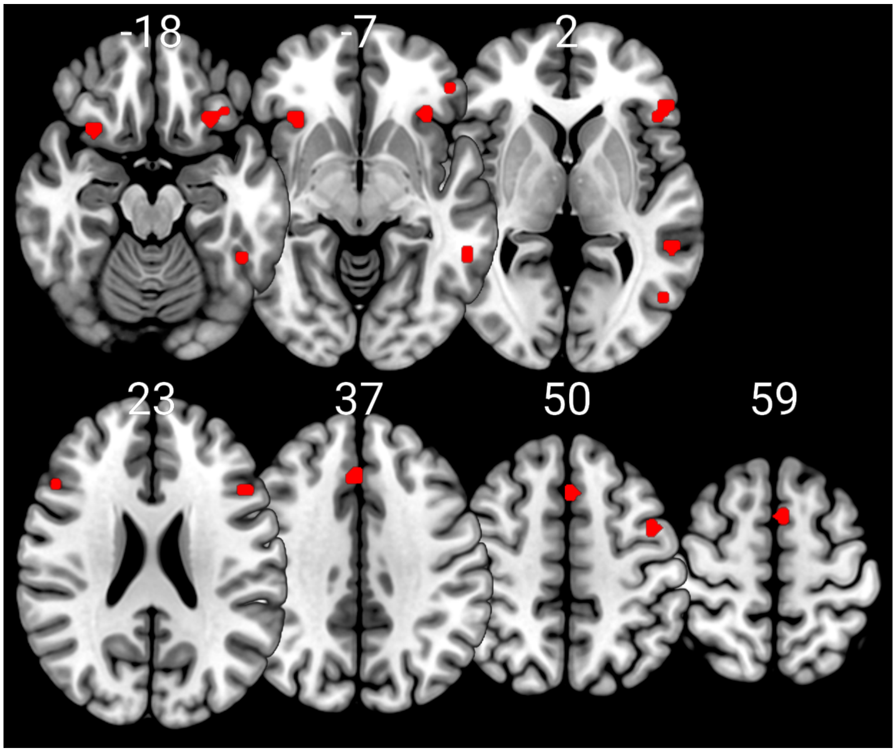

Figure 13. – Figure 7. Regions of interest as derived from a recent meta-analysis of semantic control. Numbers are axial slice locations in millimeters.

Results

Behavioral data analysis

The study included data from a total of 78 participants, including 40 younger adults, the mean (standard deviation) age in years was 24.0 (3.48) and a range of 19 to 32 years, and 38 older adults, mean (std) age in years of 66.6 (4.08) and a range of 60 to 74 years. There were 22 females and 18 males in the younger age group and 25 females and 13 males in the older age group. A X^2-test of independence confirmed no significance relationship between sex and age group counts ($X^2(1) = 0.947$, $p = 0.330$).

Tableau 2. – Table 2 Cognitive assessment results

	Younger mean (std.)	Older mean (std.)	t	p	Effect size
MoCA	28.3 (1.15)	28.4 (1.33)	0.519	0.605	0.118
PPPT	49.8 (2.13)	50.9 (1.22)	2.71	0.00838	0.613
WAIS-III	17.1 (4.01)	17.4 (3.43)	0.409	0.684	0.0926

Predicting response time, the main effects of age group (F (1, 74) = 9.78, p = 0.00253) and task demand levels (F (1, 229) = 5.54, p = 0.0194) were significant. The interaction between age group and task demand levels was not significant (F (1, 229) = 0.00883, p = 0.925) and the main effect of sex was also not significant (F (1, 74) = 0.728, p = 0.396). The main effect of age group was driven by longer response times in older (mean (standard error) = 2265 (39.1) milliseconds) than the younger adults (mean (SE) = 2096 (37.8) ms) a difference of 169 ms. The main effect of task demand levels was driven by longer response times in the high condition (mean (SE) = 2197 (28.3) ms) than in the low condition (mean (SE) = 2164 (28.3) ms), a difference of 33 ms. The random component of the model (participant, intercept) was significant (ICC = 0.774, $X^2(1) = 246$, $p < 0.0001$).

When predicting accuracy using a Fisher logit transform of mean accuracy scores a repeated measures ANOVA model was used. This is due to a minimal proportion of variation in the data attributed to between-participant differences. The main effect of task demand level was significant (F(1,74) = 138, $p < 0.0001$, $\eta^2 = 0.290$). This effect was driven by higher mean transformed accuracies at the low task demand condition (mean (s.e.) = 1.90 (0.0457)) than high task demand condition (mean (s.e.) = 1.30 (0.0394)). The interactions between task demands and sex (F(1, 74) = 0.193, p = 0.622, η^2 = 0.00) and task demands and age group (F(1, 74) = 2.62, p = 0.110, η^2 = 0.00549) were not significant. The main effects of age group (F(1, 74) = 0.0505, p = 0.823, η^2= 0.00) and sex (F(1, 74) = 0.0236, p = 0.878, η^2 = 0.00) were not significant.

fMRI analyses results

Second-level analyses used a repeated-measures univariate analysis and tested for task demand effects, age effects, and their interaction. This analysis used the sandwich estimator (SwE), which appropriately accounts for the within-subject correlation existing in repeated measures data [142]. Analyses used two images per participant. These were the first-level contrasts of low-demand versus the control condition and high-demand versus the control condition. Statistical significance was assessed using 1000 resamples and threshold-free cluster enhancement (TFCE) and family-wise error corrections for multiple comparisons across voxels [146], [147].

There were no significant voxels for the test of the interaction between task demand and age. Of the two main effects, only the effect of age group demonstrated any significant voxels within the bilateral occipital cortex and the cerebellum, see Figure 8-Figure 14 and Table 2.

Despite no task demand effects and minimal age effects, the experiment demonstrated robust task-related brain activity. Significant brain activity was evident across bilateral inferior frontal, parietal, supplementary motor, temporal, and occipital brain regions, see Figure 9-Figure 15. Tables 2-6 list the results for multiple local peaks of activity.

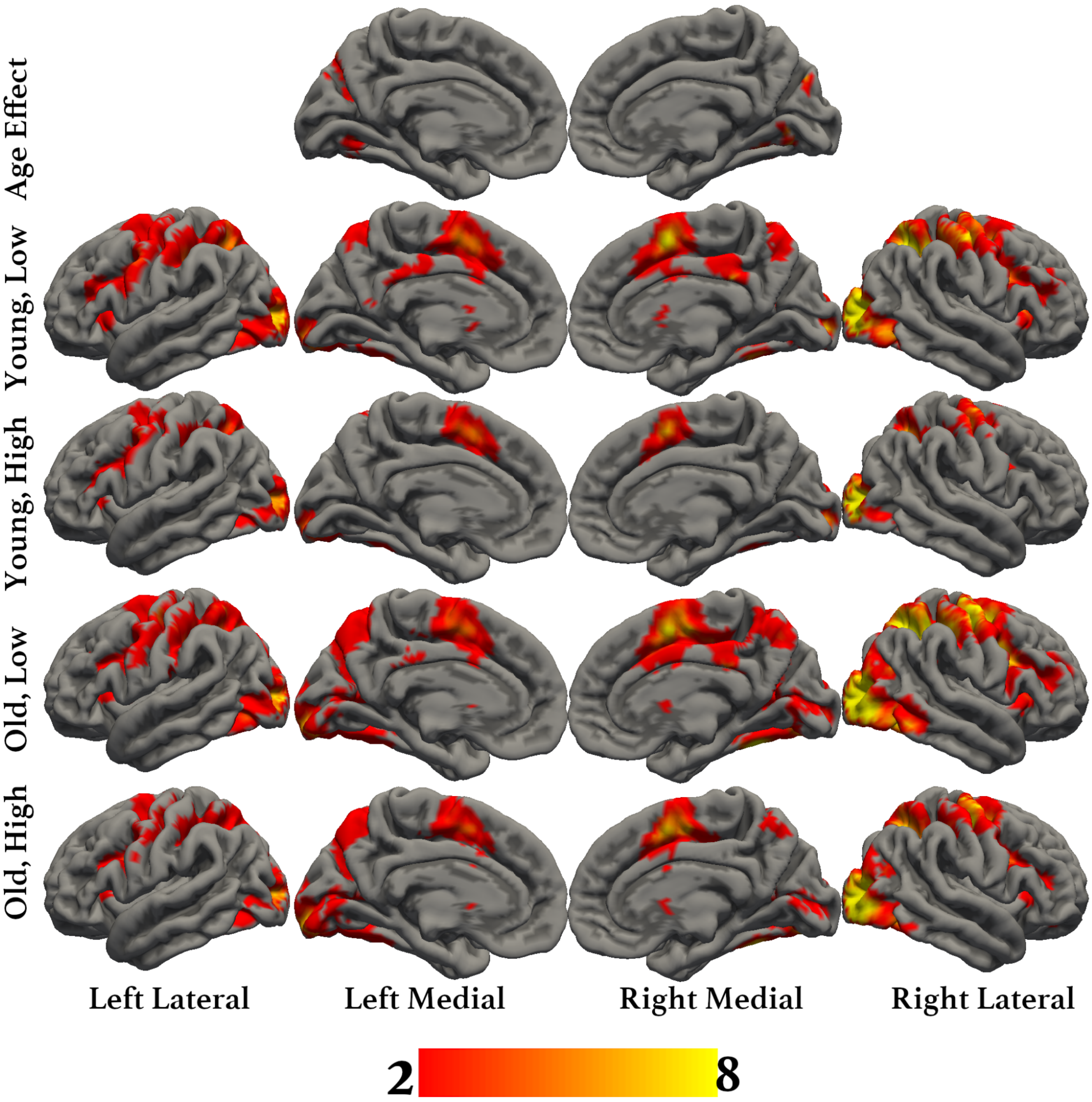

Figure 14. – Figure 8- Overlays of all results demonstrating significant brain activity using threshold free cluster enhancement family wise error correction for multiple comparisons and 1000 resamples. Colors correspond to Z-values ranging from 2 to 8.

Tableau 3. – Table 3. Main effect of age

Region	Hemi.	B.A.	x`	y	z	Z	k
Cerebellum, Crus1	R	--	15	-52	-16	4.98	221
Cerebellum, Crus1	L	--	-15	-67	-7	5.39	90
Calcarine Sulcus	L	18	-12	-76	35	5.52	174
Mid. Occipital Gyrus	R	18	12	-82	48	5.04	8

Hemi: hemisphere, k: cluster size, --: a location with no representation within the Brodman atlas. Results are corrected for multiple comparisons using threshold free cluster enhancement, family wise error correction and 1000 resamples.

Tableau 4. – Table 4 Younger, low task demand

Region	Hemi.	B.A.	x	y	z	Z	k
Lingual gyrus	R	18	-24	-91	-7	8.11	11838
Inf. occipital gyrus	L	18	24	-91	-4	7.81	--
Inf. occipital gyrus	R	19	-30	-85	-7	7.77	--
Mid. occipital gyrus	L	19	33	-88	-1	7.70	--
Sup. parietal cortex	L	7	27	-58	47	6.88	--
Sup. parietal cortex	R	7	-27	-58	53	6.78	--

Sup. occipital gyrus	R	7	-24	-67	35	6.72	--
Supp. motor area	R	6	-6	-1	53	6.67	--
Supp. motor area	L	6	6	8	53	6.54	--
Supp. motor area	R	6	-6	8	50	6.51	--

Hemi: hemisphere, k: cluster size, --: a local maxima within a larger cluster. Results are corrected for multiple comparisons using threshold free cluster enhancement, family wise error correction and 1000 resamples.

Tableau 5. – Table 5. Younger, high task demand

Region	Hemi.	B.A.	x	y	z	Z	k
Lingual gyrus	R	18	-24	-91	-7	7.74	3656
Inf. occipital gyrus	R	19	-30	-85	-7	7.24	--
Supp. motor area	R	6	-6	8	50	6.37	--
Sup. occipital gyrus	R	7	-24	-67	35	6.11	--
Precentral gyrus	R	6	-27	-4	50	6.08	--
Sup. parietal cortex	R	7	-24	-61	50	6	--
Supp. motor area	R	6	-6	-1	53	5.98	--
Precentral gyrus	R	44	-42	5	29	5.96	--
Supp. motor area	L	6	6	8	53	5.7	--
Precentral gyrus	R	6	-54	-1	44	5.53	--

Inf. occipital gyrus	L	18	24	-91	-4	7.39	2044
Sup. parietal cortex	L	7	27	-58	47	5.62	--
Precentral gyrus	L	--	36	-16	53	5.54	--
Precentral gyrus	L	6	39	-13	65	5.05	--
Precentral gyrus	L	6	27	-4	47	4.91	--
Mid. occipital gyrus	L	19	30	-70	26	4.8	--
Fusiform	L	37	36	-67	-10	4.76	--
Postcentral	L	--	54	-13	50	4.73	--
Fusiform	L	37	33	-40	-22	4.33	--
Fusiform	L	37	36	-58	-13	4.29	--
Inf. frontal oper.	L	44	42	8	29	4.71	80
--	R	47	-30	26	2	4.09	18

Hemi: hemisphere, k: cluster size, --: a local maxima within a larger cluster or a region with no atlas label. Results are corrected for multiple comparisons using threshold free cluster enhancement, family wise error correction and 1000 resamples.

Tableau 6. – Table 6. Older, low task demands

Region	Hemi.	B.A.	x	y	z	Z	k
Inf. occipital gyrus	R	18	-27	-88	-4	8.05	17869
Mid. occipital gyrus	L	19	36	-88	-1	7.95	--

Sup. occipital gyrus	R	7	-21	-64	44	7.3	--
Inf. parietal cortex	R	40	-33	-46	44	7.28	--
Precentral gyrus	L	--	36	-16	50	7.13	--
Sup. occipital gyrus	R	19	-24	-61	32	7.12	--
Sup. parietal cortex	L	7	24	-61	47	6.92	--
Precentral gyrus	L	6	33	-16	59	6.85	--
Mid. occipital gyrus	L	7	27	-61	38	6.79	--
Precentral gyrus	R	6	-39	-7	59	6.69	--
Sup. temporal gyrus	L	42	54	-43	20	3.01	12
Supramarginal gyrus	L	--	51	-37	26	2.59	--
Sup. temporal gyrus	L	--	60	-37	23	2.51	1

Hemi: hemisphere, k: cluster size, --: a local maxima within a larger cluster or a region with no atlas label. Results are corrected for multiple comparisons using threshold free cluster enhancement, family wise error correction and 1000 resamples.

Tableau 7. – Table 7. Older, high task demands

Region	Hemi.	B.A.	x	y	z	Z	k
Inf. occipital gyrus	R	18	-27	-88	-4	8.05	12010
Mid. occipital gyrus	L	19	36	-88	-1	7.68	--
Sup. occipital gyrus	R	19	-27	-64	29	7.35	--

--	R	7	-24	-61	41	7.01	--
Inf. frontal oper.	R	44	-36	5	29	6.81	--
Inf. parietal cortex	R	40	-33	-46	44	6.63	--
Supp. motor area	R	6	-6	8	53	6.56	--
Precentral gyrus	L	--	36	-16	50	6.33	--
Sup. parietal cortex	L	7	24	-61	47	6.18	--
Inf. occipital gyrus	R	19	-39	-67	-13	6.17	--

Hemi: hemisphere, k: cluster size, --: a local maxima within a larger cluster. Results are corrected for multiple comparisons using threshold free cluster enhancement, family wise error correction and 1000 resamples.

Region of Interest Analysis

Region of interest analyses only demonstrated uncorrected significant effects of task demands within the right inferior frontal gyrus. The effect in the pars triangularis region was driven by lower activity at the higher task demand level. Within the pars orbitalis the effect was driven by greater negative direction activity at the high task demand level. Despite no significant interactions or age effects, and minimal task demand effects, there were strong task related effects as demonstrated by significantly greater than zero activity shown by the estimated marginal means.

Tableau 8. – Table 8. Region of interest analyses

Region of activation	Estimates	Estimated Marginal Means

Cluster number		Age (Older - Younger)	Task demand (High - Low)	Age*Task demand	Younger, Low	Younger, High	Older, Low	Older, High
1	Left IFG (pars triangularis, orbitalis & opercularis), insula, OFC & precentral gyrus	-0.694	0.185	0.185	1.78*	1.78*	0.900*	1.085*
		-0.190	-0.0333	-0.146	0.134	0.247	0.0895	0.0562
		-0.105	0.140	-0.145	0.161	0.445	0.200	0.3399
		-0.398	-0.104	-0.0486	0.843*	0.788*	0.493*	0.3892
		0.133	0.0555	0.0291	-0.127	-0.100	-0.0228	0.0327
		-0.110	0.0304	0.0189	0.370	0.382	0.242	0.2719
		-0.151	-0.00550	0.0319	0.107	0.0696	-0.0755	-0.081
		0.848	-0.0162	-0.0165	1.42*	1.42*	2.28*	2.27*
		-0.310	0.0265	-0.0128	0.420	0.459	0.122	0.148
2	Left pMTG, pITG & pFG	-0.129	0.118	0.0182	0.775*	0.875*	0.628*	0.746*
		-0.120	0.0971	0.0278	1.09*	1.16*	0.942*	1.04*
		0.321	-0.0346	0.0391	1.33*	1.26*	1.61*	1.58*

		0.133	-0.00400	0.0252	0.103	0.0735	0.210	0.206
		0.641	-0.0658	0.106	0.205	0.0331	0.740*	0.674*
3	Bilateral dmPFC	-0.362	0.0463	0.0481	1.58*	1.57*	1.17*	1.21*
		-0.0256	-0.132	0.173	0.963*	0.658*	0.764*	0.632*
		-0.138	-0.00830	0.0754	2.28*	2.19*	2.06*	2.05*
4	Right IFG (pars orbitalis) & insula	-0.117	-0.0417	0.0203	0.841*	0.779*	0.703*	0.662*
		0.214	-0.2074*	0.0214	-0.157	-0.386*	0.0352	-0.172
5	Right IFG (pars triangularis)	-0.169	-0.3413*	0.0133	0.931*	0.577	0.749*	0.408

Bold* $p < 0.05$ uncorrected,

IFG = inferior frontal gyrus, OFC = orbitofrontal cortex, p = posterior, ITG = inferior temporal gyrus, MTG = middle temporal gyrus, FG = fusiform gyrus, dmPFC = dorsomedial prefrontal cortex.

Discussion

In this study, we aimed to examine the CRUNCH hypothesis during a semantic processing task with two levels of task demands by younger and older adults. We used a novel task that varied task demands (low versus high) in 39 younger and 39 older adults. Our participants, younger and older adults, were matched in terms of level of education, performance on questionnaires assessing engagement in cognitively stimulating activities, and performance on the MoCA and WAIS-III tests. The behavioral results confirmed that the task was successful in manipulating cognitive demands, with accuracy rates and RTs increasing with increasing task demands, namely in the high-demand condition.

There was no statistical difference in accuracy between younger and older participants regardless of the condition, so there was no age effect in accuracy. This is in line with literature that shows that accuracy in semantic tasks is overall well-preserved in older adults considering their more extensive experience with word use and a larger vocabulary than younger ones [2], [5-6], [10-13]. In terms of RTs, there was a statistically significant difference between younger and older participants, with older adults being slower to respond in general (a difference of 169 ms). This is in line with literature that shows that RTs of older adults are overall longer in comparison to younger ones [10]. As such, the semantic memory task was successful in a) manipulating task difficulty across two levels of demands as shown in differences in accuracy and RTs between the two conditions and b) demonstrating age-invariant behavioural performance for the older group (e.g. maintained in comparison with the younger), as required to test the CRUNCH model [21], [38]. We did not however find a significant interaction between task demands and age group, nor between task demands and sex for either RTs or accuracy.

In addition to lack of significant interaction between task demands and age group for RTs or accuracy, we did not find either the hypothesized age group by task demand interaction with regard to brain activation, the crucial test of the CRUNCH model. Only the age group effect demonstrated significant activation in the bilateral occipital cortex and the cerebellum, whereas no significant main effect of task demands condition was observed. Despite lack of task demand effects and only minimal age effects, the experiment demonstrated robust task-related brain activity. Independent of age, the semantic similarity judgment task activated a large bilateral fronto-temporo-parietal network. More specifically, distinct clusters of activation were observed when all task conditions were contrasted with the baseline, such as bilateral inferior frontal, parietal, supplementary motor, temporal and occipital brain regions. The activated regions correspond overall with regions reported to belong to the semantic network. The semantic network is proposed to be comprised of 7 brain regions, mainly on the left: posterior inferior parietal cortex (pIPC), lateral temporal cortex (LTC), ventral temporal cortex (VTC), dorsomedial prefrontal cortex (DMPFC), inferior frontal gyrus (IFG), ventromedial prefrontal cortex (VMPFC), and posterior cingulate gyrus (PCG) [27], [44], as well as bilaterally the anterior temporal lobes (ATLs) believed to act as a semantic hub [47] and the relative semantic control processes underpinned by the pFC, pMTG, and dAG/ IPS [55]. Semantic decisions in particular are reported to activate a large constellation of cortical regions, including bilaterally the ATLs, pFC, posterior temporal cortex and angular gyrus [27], [46], [149].

Region of interest analyses demonstrated uncorrected significant effects of task demands within the left and right inferior frontal gyrus, the left posterior middle temporal gyrus, the posterior inferior temporal gyrus and the pre-frontal gyrus. In the pars triangularis and the pars orbitalis, lower activity was observed for the high task-demand level versus the lower task demand level. This demonstrates the task demand effect in these regions. We did not find any significant interactions between task demands and activation in the regions of interest. We found only minimal task demand effects and strong task-related effects. Activation in the inferior frontal gyrus and the posterior middle temporal gyrus has been frequently reported in the literature to be associated with the more difficult conditions of semantic tasks [45], [150] in regards to both the number of competing representations and the amount of semantic information to be retrieved [45], [150], [151]. Left IFG activation is also proposed to be modulated when semantic representations are competing with each other as well as in relation to the amount of information required to be retrieved [45], [152]. Noonan et al. (2013) [46] suggested that activation of both IFG and pMTG together is crucial in establishing, maintaining and applying task-related, goal-related and contextual representations in semantic processing. The co-activation of IFG and pMTG is also associated with high executive-semantic demands [153]. Applying transcranial magnetic stimulation (TMS) to the pMTG has interfered with semantic decisions [154] the IFG or the pMTG has interfered with semantic retrieval (such as retrieval of weak semantic relationships) [155]. More specifically, it has been suggested that the left posterior IFG contributes to high-demand semantic decisions whereas the right posterior IFG contributes to picture-based decisions [153]. Whereas the BA45 portion of the left mid-IFG appeared to be strongly activated in most difficult conditions of all tasks and input modalities (words or pictures) [68], other parts of the IFG demonstrated a differential specialization and activation depending on modalities and tasks [153]. Activation in the IFG was found to be age-invariant in a semantic judgment task with two levels of difficulty and four across-the-lifespan age groups [64]. Numerous accounts in the literature have thus provided support for the co-activation of the IFG and the pMTG for the controlled retrieval and management of semantic memory [49], [55], [156], [157]. In regards to age-related IFG activation, a meta-analysis on age-related changes in the neural networks supporting semantic cognition demonstrated reduced activation in the left IFG in older adults performing semantic tasks whereas IFG recruitment was enhanced in the right IFG, especially when their performance was not maintained, in comparison to their younger counterparts [22]. Similarly, in a semantic judgment task, older adults were found to rely more on the left IFG when semantic competition was high [66].

The requirement for semantic control during semantic judgment tasks is still under investigation. Some studies have suggested that semantic judgment tasks require less effort for retrieval and control as compared to naming tasks for example [65] given the reduced demands for mental imagery [14], [158], [159]. On the contrary however, it has also been proposed that the requirement to select between competing information post-retrieval would necessitate the recruitment of the semantic control processes to a larger extent, manifested as increased activation in the multiple demand network and more specifically the left ventral PFC [65], [26], [46] and the left IFG which is thought to be typically activated in semantic judgment tasks [64]. Overactivation in the IFG however may simply reflect the longer time participants maintain triads in their working memory while comparing their semantic features [61]. Overall it is thought that semantic judgment tasks tap extensively both the semantic and multiple demand networks, as they require the integration of both internal and external representations [46]. Despite preserved behavioral performance, underactivation in the control-related IPC was observed in the older adults as a result of increased task demands which the authors justified by semantic judgment tasks generally requiring less semantic control [65].

Within the current data, the lack of a significant difference in activation between the two levels of task demand conditions may be explained by the fact that our stimuli did not capture differences sufficient to yield a difference in neurofunctional activation. For example, we did not control our stimuli for living versus non-living items, which has been shown to influence processing [121], nor did we control for motor or visual features [120]. It is possible that the task was not sufficiently challenging for either younger or older particpants, such that it would not require the recruitment of additional neural resources, or that the difference between low and high task demands was not big enough to provoke an increase in activation in either younger or older adults. It is also possible that the task was already too demanding for both younger and older adults such that no additional activation was possible, as participants had maxed out their neural resources. Indeed, since the IFG is key to semantic processing as part of the semantic network, demonstrating robust activation across numerous semantic tasks, its spare capacity for additional recruitment may be limited, either in younger or older adults [23].

Recently, Jamadar (2020) [40] tested the CRUNCH model through a visuospatial working memory with 4 levels of task demands. The results showed an effect opposite to the one predicted by CRUNCH. The author challenged the CRUNCH model as it cannot easily be tested or falsified based on imaging methodologies, since whether activation increases or decreases, it can still be claimed to be compensation, whether successful or failed (e.g., that behavioral performance would be worse without the additional activation). The author concludes that issues such as cognitive reserve, brain maintenance, compensation and de-differentiation face issues of definitions, operationalizations and falsifications. More specifically, to test CRUNCH it is necessary to manipulate task demands parametrically across 3-4 levels; however, not all cognitive fields could be amenable to such manipulations, including semantic memory.

Specifically to semantic memory preservation in aging, the above findings could be partly in line with two compensatory hypotheses proposed: the executive hypothesis, refers to the recruitment of domain-general executive processes seen as overactivation in prefrontal, dorsal premotor, inferior frontal and inferior parietal brain regions to compensate for age-related cognitive decline [6], [103]. A recent meta-analysis found that activation shifts from neurally specialized regions to more task-general areas with aging [22]. For example, in a study where participants had to decide whether two words share a common feature, better-performing older adults had increased activation in comparison to both young and poorer-performing older adults, notably in bilateral premotor cortex as well as inferior parietal, and lateral occipital cortex, regions important for executive functions and object knowledge, in support of the executive hypothesis [56]. In a semantic judgment task using MEG where participants decided whether a word was concrete or abstract, older participants activated the posterior middle temporal gyrus, inferior parietal lobule and the ATL more in comparison to the young, whereas the young activated the left inferior prefrontal cortex (IPC) to a greater extent than the elderly, leading the authors to conclude that elderly overactivated executive control regions to compensate and maintain their performance. Alternatively, the semantic hypothesis also known as left anterior-posterior aging effect (LAPA), refers to the recruitment of supplementary semantic processes and representations seen as overactivation in the old in the left posterior temporo-parietal cortex [104], [105]. Given the larger decline in older adults of executive over language functions could partly justify this latter hypothesis assuming the compensatory recruitment of semantic over executive processes [106]. For example, in a semantic judgment study where participants had to decide if a word is an animal or not, older participants had more bilateral parietal, temporal and left fusiform activations than young who presented more dorsolateral activations, leading the authors to suggest that older participants compensate with more semantic processes whereas younger participants rely on frontal-based executive strategies [107]. It is important to note however that regions such as the left inferior frontal gyrus and PFC serve both executive and language functions as described in the semantic network [53], somehow blurring the intersection between the semantic and executive hypothesis. Additional analyses are expected to elucidate the role of the semantic control network when performing a semantic judgment task with two levels of task demands in younger and older adults.

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Chapter 5 – Fourth article. Evolution of taxonomic vs. thematic semantic relations: an fMRI study

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Abstract

Semantic relationships between words can be classified as taxonomic or thematic depending on whether they are members of the same category or co-occur in space and time. In dual-hub theory, the two types undergo distinct neurofunctional processing: the anterior temporal lobes (ATLs) bilaterally act as semantic hub for taxonomic relations, while the left temporoparietal junction (TPJ) performs this function for thematic relations. According to Controlled Semantic Cognition or single-hub theory, only one hub, the ATLs bilaterally, subserves both types of relationships, and TPJ activation TPJ differs depending on task demands and semantic control requirements. This study aimed to assess how aging affects the processing of taxonomic versus thematic relationships and their respective hub(s), given that exposure to vocabulary and life events increases throughout the lifespan, potentially favoring both types of semantic relationships. This study compares 39 younger (20–35 years) and 39 older (60–75 years) adults who performed a triad-based semantic judgment task in an fMRI scanner while the type of semantic relationship (taxonomic versus thematic) and task difficulty (low versus high-demand) were manipulated. If the ATLs and TPJ act as neural hubs of the network of brain regions underlying the semantic network, then aging was expected to affect connections between semantic hubs and their spokes, manifested as differential activation in the bilateral ATLs and left TPJ regions of interest in the older and younger participants. Our findings partly confirmed our hypotheses. We found significant behavioral differences between younger and older adults in terms of response times, but similar accuracy. We found an interaction between age group and task demands and an age effect only on the taxonomic and high-demand conditions. Overall, our task activated a large bilateral fronto-temporo-parietal semantic network, including the left inferior frontal gyrus and the right parietal and temporal inferior gyri. We did not find significant activations when contrasting taxonomic vs. thematic conditions. In younger participants, the taxonomic condition activated both the ATLs and the left TPJ, whereas in the thematic condition, when the TPJ was activated bilaterally, the ATLs were not significantly activated. In older participants, however, activation patterns of semantic hubs varied depending on the condition, with taxonomic relationships activating the ATLs more robustly than the TPJ and thematic relationships having the opposite effect. For both taxonomic and thematic conditions, TPJ activation increased as a function of task demand in younger participants, but not in older adults. The findings thus lend partial support to both the single- and dual-hub hypotheses depending on age group. Additional analyses of the ATLs and the TPJ will elucidate the processing of the two semantic relationships by younger and older adults.

1. Introduction

Our conceptual knowledge of the world, termed semantic memory, is thought to be organized as a web-like network of interconnected nodes, known as semantic relationships, which form what is called the semantic network (Nocentini et al., 2001; van der Meer, 1980). Words are therefore not processed independently from each other; rather, when a word is recognized, multiple other words are also activated, facilitating the retrieval and manipulation of semantic representations (Bonner & Price, 2013; Landis & Regard, 1988). The semantic network of nodes is subserved by the brain areas that typically activate during semantic memory tasks, the semantic network (Baciu et al., 2016; Badre & Wagner, 2002; Binder et al., 2009; Diaz et al., 2018; Noonan et al., 2013).

Depending on whether semantic relationships are are the product of more formal learning or are naturally learned from direct experience, they can be classified as taxonomic or thematic, respectively. Taxonomic relationships such as *dog–fox* represent members of the same category (e.g., animals), share some perceptual/functional features (e.g., four legs) (de Zubicaray et al., 2013) and are organized in logical taxonomies or hierarchies **(Belacchi & Artuso, 2018; Devlin et al., 2002; Estes et al., 2011; Lin & Murphy, 2001; Sachs, Weis, Krings, et al., 2008)**. Thematic relationships such as *dog–bone,* on the other hand, are external and complementary; are based on personal experience and co-occurrence in space and time **(de Zubicaray et al., 2013; Dilkina & Lambon Ralph, 2012; Estes et al., 2011; Schmidt et al., 2012)**, action experience (Kalénine et al., 2009) or interaction in a scene or event (Sachs, Weis, Zellagui, et al., 2008); and are directly stored as such in long-term semantic memory (Klix, 1978; Mirman et al., 2017). Overall, there is evidence that both types of relationships represent equally valid types of organization of our conceptual knowledge of the world, and there is no particular preference for either **(Estes et al., 2011; Lin & Murphy, 2001; Nedergaard, 2017; Sachs, Weis, Krings, et al., 2008)**. It is not yet known, however, how processing of both types of relationships evolves throughout one's lifetime, given that older adults have greater experience with both words and life events, and generally have a well-maintained semantic memory **(Kavé et al., 2009; Prinz et al., 2004; Salthouse, 2009; Verhaegen & Poncelet, 2013; Wingfield & Grossman, 2006)**.

Differences in neurofunctional activation during the processing of taxonomic versus thematic relationships have been reported in younger adults (16–42 years old) **(Kalénine & Buxbaum, 2016; Kalénine et al., 2009; Mirman et al., 2017; Satterthwaite et al., 2016)**. The level of effort required to process each type of relationship is often discussed in the literature given the assumption that thematic relationships are more natural, and therefore more accessible, whereas taxonomic ones are taught or made-up and therefore more demanding. Some neuroimaging studies, for example, found that taxonomic relationships are more difficult to process than thematic ones, activating a larger or more right-lateralized neural network **(Kotz et al., 2002; Noppeney & Price, 2004; Paivio, 1991; Sachs, Weis, Krings, et al., 2008; Sachs, Weis, Zellagui, et al., 2008; Sass et al., 2009; Schmidt et al., 2012; Scott et al., 1982, 1985)**. Taxonomic relationships are thought to require more effort, probably because they are learned later in life and are therefore weaker (Kotz et al., 2002; Scott et al., 1985; Scott et al., 1982) or because their processing requires the selective abstraction of shared features and ignoring of others **(Noppeney & Price, 2004; Paivio, 1991; Sass et al., 2009)**.

Conversely, other studies have found that thematic relationships are more difficult to process than taxonomic ones (Kalénine et al., 2009; Kuchinke et al., 2009). The rationale is that they require more contextual processing than taxonomic relationships (Kalénine et al., 2009) or that they are more relevant for abstract than concrete words, and the former require more effort to process (Hoffman et al., 2013). Overall, findings about the neurofunctional activation pattern for taxonomic versus thematic relationships, their perceived difficulty or preferences for one type of relationship or the other are fairly divergent. This divergence may be partly explained by the use in different studies of different methodologies and stimuli (e.g., nouns, verbs, pictures, auditory stimuli); the different definitions adopted for the two types of relationships, including various subtypes (e.g., sequential thematic relationships, action/non-action, natural objects versus artifacts, etc.); individual differences; and even different task instructions (for a review, see Mirman et al. 2017). Few studies, however, have focused on how the differential processing of taxonomic versus thematic relationships is affected by aging, characterized by increased semantic network size and connections, as well as increased life experiences.

Some age-related changes in processing taxonomic and thematic relationships seem plausible. Studies of the evolution of the semantic network in aging (Dubossarsky et al., 2017; Siew et al., 2019; Wulff et al., 2019; Wulff et al., 2016) report increases not only in its size – increased vocabulary (Balota et al., 2004; Kahlaoui et al., 2012; Wulff et al., 2019) – but also in its density – increased connections among its nodes (Zortea et al., 2014). Longer life experience could entail increased exposure to events, reinforcing thematic relationships. Indeed, thematic relationships are thought to become more robust depending on the frequency with which they are experienced (Estes et al., 2011; Jouravlev & McRae, 2015), which represents an advantage for older adults, who have more experience with life events. Not all thematic relationships are expected to be reinforced equally, however, as some are thought to be encountered more frequently and thus to become stronger than others (Estes et al., 2011). Longer life experience could also mean greater exposure to words and therefore a larger vocabulary (Dubossarsky et al., 2017; Zortea et al., 2014). Indeed, older adults are found to perform better than younger ones in tests assessing vocabulary size (Krieger-Redwood et al., 2019); however, they perform less well when tasks require semantic selection (Hoffman & Morcom, 2018).

On the contrary, it has also been suggested that, with age, the lexicon becomes less connected, less organized and less efficient with overall declining clustering coefficients throughout the lifespan (Dubossarsky et al., 2017; Wulff et al., 2018). Older adults' semantic network is claimed to become less flexible even though their semantic memory is preserved across the lifespan, potentially resulting in differences between younger and older adults' response times and language production (Cosgrove et al., 2021). Given that older adults have a larger vocabulary, implying a larger network with more nodes between semantic representations, it may be more “costly” for them to access and navigate the semantic network, resulting in longer reaction times (Siew et al., 2019). In addition, structural changes in semantic networks could affect the speed of accessing and processing semantic representations (Ramscar et al., 2014; Ramscar et al., 2017; Wulff et al., 2019). In other words, searching the semantic network may be more demanding for older adults because this network is larger, and in turn, these higher demands may account for the general cognitive decline observed in aging **(Pakhomov & Hemmy, 2014)**. On the other hand, it has been reported that, when the default mode network connectivity between the right anterior temporal lobe (ATL) and the prefrontal cortex increased, behavioral outcomes improved, especially for older adults. This suggests that increased connectivity favors access to conceptual representations, especially in older adults (Krieger-Redwood et al., 2019).

Some studies on processing of taxonomic versus thematic relationships have questioned whether their distinct neural processing reflects a single or two parallel and complementary knowledge systems, and whether specific hub areas are assigned to each type of semantic relationship to converge information. In dual-hub theory, if two distinct systems exist, the ATLs bilaterally have been suggested to serve as a hub for taxonomic relationships and their features (e.g., function, location), while the left temporoparietal junction (TPJ) acts as a hub for thematic ones **(Geng & Schnur, 2016; Jackson et al., 2015)**. Several studies have found evidence of such a dissociation **(Geng & Schnur, 2016; Lewis et al., 2015; Schwartz et al., 2011; Tsagkaridis et al., 2014)**. Other studies, however, have not found evidence of the reported dissociation (Devlin et al., 2002; Hoffman et al., 2013; Jackson et al., 2015; Lewis et al., 2015). A study comparing taxonomic with thematic concepts found that both types of relationships activated equally the same semantic neural network; any differences were mainly attributed to different difficulty levels and requirements for semantic control (Jackson et al., 2015). The ATLs were significantly activated bilaterally for both types of relationships, whereas the TPJ showed no difference in activation for either one (Jackson et al., 2015). In a magnetoencephalography (MEG) study, the ATLs were activated more for taxonomic than thematic relationships, whereas the TPJ was activated equally for both (Lewis et al., 2015).

The ATLs bilaterally, including the middle temporal gyrus (BA 21), seem to play a central role in semantic processing. Converging evidence from functional neuroimaging studies suggests that they are critically involved in semantic representation (Lambon Ralph et al., 2017; Pobric et al., 2010; Rice et al., 2018; Rice et al., 2015; Visser, Embleton, et al., 2010). Within the Single-Hub theory, the ATLs are described as an amodal hub, connected bidirectionally with modality-specific spokes and responsible for converging representations into coherent conceptual knowledge (Binney et al., 2016; Jefferies, 2013; Lambon Ralph et al., 2017; Lambon Ralph et al., 2010; Patterson & Lambon Ralph, 2016; Patterson et al., 2007; Rice et al., 2015; Rogers et al., 2004). The ATLs are important for identifying and naming objects (Mirman et al., 2017) and are also thought to subserve judgments about whether a concept is a member of a category or not (Kemmerer, 2015; Lambon Ralph et al., 2010; Patterson et al., 2007; Visser, Embleton, et al., 2010), therefore important for taxonomic processing. In addition, neuropsychological evidence from patients with semantic dementia having lesions in the ATLs present, as a first symptom, anomia, a difficulty in naming objects (Jefferies, 2013; Visser, Jefferies, et al., 2010). Some patients with semantic dementia produced more taxonomic than thematic errors (Schwartz et al., 2011), whereas others are worse at identifying thematic than taxonomic relationships (Hoffman et al., 2013). Consequently, atrophy in the ATLs seems to affect the integrating hub in charge of monitoring the coherence of semantic memory and therefore taxonomic relationships (Hoffman et al., 2013; Patterson et al., 2007; Rice et al., 2018).

While the ATLs have been coined the “what” visual pathway, specializing in processing color and shape, the TPJ on the other hand, has been coined the “where/how” pathway, specializing in action and location and contributing to episodic memory and the completion of events (Kravitz et al., 2013; Mirman et al., 2017; Spunt et al., 2015) or else, in “event semantics” (Binder & Desai, 2011). The TPJ, including the angular gyrus (AG), is thought to be crucially involved in retrieving and integrating concepts in coherent representations, and has consistently been found to be activated during such tasks, according to meta-analyses of neuroimaging studies of semantic memory (Binder et al., 2009; Cabeza & Nyberg, 2000; Humphreys & Lambon Ralph, 2015; Mirman et al., 2017; Seghier et al., 2010). Like the ATLs, its anatomical position and connections with multiple modality systems make the TPJ an ideal transmodal convergence hub (Binder & Desai, 2011; Patterson et al., 2007; Price et al., 2015; Price et al., 2016). In a task combining adjectives with nouns across four different categories, for example, it was reported that the AG was involved in thematic relationships (combinatorial semantics) independently of task difficulty, since increased AG activation was not observed during the most difficult condition (Price et al., 2015).

Other studies, however, have emphasized the role of the AG in semantic control rather than semantic representations, thus questioning its role in the processing of thematic relationships. For example, in a large-scale meta-analysis of the role of the parietal lobe in cognition, the AG was found to be consistently activated as part of the default mode network but was also found to demonstrate increasing task-related deactivation when task difficulty increased **(Humphreys & Lambon Ralph, 2015; Lambon Ralph et al., 2017)**. Similarly, the AG has been found to be consistently recruited by the most difficult semantic tasks (Noonan et al., 2013). It was therefore proposed that the TPJ has a central role in the semantic control system **(Davey, Rueschemeyer, et al., 2015; Jefferies & Lambon Ralph, 2006; Lambon Ralph et al., 2017; Noonan et al., 2013)** and perhaps the frontoparietal multi-demand control system (Duncan, 2010; Krieger-Redwood et al., 2019).

No study to our knowledge has compared the processing of taxonomic versus thematic semantic relationships in light of aging theories, the aging lexicon and the respective roles of the ATL and TPJ semantic hubs. The question arises of how the differential processing of taxonomic versus thematic relationships and their potentially different semantic hubs evolve throughout the lifespan. Given the inconsistent results in the literature about the differential or similar processing of taxonomic versus thematic relationships, in this study we aim to fill this gap by examining these two types of semantic relationships within the aging semantic memory framework. Only a few behavioral studies have explored this question and none have explored the underlying brain functions.

Some behavioral studies have suggested that taxonomic relationships are more affected by aging than thematic ones **(Barulli & Stern, 2013; Maintenant et al., 2011; Maintenant et al., 2013; Rozencwajg & Bertoux, 2008)**. For example, a study comparing taxonomic with thematic relationships in long-term recall memory found that taxonomic relationships facilitated recall memory until the age of 65 years. After 65, the pattern appeared to be inverted, suggesting that the thematic component of recall memory is better preserved than the taxonomic one **(Belacchi**

& Artuso, 2018). Another study reported that taxonomic processing increases compared to thematic processing from childhood to adulthood and again decreases over thematic as a function of aging (Rozencwajg & Bertoux, 2008).

Children are thought to have a preference for “primitive” thematic relationships and these relationships remain important for adults, even after similarity of features and taxonomic membership become the default sorting rules (Lin & Murphy, 2001). It appears that personal circumstances such as exposure to different experiences, education level, Western culture and individual characteristics are some of the factors that influence more taxonomic or more thematic thinking (for a review, see Lin & Murphy, 2001). The only fMRI study comparing stroke patients with left-hemisphere lesions to healthy older adults found that artifact (manipulable human-made objects) concepts present an advantage for thematic relationships, regardless of age (Kalénine & Buxbaum, 2016). In a study with 10 experiments that tested different factors, Lin and Murphy (2001) stressed the importance of the salience of different types of relationships and found that, although thematic relationships are still important in adulthood, they are rarely sufficient to organize the world around us. This difference in inclination toward taxonomic or thematic relationships may depend on individual preferences regardless of age, as younger and older adults are equally sensitive to the strength of association between the two types of relationships (Pennequin et al., 2006). According to Pennequin et al., any age differences in preference for either type of relationship would reflect behaviors related to perceiving and organizing the environment rather than cognitive decline.

In this study, we aim to bridge the gap in the literature concerning the existence and evolution of semantic hubs in aging, in light of dual- and single-hub theories. We evaluate the effect of aging on the role of the ATLs and the TPJ as neural representations of the semantic hubs responsible for taxonomic and thematic processing, respectively, hypothesizing that age-related increases in semantic network connections among semantic nodes are manifested as differential activation in the brain regions subserving them (ATLs and TPJ). We compared younger and older adults when processing taxonomic versus thematic relationships in a semantic judgment task and studied the respective roles of the ATLs and TPJ as neural hubs of the brain network underlying the semantic network, while manipulating for semantic control demands (Jackson et al., 2015). The semantic distance variable manipulated in this study adds a quantitative aspect, and helps differentiate the two effects in terms of performance and brain activation (Sabsevitz et al., 2005). Independent variables in this study include age group, type of semantic relationship (taxonomic or thematic) and task demands (low or high), while dependent variables include brain activation and behavioral performance (accuracy and response times (RTs)). The study's hypotheses are:

1. If dual-hub theory (Geng & Schnur, 2016; Jackson et al., 2015) is correct, then we expected a double dissociation across age groups such that processing of taxonomic relationships would significantly activate the ATLs but not the TPJ, whereas processing of thematic relationships would significantly activate the TPJ but not the ATLs. This would confirm that the ATLs and TPJ act as semantic hubs in both younger and older adults.

2. If single-hub theory is correct (Binney et al., 2016; Jefferies, 2013; Lambon Ralph et al., 2017; Lambon Ralph et al., 2010; Patterson & Lambon Ralph, 2016; Patterson et al., 2007; Rice et al., 2015; Rogers et al., 2004), we expected to find increased activation in the ATLs in both younger and older adults and for both taxonomic and thematic semantic relationships, whereas activation in the TPJ would vary only as a function of task demand,

given its role in semantic control. Thus, any differences in brain activation would depend on task demand but not on the type of semantic relationship.

3. Given older adults' greater life experience and word exposure, as well as behavioral evidence that thematic relationships are better preserved in aging than taxonomic ones, and irrespective of whether dual- or single-hub theory is found to be valid, we expected to find differential activation in the ATLs and TPJ in older and younger adults, supporting the idea that aging may impact the brain regions subserving the semantic hubs.

2. Materials and methods

This study complied with the OHBM COBIDAS report (Nichols et al., 2017) and guidelines (Poldrack et al., 2008) as much as possible. It used the same data acquisition protocol and preprocessing methodology reported in the study by Haitas et al. (2021). This study has a unique focus on the effect of aging on taxonomic versus thematic relationship processing, whereas the other study focused on the effect of task demands in aging.

2.1 Participants

In order to have sufficient power, 80% (alpha = 0.05), to distinguish between two age groups in terms of activation in the ATLs bilaterally and the left TPJ, 80 participants were required: 40 younger adults (20–35 years) and 40 older adults (60–75 years) (male = female). This sample size was based on power calculations using the fMRIPower tool (http://fmripower.org/; **Mumford & Nichols, 2008)** using data from an age group comparison (healthy younger and older adults) in a similar task (Boston naming; Ferré et al., 2020). (Although efforts were made to find statistical maps from a semantic similarity task comparing younger with older adults to base our power calculations on, these were not available.) In addition, to have sufficient power to detect condition and age group effects, this study quadrupled the sample size used by Geng and Schnur (2016), who had a sample of 10 people in each group to identify differences in taxonomic versus thematic brain activation, with 90% predictive power (alpha = 0.05). The number of stimuli used in this study is approximately three times more than the one used in Geng and Schnur's.

To account for potential exclusions due to excessive motion, poor performance or technical difficulties, we aimed to recruit 86 participants. We contacted 265 participants in total (194 younger and 71 older). We ultimately recruited 84 participants (instead of the 86 initially planned). Recruitment took place from June 17 to December 24, 2021. Of the 84 participants scanned, 3 were excluded because they experienced panic attacks during the scan. At the analysis level, 3 participants were excluded because data (either behavioral or imaging) were missing, and 4 were excluded due to excessive motion. We ended up with 78 participants in total, 39 younger (Y = 20–35 years) and 39 older adults (O = 60–75 years) (these are the same participants as the ones mentioned in the previous study).

Participants were recruited from the Centre de Recherche Institut Universitaire de Gériatrie de Montréal (CRIUGM) research center's pool of participants and poster announcements in neighboring buildings and social media. All participants had completed a minimum of CEGEP (junior college) education. French was their dominant language and the one they used every day; multilingual participants were excluded (Perquin et al., 2013). Participants were screened for fMRI compatibility and for health and neuropsychological inclusion/exclusion criteria to exclude any history of neurological illness. They provided written informed consent and were financially compensated for their participation according to the Institute's Ethics Committee policies.

2.2 Material

The methodology described here below is identical to the one described in the previous study.

2.2.1 Neuropsychological tests

During a first phone interview, we collected demographic information on every participant's age, gender, years of education, mother tongue and handedness, and administered a health questionnaire to exclude people with a history of dementia, drug addiction, major depression, stroke, aphasia, cardiovascular disease or any drugs that could affect results. To control for the use of French and other languages, given that many people in the recruitment region are bilingual or multilingual, we assessed the frequency of use of French and other languages (multilinguals were excluded). Questions were asked about the frequency of use of French and other language use during work/education, communication with partners and friends, reading books, watching television and writing. Potential responses were daily, several times a week, several times a month, several times a year and never. We excluded participants whose native language or most frequently used language was not French (from the 265 participants contacted in total (194 younger and 71 older), 29 were excluded because French was not their native or most frequently used language).

During the first in-person session, we administered the following tests:

1. The Edinburgh Handedness Inventory: participants were right-handed with a minimum right-handedness score of 80 (Oldfield, 1971).
2. The MoCA (Montreal Cognitive Assessment) with a minimum cutoff score of 26 (Nasreddine et al., 2005; Waldron-Perrine & Axelrod, 2012).

3. The MRI-compatibility checklist (Unité Neuroimagerie Fonctionnelle/UNF) (available at https://unf-montreal.ca/forms-documents/).
4. The Pyramids and Palm Trees Test (PPTT; image version; **Howard & Patterson, 1992)**, which was used as a measure of semantic performance.
5. The Similarities section of the Wechsler Adult Intelligence Scale (WAIS-III; Axelrod, 2002; Schrimsher et al., 2007).
6. The Habitudes de Lecture (Reading Habits) questionnaire, based on Wilson et al. (2003), as a measure of cognitive reserve (Stern, 2009). We derived a global score that reflected the mean frequency of engagement in cognitively stimulating activities during the lifetime, from 6 years old to the present, called "Life Activities."

Older (O) and younger (Y) participants differed significantly on age (mean = Y = 23.97; mean O = 66.72); the frequency of the use of English in their daily life, with younger participants using it more frequently (t = 6.11, p < .001; mean Y = 2.15; mean O = 0.75); and less on the PPTT semantic score (t = –2.8, p < .05; mean Y = 49.9; mean O = 50.9). Participants (n = 78) were equally distributed in terms of gender (All participants: n = 78, Y: F = 17, M = 22, O: F = 14, M = 25, all: F = 30, M = 47). We did not find any other statistical differences between older and younger participants regarding demographic and neuropsychological variables (p < .05). Younger and older participants were matched for education (years; t = 0.17, NS; mean Y = 17.36; mean O = 17.28); frequency of engagement in cognitively stimulating activities from age 6 to present (Life activities: t = 1.18, NS; mean Y = 3.51; mean O = 3.36); handedness (Edinburgh Inventory score; t = –1.96, NS; mean Y = 88.15; mean O = 92.2); general cognitive level (MoCA; t = –0.17, NS; mean Y = 28.28; mean O =

28.33); and verbal reasoning (WAIS-III Similarities; *t* = –0.45, NS; mean Y = 17.03; mean O = 17.41). See Table S1 in the Supplementary Material for statistical details.

2.2.2 Semantic Similarity Judgment (fMRI) task

A semantic similarity judgment task in French, similar to the Pyramids and Palm Trees Test (PPTT) (Howard & Patterson, 1992), was administered to participants; it is also similar to the tasks used in earlier studies (Binney et al., 2016; Jackson et al., 2015; Sachs, Weis, Krings, et al., 2008). The semantic similarity judgment task was chosen because it was expected to elicit deep semantic processing as it requires explicit access and retrieval of semantic knowledge in order to judge similarity (Baciu et al., 2016; Sabsevitz et al., 2005); it activates large semantic networks as in semantic priming and independently of working memory processes (Allen et al., 1993; Evans et al., 2012; Reilly et al., 2011). As such, it is thought to require less effort for semantic retrieval than a naming or other word production task (Lacombe et al., 2015), since when a word is recognized, semantic representations and associations are automatically created, minimizing mental imagery demands (Bonner et al., 2013; McLeod, 2007; Pulvermüller et al., 2005). Therefore, this task's demands on attention and memory, factors known to be most affected by aging (Stebbins et al., 2002), are reduced compared with other tasks. Also, because processing of taxonomic versus thematic semantic relationships has been shown to stimulate differential activation (Schmidt et al., 2012). The semantic distance (distant versus close) variable that was manipulated in this study added a quantitative aspect, and helped differentiate one effect from the other in terms of performance and brain activation (Sabsevitz et al., 2005). However, this type of semantic task has been criticized on the basis that semantic decision tasks may not fully activate all the features involved in word pairs (Pecher et al., 1998) or engage deep semantic processing (Becker et al., 1997). It has also been criticized that this kind of task may not fully activate the features important in the distinction between taxonomic versus thematic relationships (Geng & Schnur, 2016).

The task involves triads of words presented on a screen in a pyramidal structure. Participants needed to decide, as fast and accurately as possible, within a maximum of 4 seconds, which of the two words presented at the bottom of the triad (target or distractor) was more closely related to the third word, presented above (stimulus). The task consisted of 150 triads divided into two experimental conditions: 60 taxonomic (TAX) triads and 60 thematic (THEM) ones. In addition, there was a baseline condition of 30 control triads, which required participants to indicate which of two consonant strings, pseudo-randomly presented, was in the same case as the target string (e.g., DKVP: RBNT or kgfc).

The baseline condition served as a positive control, with activation expected in the primary visual and motor cortices when group comparisons were conducted with the baseline condition (Geng & Schnur, 2016; Sachs, Weis, Krings, et al., 2008). The baseline condition was designed to maximize perceptual processing while minimizing semantic processing (Binney et al., 2016; Gutchess et al., 2010), based on the task used by Sachs, Weis, Krings, et al. (2008). This baseline condition was chosen because it is considered to be a "high-level" active condition, requiring judgments on the basis of perceptual identification, and does not include a semantic processing component (Binney et al., 2016; Gutchess et al., 2010). The triads appeared as in Figure 1:

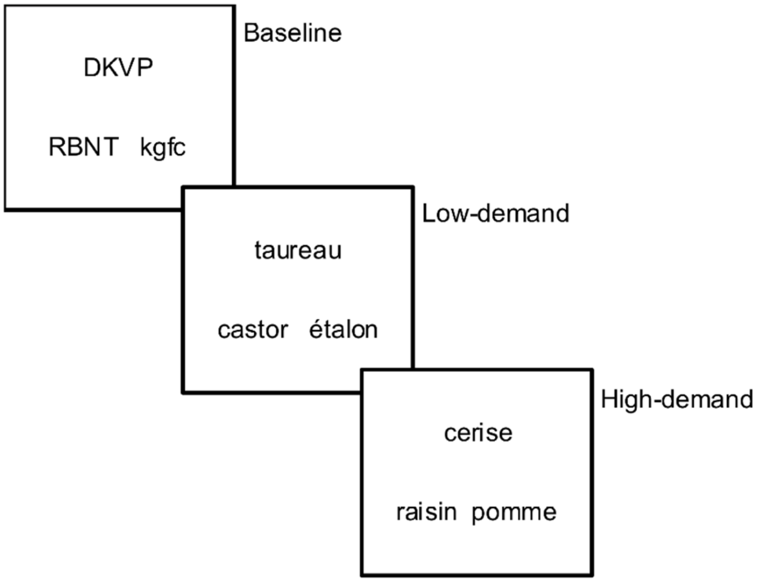


Figure 15. – Figure 1. Examples of experimental triads in three conditions

2.2.3 Stimuli

Thematic relationships were developed following the criteria described below, based on the definition that “Two words are considered associated if participants tend to produce one when prompted by the other” (Mirman et al., 2017). Thematic relationships were calculated with the help of the *Dictionnaire des associations verbales (sémantiques) du français* (Dictaverf: http://dictaverf.nsu.ru/dict, version accessed in 2014) as a function of the number of respondents who associated two words (i.e., the larger the number of respondents, the more closely associated the two words, and vice versa). As such, a score of 1 means that only one person provided this word (distant thematic relationship), whereas a score of 100 means that 100 people provided this word (close thematic relationship). To control for the level of effort required, half of the experimental triads required less effort (low-demand) and half required more effort (high-demand). The variable task demands allowed us to test the dual- versus single-hub theories.

The following definitions were used:

Taxonomic relationships (TAX)

- Low-demand:

All items (stimulus, target, distractor) belong to the same semantic category (e.g., animals). Stimulus and target words belong to the same semantic subcategory (e.g., birds); for example, *taureau: ÉTALON–castor* (bull: STALLION–beaver).

- High-demand:

All items in the triad come from the same semantic subcategory (e.g., birds). The stimulus and target items share a visual or structural feature whereas the distractor word does not; for example, *cerise: RAISIN–pomme* (cherry: GRAPE–apple), where cherries and grapes have a similar size and bunch structure, but apples do not.

Thematic relationships (THEM):

- Low-demand:

Both the target and distractor words are thematically related to the stimulus and occur in the list of answers presented by Dictaverf. To ensure the largest possible distance, the target was the first appropriate answer mentioned in Dictaverf, and the distractor was the last or almost the last answer, meaning that it had a score close to 1; for example, *sorcier: village–BAGUETTE* (wizard: village–WAND).

Alternatively, to ensure the largest possible distance, the following criteria were used: the distractor word has a score of 1 (which means only 1 person provided this answer); the distractor word scores between 2 and 5 and the target word scores above 10; or the difference between the target and distractor words' scores is greater than 100.

- High-demand:

Both the target and distractor words are thematically related to the stimulus. The target was the first appropriate answer mentioned in Dictaverf and the distractor had a score smaller than or equal to half of the target's score and scored at least 4. This criterion was used to ensure that the distractor was a frequently mentioned answer but distant enough from the target (e.g., half of the people mentioned the distractor as opposed to the target); for example, *enfant: JOUET–sourire* (child: TOY–smile). Additional information about the development of stimuli is available in Haitas et al. (2021) .

2.3 Experimental Design

2.3.1 Session 1: Neuropsychological tests

Participants were initially tested for eligibility (health questionnaire and MRI screening form) by phone. If eligible, they could then participate in the first experimental session (approximately 45 minutes), where they provided written informed consent, took neuropsychological tests and practiced with 15 practice triads (five for each condition). Participants who were eligible for the fMRI scanning session were scheduled for the second session one week later.

2.3.2 Session 2: fMRI scanning

In the second experimental session (approximately 90 minutes), participants prepared to go in the scanner, where they listened to task instructions and practiced with three triads (one per condition). They were instructed to remain still in the scanner, and foam rubber pads in the head coil restricted their movement. Earplugs were provided to reduce machine noise. Their vision was corrected if necessary, with MRI-175 compatible lenses according to the prescriptions they shared in earlier sessions. Stimuli were presented to participants with E-Prime software, version 2.0.10.356, run on Microsoft Windows 10 (for the first 13 participants), and E-Prime 3.0 for the remaining ones, through an LCD projector projecting to a mirror over the participant's head. Participants selected their responses with an MRI-compatible response box, using any fingers on either hand to respond. Response data and RTs were recorded but no feedback was shared with participants. The trials of different conditions were presented randomly and counterbalanced and the location of the correct (target) choice was varied randomly and counterbalanced across trials. Participants were instructed to respond as fast as possible and to guess the answer if they did not know the meaning of any of the three words. Participant testing alternated between younger and older adults to minimize any bias due to scanner changes or upgrades. To assess perceived task difficulty, an additional session with participants took place following the fMRI acquisitions, at which they rated each triad for difficulty on a 7-point Likert scale (1: very easy; 7: very difficult).

The semantic task was event-related. Triads were presented for 4 seconds, during which participants needed to make a selection by pressing on any of the buttons on their left or right hand. A black screen followed for approximately 2.2 s. This interstimulus interval (ISI) varied randomly between 0.67 s and 3.8 s to remove possible correlations with the BOLD signal, or else to maximize variance in the BOLD signal and ensure unpredictability. A fixation point then appeared for 1.3 s, to prepare the participant for the next trial. More information on the methods used to define the ISIs is available in section 2.3.3. The whole trial lasted between 5.97 s and 9.1 s, with a mean of 7.5 s. Black screens were presented at the beginning and end of the Runs to allow for steady-state magnetization. The scanning flow is shown in Figure 2:

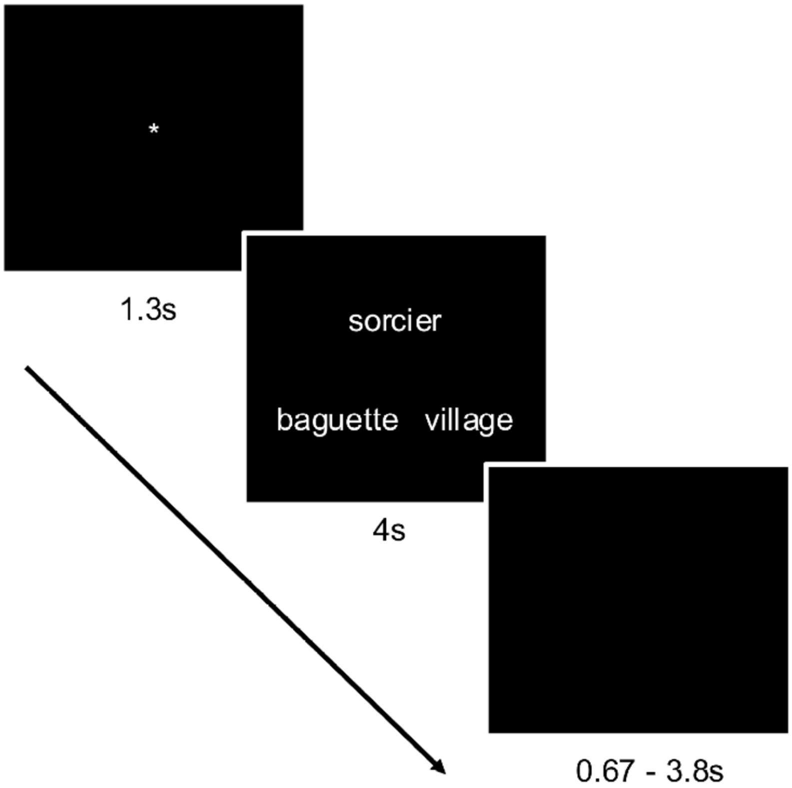


Figure 16. – Figure 2 Example of trial duration (triad and interstimulus interval)

The task was divided into two Runs with 75 triads each: 30 taxonomic triads, 30 thematic triads and 15 baseline triads, interspersed pseudo-randomly, so that no more than four triads of the same condition or type are repeated in a row, as described above. The duration of each Run was approximately 9:45 minutes. There was a short break (1 minute) between Run 1 and Run 2. The whole session lasted around 45 to 60 minutes.

2.3.3 Stimuli order and ISIs

To design the experiment in order to maximize design efficiency, optimal trial ordering and ISIs were chosen (Smith et al., 2006). The methodology used simulated random ordering designs in the three conditions. In addition, the ISIs were randomly drawn from Gamma distributions across a range of parameter values (shape: 0.1 to 10, scale: 0.1 to 5). This approach included expected error rates produced during the stimulus pilots to maximize design efficiency in the face of errors. A total of 800,000 simulations were performed. The ISI distribution and specific lists were chosen, as well as the condition order in which there was the smallest decrease in required BOLD signal response for detection as errors increased. The E-Prime files for the stimuli will be available at the OSF repository. Stimuli were not repeated.

2.3.4 fMRI data acquisition

Acquisition parameters were determined for an optimal temporal signal-to-noise ratio in the ATLs, as this area is thought to act as a hub for semantic memory (Binney et al., 2016; Chiou et al., 2018; Lambon Ralph et al., 2017), given the technical difficulty of ensuring good signals in this area due to air-filled sinuses (Devlin et al., 2000). To do this, a protocol for optimized EPI sequencing developed by colleagues (Julien Cohen-Adad and team) was followed to reduce signal dropout by using field maps to perform distortion correction and optimize signals in the ATLs bilaterally. The protocol also included a negative 30° angle from the axial plane to reduce signal dropout. Functional scans were performed on a 3 Tesla Syngo MR E11 Prisma_fit Siemens MRI machine with 32 channels at the CRIUGM's functional neuroimaging unit. The start of stimulus presentation was triggered by a pulse sent from the MRI to the stimulus laptop. To detect effects between conditions and to ensure a good fMRI signal in the brain, pilot data collected using the scanning protocol described here suggested a minimum temporal signal to noise ratio (TSNR) of 40 throughout the brain (Wang et al., 2013); this is considered to be the minimum TSNR required to reliably detect differences in signal (Murphy et al., 2007; Wang et al., 2013). Participant data were excluded if the TSNR, assessed for each participant's time series, was below 40. We acquired T1-weighted MRI images for co-registration with fMRI data and atlases and to identify regions of interest (ROIs) to be used as masks in the functional data analysis. An meMPRAGE (multi-echo MPRAGE) sequence (704 total MRI files) was acquired with 1 x 1 x 1 mm resolution, 2.2 s repetition time, 256 x 256 acquisition matrix, a Field of View (FOV) of 256 mm covering the whole head, and echo times of 1.87 ms, 4.11 ms, 6.35 ms, 8.59 ms, 13 ms and 15 ms. The phase encoding orientation was sagittal with a flip angle of 8°.

For the functional scans (Runs 1 and 2), T2-weighted BOLD data were acquired on the entire brain (including the cerebellum) using an Echo Planar Imaging (EPI) sequence with 50 slices, resolution 2.5 x 2.5 x 3 mm, echo time of 20 ms, repetition time of 3 s and flip angle of 90°. Field of view was 220 x 220 mm and the acquisition matrix was 88 x 88, in the AC–PC direction, covering

150 mm in the *z*-direction. Slice order was ascending interleaved. For each Run, 195 scans were collected. The SIEMENS default double-echo FLASH sequence for field map distortion correction with the same parameters was acquired after each sequence to correct for inhomogeneity. Functional images were reconstructed to the collected matrix size with no prospective motion correction. Two initial dummy scans were collected and discarded by the MRI, allowing for T1 saturation.

3. Analyses

3.1 Neuroimaging data analysis

3.1.1 Preprocessing

Preprocessing analysis was performed with SPM12 software (Penny et al. 2011). Images were corrected for slice timing (differences in slice acquisition time), with ascending slice order and using the acquisition time for the middle slice as the reference. We used field map correction to correct EPI images for distortion using the Calculate VDM toolbox and the first EPI image as reference. The gradient field map images were pre-subtracted by the scanner to provide phase and magnitude data separately. Motion correction was applied for within-subject registration and unwarping. Motion parameters were used later as confound variables. Data were visually inspected for excessive motion. Four participants (3 younger females and 1 older male) with estimated motion parameters of more than 2 mm, or 1° rotation, in any direction, were excluded. EPI functional volumes were registered to the average anatomical volume calculated by the machine over the four echoes of meMPRAGE T1-weighted anatomical scan. The mean anatomical image was used as the reference image and for quality control. Anatomical variations between participants were reduced by aligning the structural images to the standard space MNI template, followed by visual inspection of their overlay. An 8 mm full width at half maximum (FWHM)

Gaussian blur was then applied to smooth images within each Run. The final voxel size after preprocessing was 3 x 3 x 3 mm.

3.1.2 fMRI analysis

fMRI data analysis was performed with SPM12, focusing on the ATLs bilaterally and the left TPJ as primary ROIs. Using files created by E-Prime during stimulus presentation, stimulus onset files were created and four event-related regressors were defined for the taxonomic and thematic conditions at low and high-demand levels. For the first-level (intrasubject) analysis, a General Linear Model (GLM) employing the canonical Hemodynamic Response Function was used to estimate BOLD activation for every subject as a function of condition in the fMRI task. Each participant's fMRI time series (2 Runs) were analyzed in separate design matrices using a voxel-wise GLM (first-level models). Movement parameters obtained during preprocessing were included as covariates (regressors) of no interest to reduce the residual variance and the probability of movement-related artifacts. A high-pass filter with a temporal cutoff of 200 s and a first-order autoregressive function correcting for serial autocorrelations was applied to the data before the models were assessed. To test the main hypotheses, several contrasts of interest were calculated across both Runs, namely:

- All conditions of the task (High and Low demand, TAX and THEM relationships) versus the baseline condition (Baseline)
- TAX versus Baseline
- THEM versus Baseline
- TAX versus THEM
- TAX_Low versus Baseline
- TAX_High versus Baseline
- THEM_Low versus Baseline
- THEM_High versus Baseline

We also conducted additional contrasts (High versus Baseline; Low versus Baseline; High versus Low) not directly linked to our study hypotheses. The results of these contrasts are presented in the Supplementary Material (Tables S4 and S5).

For the second-level group analysis, individual contrasts were entered into a one-sample *t*-test. For all effects, activations were reported at a $p<.05$ significance level corrected for multiple comparisons (family-wise error- corrected). Group brain maps were calculated for all participants and each age group.

3.2 Statistics

Task performance

3 participants (2 older male, 1 younger female) with missing or incomplete behavioral or imaging data were excluded and 4 participants (3 younger females and 1 older male) were excluded due to excessive motion. 78 participants were finally analyzed (38 younger and 3 older). Accuracy (ACC), response time (RT) and self-reported Likert scores were estimated at each trial and then averaged for each group (All, Younger, Older), condition (baseline, TAX, THEM) and subcondition of the task (TAX_Low, TAX_High, THEM_Low, THEM_High).

To account for overall performance, we calculated a score that included both RT and ACC. This composite score represents the mean, for each trial individually, of ACC relative to 100 (ACC% = ACC*100), and RT relative to the total timespan of each trial (4 s) and multiplied by 100 (RT% = [RT/4000] * 100). Note that the RT% was then reversed (100 – RT%) so that, as with ACC, a high value (i.e., close to 100) reflects good performance on the test. For the other behavioral measures, the composite scores obtained for each trial were averaged according to group, condition or subcondition.

We conducted statistical analyses on behavioral measures using factorial ANOVAs. Behavioral differences between age groups were examined using standard statistical tests (*t*-test). To investigate the relationships between task performance (composite score) and the demographic and neuropsychological variables, simple and multiple linear regressions were performed. The composite scores were used as the scores of interest for this study. The details of the ACC, RT and Likert scores are presented in the Supplementary Material (Table S1 and Figure S1) for reference.

Neurofunctional activations

To evaluate our hypotheses concerning the semantic hubs, namely the modulation of neurofunctional activity according to task conditions or participant groups, we extracted the beta values using nilearn tools (https://nilearn.github.io/stable/index.html). Beta values were extracted for two ROIs in particular: the TPJ and the left ATL. To define the regions, we created masks from the Atlas of Intrinsic Connectivity of Homotopica Areas (AICHA) functional atlas (Joliot et al., 2015). Because the TPJ is located at the intersection of different functional regions, we assembled the following regions into a single mask: S_Sup_Temporal-4-L (–56.54 x –48.36 x 13.36); S_Sup_Temporal-5-L (–48.12 x 58.17 x 25.78); and G_SupraMarginal-7-L (–55.21 x –51.66 x 25.51). For the ATL, the AICHA region G_Temporal_Pole_Mid-1-L (–45.17 x 7.20 x –33.92) was used. See Figure 5 for an illustration. On the basis of the beta activation values extracted from the individual maps for these two regions, we carried out classic *t*-test analyses between the different conditions, ROIs and groups of participants. For all statistical analyses, a minimum threshold of $p < .05$ was considered as significant.

4. Results

4.1 Behavioral data

Task condition and group differences

For the composite performance score reflecting both ACC and RT, we found a significant difference at $p < .001$ between all conditions (Baseline, TAX, THEM; see Figure 3A). On the other hand, we did not find any difference between conditions that differentiated the Y and O groups.

The interaction between group and condition was not significant ($F = 1.6$, $p > .05$). Thus, both groups of participants were less successful in the THEM condition than the TAX condition or the baseline (see Tables S1 and S2). In all trials, the THEM condition induced more errors and longer RTs than the TAX condition (ACC; $F = 417.64$, $p < .001$) and was also perceived as more difficult (Likert scale; see also Table S1 and Figure S1 in the Supplementary Material).

Examining the subconditions in detail, it was found that all participants had the lowest performance in the THEM_High condition (see Figure 3A); they presented their worst ACC and longest RTs and also perceived it to be the most difficult condition (Figure S1). This is the only condition where there is a significant group effect on the composite performance score ($t = 3.64$, $p < .001$); the O group performed worse than the Y group (Figure 3A). Indeed, older participants were less accurate than their younger counterparts in this condition only. On the other hand, regardless of task condition, including for the baseline, older participants' RTs were significantly slower than younger participants' RTs. This difference was largest in the THEM_High condition, indicating an interaction between age group and task condition. Figure S1 in the Supplementary Material presents the responses observed on the different measures (ACC, RTs and self-reported difficulty on the Likert scale) for each subcondition.

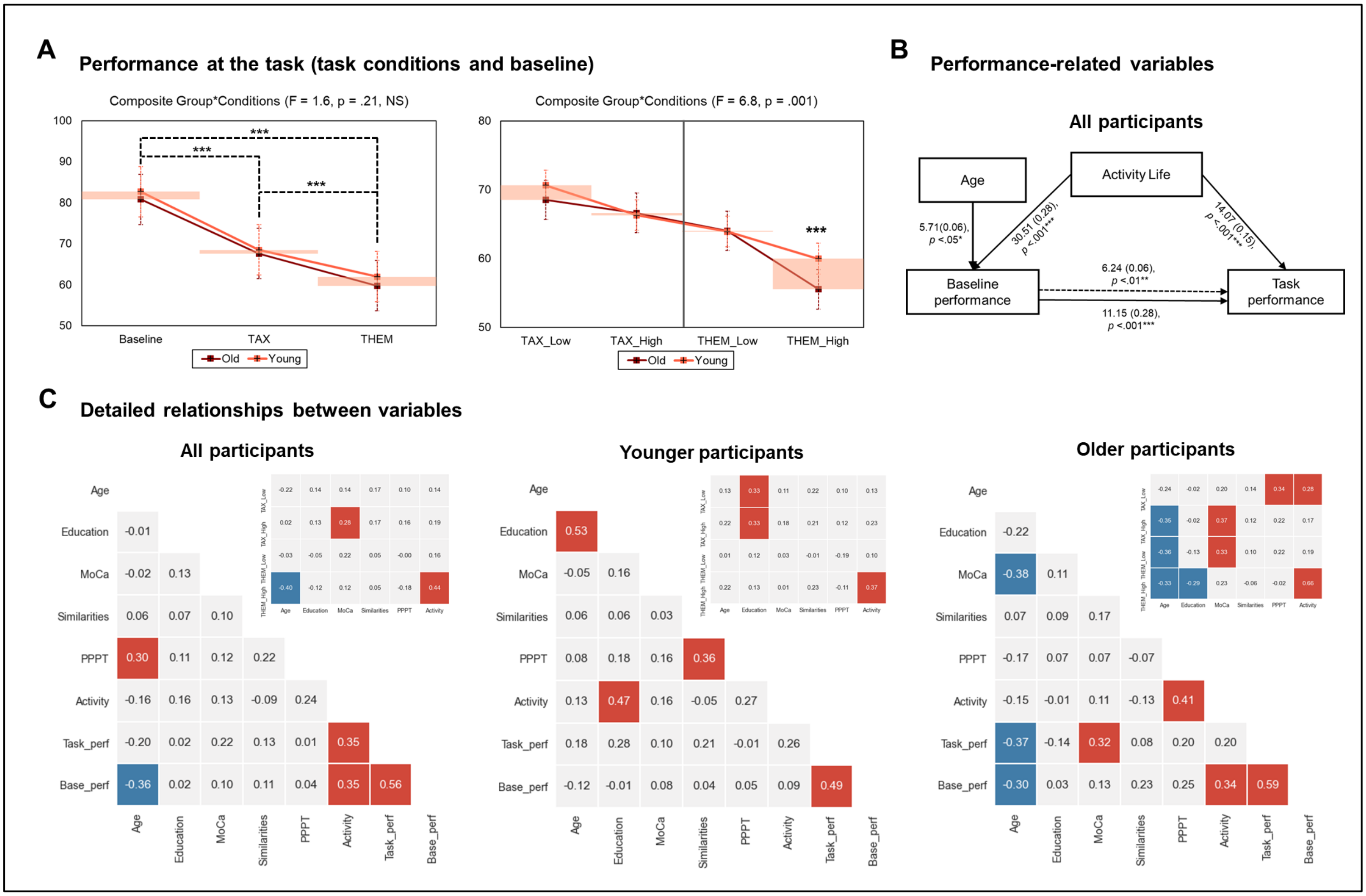
It should be noted that both groups of participants' RTs decreased overall between the two Runs (i.e., the two sessions of the task), which may reflect a learning effect (Table S1).

Associations between task performance and other variables

In all participants, task performance (i.e., the composite scores of all task conditions taken together) was significantly correlated with performance in the Baseline condition (i.e., the Baseline composite scores; $F = 11.15$, $p < .001$). Baseline scores and task scores are therefore interdependent. Performance in the Baseline condition was also significantly affected by age ($F = 5.71$, $p < .05$); the older the individual, the lower the performance.

In addition, we found a correlation between the baseline composite score and life activities ($F = 30.51$, $p < .001$). We found the same correlation with life activities for the overall composite task score (Task performance: $F = 14.07$, $p < .001$). The more often individuals had engaged in cognitively stimulating activities throughout their lives, the better their performance was. The relationship between baseline and task performance decreased (*F* = 6.24, *p* < .01) but remained significant at a threshold of *p* < .05. Figure 3B presents the statistical diagram of significant correlations. We did not observe any other significant and direct correlations with task performance.

Figure 3C demonstrates in detail the correlations between all variables included in this study, and not only the ones that are correlated with behavioral performance. It also shows the correlations observed according to groups of participants (younger and older) and for task subconditions (TAX_Low, TAX_High, THEM_Low, THEM_High).



All participants

	Age	Education	MoCa	Similarities	PPPT	Activity	Task_perf	Base_perf
Age								
Education	-0.01							
MoCa	-0.02	0.13						
Similarities	0.06	0.07	0.10					
PPPT	0.30	0.11	0.12	0.22				
Activity	-0.16	0.16	0.13	-0.09	0.24			
Task_perf	-0.20	0.02	0.22	0.13	0.01	0.35		
Base_perf	-0.36	0.02	0.10	0.11	0.04	0.35	0.56	

	Age	Education	MoCa	Similarities	PPPT	Activity
TAX_Low	-0.22	0.14	0.14	0.17	0.10	0.14
TAX_High	0.02	0.13	0.28	0.17	0.16	0.19
THEM_Low	-0.03	-0.05	0.22	0.05	-0.00	0.16
THEM_High	-0.40	-0.12	0.12	0.05	-0.18	0.44

Younger participants

	Age	Education	MoCa	Similarities	PPPT	Activity	Task_perf	Base_perf
Age								
Education	0.53							
MoCa	-0.05	0.16						
Similarities	0.06	0.06	0.03					
PPPT	0.08	0.18	0.16	0.36				
Activity	0.13	0.47	0.16	-0.05	0.27			
Task_perf	0.18	0.28	0.10	0.21	-0.01	0.26		
Base_perf	-0.12	-0.01	0.08	0.04	0.05	0.09	0.49	

	Age	Education	MoCa	Similarities	PPPT	Activity
TAX_Low	0.13	0.33	0.11	0.22	0.10	0.13
TAX_High	0.22	0.33	0.18	0.21	0.12	0.23
THEM_Low	0.01	0.12	0.03	-0.01	-0.19	0.10
THEM_High	0.22	0.13	0.01	0.23	-0.11	0.37

Older participants

	Age	Education	MoCa	Similarities	PPPT	Activity	Task_perf	Base_perf
Age								
Education	-0.22							
MoCa	-0.38	0.11						
Similarities	0.07	0.09	0.17					
PPPT	-0.17	0.07	0.07	-0.07				
Activity	-0.15	-0.01	0.11	-0.13	0.41			
Task_perf	-0.37	-0.14	0.32	0.08	0.20	0.20		
Base_perf	-0.30	0.03	0.13	0.23	0.25	0.34	0.59	

	Age	Education	MoCa	Similarities	PPPT	Activity
TAX_Low	-0.24	-0.02	0.20	0.14	0.34	0.28
TAX_High	-0.35	-0.02	0.37	0.12	0.22	0.17
THEM_Low	-0.36	-0.13	0.33	0.10	0.22	0.19
THEM_High	-0.33	-0.29	0.23	-0.06	-0.02	0.66

Figure 17. – Figure 3. Behavioral performance on the semantic judgment task and correlations with demographic and cognitive factors

A. Task performance (composite scores; composed of ACC and RT; see section 3.2.1) obtained for the conditions and subconditions of the semantic task protocol. Performance is broken down by age group. Note: NS = not significant (*p* > .05); * = significant at *p* < .05; ** = significant at *p* < .01; *** = significant at *p* < .001.
B. Statistical diagrams of variables that have a significant (*p* < .05) and direct correlation with task performance (composite scores), for all participants (*n* = 78).

C. Patterns of correlation between the continuous variables included in the study in relationship to age group (all participants, older participants only (O) and younger participants only (Y)). The colored boxes reflect significant correlations (*p* < .05). Positive correlations are depicted in red, and negative correlations in blue.

Neurofunctional mappings of semantic judgment

Task-evoked activation

All task conditions versus baseline

Independently of age, the semantic similarity judgment task activated a large bilateral fronto-temporo-parietal semantic network (Figure 4A). At a threshold corrected for multiple comparisons across voxels (FWE corrected, *k* > 5), 10 distinct clusters of activation were recruited during the task at a statistically significant level (Table 1). See Table S3 (Supplementary Material) for the complete table (*p* < .001, uncorrected).

Tableau 9. – Table 1: Activation clusters for all task conditions (versus baseline)*

Clusters	Vol.	*t* Peak	*xyz* Peak	Peak Structure (AAL)	Lobe	Hem.
9	957	6.8	–41.8×19.8×44.0	Frontal_Mid_L	Frontal	L
10	928	6.7	–11.6×28.6×61.7	Frontal_Sup_Medial_L	Frontal	L
1	34415	12.1	–53.6×–49.6×32.2	SupraMarginal_L	Parietal	L
2	9785	11.8	0.2×–85.0×32.2	Cuneus_L	Parietal	L
5	909	9.7	–30.0×–42.9×–6.9	ParaHippocampal_L	Temporal	L
8	1070	7.1	–50.7×16.8×–12.8	Temporal_Pole_Sup_L	Temporal	L

4	7427	9.8	23.8×28.6×55.8	Frontal_Sup_R	Frontal	R
7	3225	7.6	53.3×40.4×–7.6	Frontal_Inf_Orb_R	Frontal	R
3	20466	10.6	51.1×–54.7×35.2	Angular_R	Parietal	R
6	3576	9.7	65.8×–22.3×–12.8	Temporal_Mid_R	Temporal	R

*Obtained at a statistically corrected threshold

Effect of semantic relationship

- TAX versus Baseline

Seven distinct activation clusters were identified for the taxonomic relationship condition (*p* < .05, FWE corrected; Table 2). These clusters engaged the fronto-temporo-parietal cortex, which is known to be engaged in language processing (Figure 4B). Interestingly, in addition to the frontal lobe and left TPJ, the ATLs in both hemispheres were robustly activated. See Table S6 (Supplementary Material) for the complete table (*p* < .001, uncorrected).

Tableau 10. – Table 2: Activation clusters for the taxonomic condition of the semantic similarity judgment task (versus baseline)*

Vol.	*t* Peak	*xyz* Peak	Peak Structure (AAL)	Lobe	Hem.
9221	6.1	–11.6×53.0×41.1	Frontal_Sup_L	Frontal	L
6479	6.1	–51.4×–61.4×26.3	Angular_L	Parietal	L
1849	5.4	–45.5×–40.0×2.0	SupraMarginal_L	Parietal	L
1281	5.7	–35.9×15.3×–30.5	Temporal_Pole_L	Temporal	L
1197	5.3	54.0×40.4×–9.8	Frontal_Inf_Orb_R	Frontal	R
606	5.2	39.3×–19.3×52.9	Postcentral_R	Parietal	R
3832	5.3	45.2×8.0×–37.1	Temporal_Pole_R	Temporal	R

* Obtained at a statistically corrected threshold

- THEM versus Baseline

We found activation in 10 distinct clusters in the thematic relationship condition. THEM relationships engaged numerous regions of the semantic network (Figure 4, Panels A and B) distributed across both hemispheres, including the TPJ bilaterally (Table 3). See Table S7 (Supplementary Material) for the complete table (*p* < .001, uncorrected).

Tableau 11. – Table 3: Activation clusters for the thematic condition of the semantic similarity judgment task (versus baseline), obtained at a corrected statistical threshold.

Clusters	Vol.	*t* Peak	*xyz* Peak	Peak Structure (AAL)	Lobe	Hem.
5	2196	5.2	–54.4×20.5×2.0	Frontal_Inf_Tri_L	Frontal	L
7	1265	5.0	–41.8×17.6×44.0	Frontal_Mid_L	Frontal	L
9	1517	5.0	–0.2×–84.0×32.2	Occipital_Sup_L	Occipital	L
1	14848	7.8	–51.4×–58.4×26.3	Angular_L	Parietal	L
6	5513	5.1	–65.4×–22.3×–12.8	Temporal_Mid_L	Temporal	L
4	2609	5.6	54.0×40.4×–9.8	Frontal_Inf_Orb_R	Frontal	R
10	1843	5.0	14.9×35.3×55.8	Frontal_Sup_R	Frontal	R
2	5517	6.0	0.2×–85.0×32.2	Occipital_Sup_R	Occipital	R
3	6067	5.7	57.0×–63.6×23.4	Angular_R	Temporal	R
8	2175	5.0	65.8×–22.3×–12.8	Temporal_Mid_R	Temporal	R

- TAX versus THEM

The direct contrast between task conditions (taxonomic versus thematic) did not find any robust activation, including at an uncorrected threshold of *p* < .001.

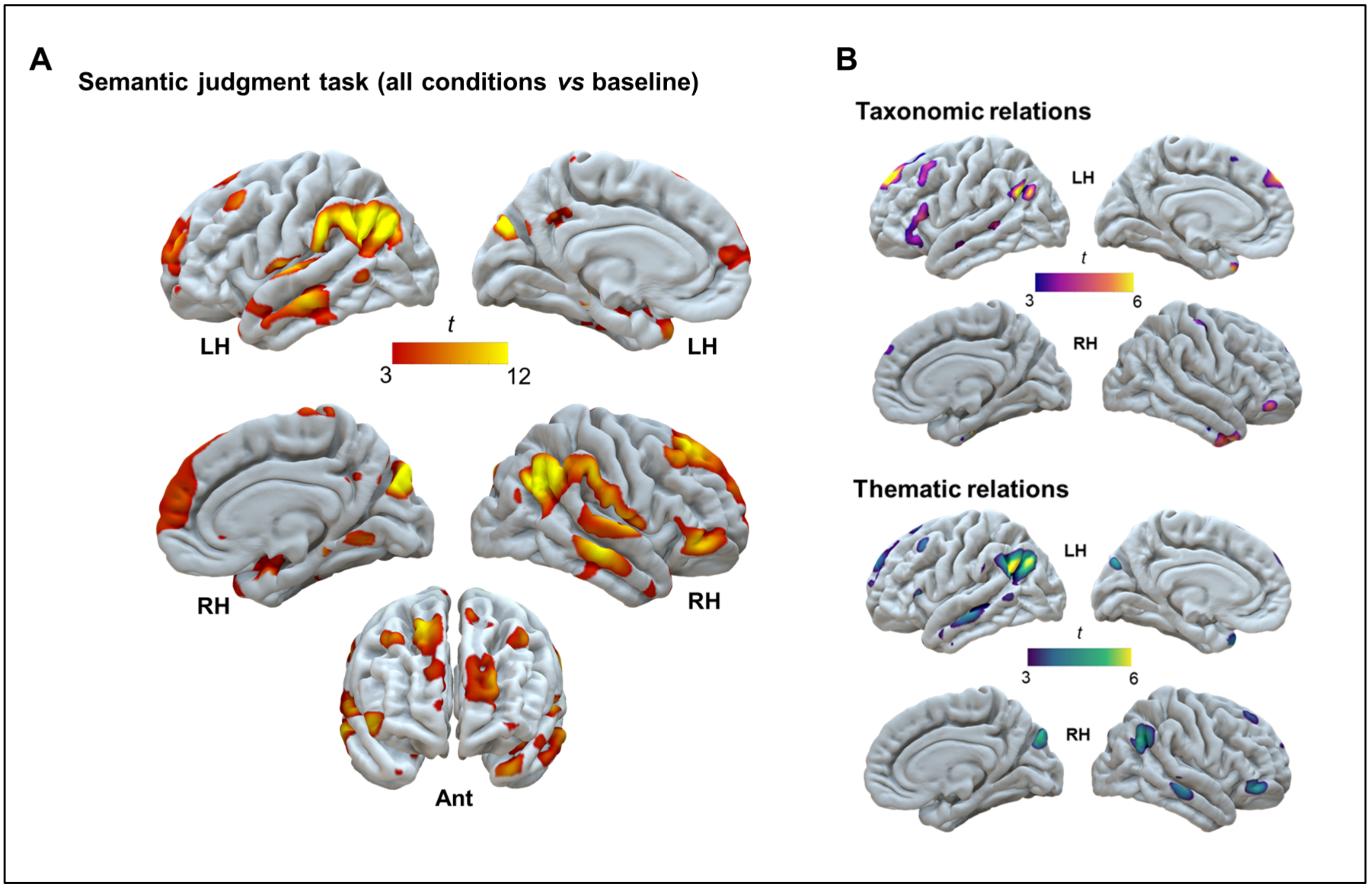


Figure 18. – Figure 4: Brain map activation during the semantic task (all participants)

A. Whole-brain mapping of the task-related semantic network activation ($p <. 001$, uncorrected, $t = 3.14$, $k > 5$) at the group level. The yellow voxels are above the corrected activation threshold ($p < .05$, FWE corrected; see Table 2 for an overview of significantly activated clusters).

B. Whole-brain mapping related to every task condition of the semantic similarity judgment task ($p <. 001$, uncorrected, $t = 3.14$, $k > 5$). See Supplementary material S3-S6 for an overview of significantly activated clusters at a corrected threshold for every condition.

NB: For each brain mapping presented here, all participants were included ($n = 78$), and conditions of interest were contrasted with the Baseline condition.

Neurofunctional activity in the TPJ and ATL semantic hubs

Task condition differences

To explore the relationships between the two semantic hubs, task condition, task demand, and age group, a repeated measures 2x2x2x2 analysis of variance was performed. Age group was a between subjects factor while the remaining factors were repeated measures factors. Results demonstrated a significant interaction between all factors ($F(1,76) = 20.7$, $p < 0.0001$, $\eta^2 = 0.214$). All lower interactions and main effects were also significant (condition X demand X ROI: $F(1,76) = 13.1$, $p = 0.0005$, $\eta^2 = 0.147$; demand X ROI X age group: $F(1,76) = 129$, $p < 0.0001$, $\eta^2 = 0.630$; demand X ROI: $F(1,76) = 88.5$, $p < 0.0001$, $\eta^2 = 0.538$; condition X ROI X age group: $F(1,76) = 230$, $p < 0.0001$, $\eta^2 = 0.752$; condition X ROI: $F(1,76) = 242$, $p < 0.0001$, $\eta^2 = 0.761$; condition X demand X age group: $F(1, 76) = 13.2$, $p = 0.0005$, $\eta^2 = 0.148$; condition X demand: $F(1, 76) = 48.7$, $p < 0.0001$, $\eta^2 = 0.390$); ROI x age group: $F(1, 76) = 901$, $p < 0.0001$, $\eta^2 = 0.922$; ROI: $F(1, 76) = 999$, $p < 0.0001$, $\eta^2 = 0.929$; demand X age group: $F(1, 76) = 297$, $p < 0.0001$, $\eta^2 = 0.796$; demand: $F(1, 76) = 33.4$, $p < 0.0001$, $\eta^2 = 0.306$; condition X age group: $F(1, 76) = 30.1$, $p < 0.0001$, $\eta^2 = 0.284$; and condition: $F(1, 76) = 5.62$, $p = 0.020$, $\eta^2 = 0.0688$). Marginal mean brain activation from repeated measures ANOVA ROI analyses are shown in Table 4. Post-hoc tests for all comparisons corrected for multiple comparisons using Bonferroni's method, are in Supplementary Table S1.

Tableau 12. – Table 4. Marginal mean brain activation from repeated measures ANOVA region of interest analysis

			Condition	
Age Group	Demand	ROI	Tax	Them
Young	High	ATL	0.71976	0.74816
Young	High	TPJ	0.42519	0.46964
Young	Low	ATL	0.73943	0.74352
Young	Low	TPJ	0.21102	0.20753
Old	High	ATL	0.37581	0.25812
Old	High	TPJ	0.22469	0.36476
Old	Low	ATL	0.53085	0.19444
Old	Low	TPJ	0.29925	0.42819

In younger participants, neurofunctional activation in the ATLs did not vary depending on conditions (or subconditions) but was higher on average than the activation observed in the TPJ (Figure 5A). Like activation in the ATL, activation in the TPJ did not vary as a function of the TAX or THEM condition. It did, however, vary as a function of task demand (0.263 points for THEM and 0.214 points for TAX). In older participants, the semantic hubs' activation patterns varied depending on condition. For TAX relationships, activation in the ATLs was higher than in the TPJ. For THEM relationships, activation in the TPJ was higher than in the ATL. Finally, we did not observe any significant modulation of activation according to task demand (Low or High), whether in the ATL or the TPJ (Figure 5B).

Age group affected activation levels in the two semantic hubs (ATLs and TPJ) regardless of the condition or subcondition. The ATLs were consistently less engaged in the O than the Y group, and this gap widened for THEM conditions (see Figure 5B). TPJ activation was higher in Group O than Group Y in Low-demand conditions. In the High-demand conditions, on the other hand, the TPJ appeared to be more active in the Y than the O group. The increase in engagement of the TPJ according to task demands therefore appears to be specific to Group Y (Figure 5B).

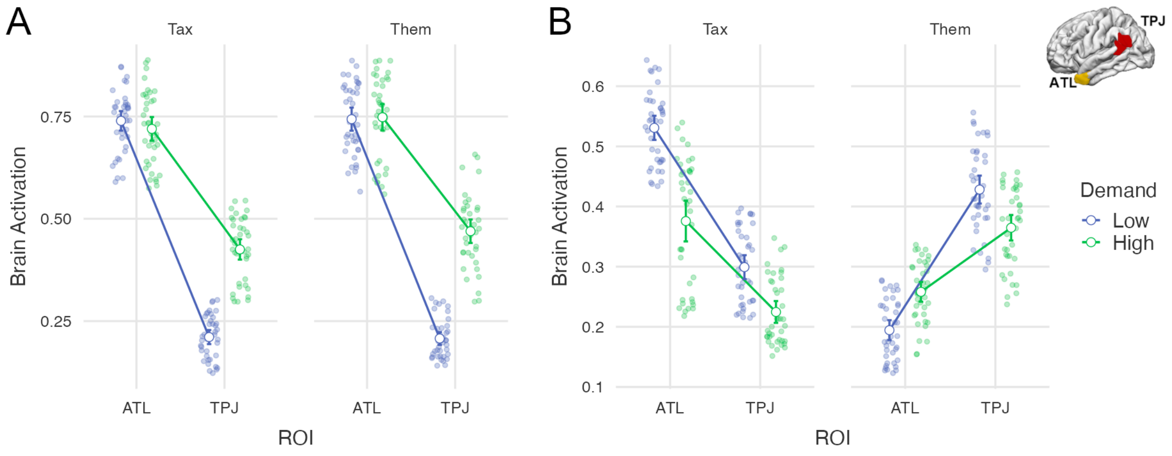


Figure 19. – Figure 5: Modulation of hub activations according to condition or group

A. Differences in neurofunctional activation for the younger age group.

B. Differences in neurofunctional activation for the older age group.

On an exploratory basis, we also investigated the correlation between neurofunctional activation in semantic hubs and performance for the THEM_High condition, given the observed behavioral differences between groups Y and O (Section 4.1.1; Figure 3).

In younger participants, THEM_High composite scores correlate positively and significantly with TPJ activation on this condition ($r = 0.58$, $p < .05$). Thus, the more active the TPJ during this condition, the better the younger participants' performance. We did not find any correlation with ATL activation values ($r = 0.13$).

Interestingly, we found the same correlation between performance and TPJ activation in Group O ($r = 0.49$, $p < .05$). Although the TPJ is less active in the THEM_High condition in Group O than Group Y, the more the older participants activated this semantic hub, the better their performance. In addition, unlike the Y group, we also found a positive and significant correlation in the O group between performance and ATL activation values ($r = 0.39$, $p < .05$). Overall, the more similar their activation patterns in the left ATL and TPJ are to Group Y's, the better the older participants performed in this condition.

Discussion

In this study, we examined the single-hub and dual-hub hypotheses about activation in their respective proposed hubs (ATLs and TPJ), as well as expected differential processing of taxonomic versus thematic relationships, in relation to aging. We administered a novel experimental task that varied the type of semantic relationship (taxonomic versus thematic) and task demand (low versus high) to 39 younger and 39 older adults. Overall, our younger and older participants were matched for level of education, and their results on questionnaires assessing engagement in cognitively stimulating activities (Life activities), general cognition (MoCA) and Weschler Adult Intelligence Scale (WAIS-III) tests. The behavioral results confirmed that task demands were manipulated successfully: errors and RTs increased with increasing task demands, as well as self-reported difficulty. Unexpectedly, the thematic condition proved more demanding for all participants, as manifested in increased RTs and lower accuracy, as well as higher self-reported difficulty scores. Overall, the most demanding condition for all participants was the high-demand thematic condition, which was the only condition where we found a significant group effect in behavioral measures. We found that engaging in cognitively stimulating activities had a positive impact on baseline RTs and accuracy for both age groups. Furthermore, higher scores on the MoCA were positively correlated with older adults' performance. Performance on the baseline condition of the task positively correlated with performance at the two semantic relationship conditions for both age groups.

Accuracy did not differ significantly between younger and older participants, regardless of the condition. This is in line with previous studies that show that accuracy in semantic tasks is generally well preserved in older adults, given their extensive experience with word use and large vocabulary **(Balota et al., 2004; Kahlaoui et al., 2012; Kavé et al., 2009; Laver, 2009; Methqal et al., 2019; Verhaegen & Poncelet, 2013; Wingfield & Grossman, 2006)**. For RTs, there was a statistically significant difference between younger and older participants for both the task and baseline conditions; in general, older adults were slower to respond. The older the participant, the longer their RTs. This is in line with previous findings that older adults' RTs tend to be longer than younger adults' (Balota et al., 2004), possibly because older adults are slower at accessing and retrieving conceptual representations from their semantic store (Bonner et al., 2013; Huang et al., 2012; Wierenga et al., 2008), and engaging the required necessary function resources (Diaz et al., 2018) and motor responses (Falkenstein et al., 2006). When baseline RTs were accounted for, or when we took into account older adults' inherently longer RTs, performance in the different conditions was positively correlated for both age groups. The greatest behavioral differences between the two age groups were found in the high-demand and thematic conditions.

At the neural level, regardless of age, the semantic similarity judgment task activated a large bilateral fronto-temporo-parietal network. In our study, 10 distinct activation clusters were observed when both task conditions were contrasted with the baseline, including the left supramarginal gyrus, the left cuneus, the right angular gyrus, the left middle frontal and superior gyri, and the dorsolateral and medial superior frontal gyri (see Table 2). Overall, the activated areas correspond with seven semantic network regions mainly on the left, namely the posterior inferior parietal cortex, lateral temporal cortex, ventral temporal cortex, dorsomedial prefrontal cortex, inferior frontal gyrus, ventromedial prefrontal cortex, and posterior cingulate gyrus (Baciu et al., 2016; Binder et al., 2009). The semantic network is believed to be subserved bilaterally by the ATLs, which act as a semantic hub (Patterson et al., 2007) and also, semantic control processes underpinned by the prefrontal cortex, posterior middle temporal gyrus, and dorsal angular gyrus/intraparietal sulcus (Jefferies, 2013). Semantic decision tasks have been found to activate a large constellation of cortical regions, including the ATLs bilaterally, prefrontal cortex, posterior temporal cortex and angular gyrus (AG) (Binder et al., 2009; Noonan et al., 2013; Visser, Jefferies, et al., 2010).

With regard to the semantic relationship effect, such as the effect of processing taxonomic versus thematic relationships on brain activation, direct contrast of the taxonomic and thematic conditions did not find any brain activation at a corrected or uncorrected threshold. When the taxonomic and baseline conditions were contrasted, seven distinct clusters in the fronto-temporo-parietal cortex were activated across the two hemispheres, including the ATLs and the left TPJ. In addition, activation was significant in the left frontal superior gyrus, the left AG and the inferior frontal gyrus (orbital part) in the right hemisphere (see Table 2). This finding for all participants in the taxonomic condition may be partly in line with dual-hub theory, which proposes that the ATLs and the TPJ act as semantic hubs when processing taxonomic relationships. When the thematic condition was contrasted with the baseline, 10 distinct clusters were activated, including the TPJ bilaterally; however, the ATLs were not robustly activated. More specifically, activated regions included the AG bilaterally, the middle temporal gyrus, the inferior frontal gyrus (triangular part) and the middle frontal gyrus (see Table 3).

A closer look at the ROIs in younger participants demonstrated that activation in the ATLs or TPJ did not vary as a function of the taxonomic or thematic condition, so we did not find a double dissociation. However, activation in the TPJ was mostly modulated by task demand, with increased TPJ activation observed during the high-demand condition, for both taxonomic and thematic conditions (we did not find any interaction effect) in younger participants. This activation contributed positively to performance. In older participants, on the other hand, we found an almost opposite pattern, specifically a condition effect (taxonomic versus thematic), with taxonomic relationships mostly activating the ATLs and thematic relationships activating mostly the TPJ, regardless of task demands. Older adults recruited the ATLs less than younger, whereas TPJ activation was higher in older adults than in younger only in the low-demand condition. In the high-demand condition, the TPJ was more robustly activated in younger than in older adults. Both TPJ and ATL activation seemed to contribute positively to older adults' performance.

Indeed, age group affected activation levels in the ATL and TPJ ROIs regardless of the condition or subcondition. The ATLs were significantly less engaged in the older versus the younger group, especially for the thematic condition, regardless of demand levels. The older participants had greater TPJ activation than the younger ones in the low-demand condition, whereas in the high-demand condition, the younger participants had more activation than the older ones. Interestingly, both younger and older participants' performance was positively and significantly correlated with an increase in activation in the TPJ. A positive correlation between performance and activation in the ATLs was found only for the older participants. In the most demanding condition as evidenced by behavioral and self-reported findings, which was the thematic high-demand condition, performance scores correlate positively and significantly with TPJ activation in younger participants. No such correlation was found with activation in the ATLs.

The above findings are partly in line with reports in the literature of activation in more difficult conditions of semantic tasks. The Controlled Semantic Cognition (CSC) hypothesis (Lambon Ralph et al., 2017) proposes that semantic memory is organized as a dual system composed of two distinctive but interacting systems, one specific to representations (the ATLs) and the other specific to cognitive-semantic control (the TPJ) **(Badre et al., 2005; Chiou et al., 2018; Davey, Cornelissen, et al., 2015; Davey et al., 2016; Diaz et al., 2016; Jefferies, 2013; Jefferies & Lambon Ralph, 2006; Noonan et al., 2013)**. The semantic control network would then be significantly recruited during more complex tasks underpinned by left-hemisphere regions **(Badre & Wagner, 2002; Davey, Cornelissen, et al., 2015; Davey et al., 2016; Diaz et al., 2016; Duncan, 2010; Jefferies, 2013; Lambon Ralph et al., 2017; Noonan et al., 2013)**, potentially extending to the right inferior frontal gyrus and prefrontal cortex (when demands intensify further (Noonan et al., 2013). Accordingly, a single transmodal hub situated bilaterally in the ATLs would act as the convergence zone for various modality-specific regions (the spokes) (Lambon Ralph et al., 2017). Both taxonomic and thematic relationships would thus be subserved by a single hub located in the ATLs, and differential processing of the two would be attributed to different semantic demand requirements, subserved by the TPJ, among others.

Our findings could lend differing support to the two hypotheses, depending on age group. In younger adults, neither ATL nor TPJ activation varied as a function of type of semantic relationship. TPJ activation did, however, vary as a function of task demands, potentially supporting the CSC hypothesis, with the TPJ playing a role in regulating semantic control. In the older age group, the ATLs were recruited less than in the younger group. This could potentially be explained by the dedifferentiation hypothesis, referring to reduced neural efficiency, and the detrimental effect that aging may have on the recruitment of the ATLs as a semantic hub (Baltes & Lindenberger, 1997; Jiang et al., 2017; Park et al., 2004; Reuter-Lorenz & Lustig, 2005). Alternatively, it could support the CRUNCH (Compensation Related Utilization of Neural Circuits Hypothesis), whereby underactivation is seen in areas subserving “redundant” tasks and neural resources migrate to serve more urgent task requirements (Reuter-Lorenz & Cappell, 2008). In the low-demand condition, older adults recruited the TPJ more than younger ones, potentially demonstrating a compensation effect, that is, recruiting additional resources to meet task demands (Cabeza & Dennis, 2012; Reuter-Lorenz & Cappell, 2008). In the high-demand condition, however, when potentially they could have exhausted their resources, there was less activation in the TPJ than in the younger participants, which is somewhat in line with CRUNCH. Focusing on task complexity and demands regardless of age, CRUNCH proposes that both younger and older people can benefit from overactivation in these regions when task demands require additional resources (Reuter-Lorenz & Cappell, 2008). For older adults, however, the benefit of overactivation reaches a threshold above which the neural resources recruited are not adequate and performance declines (Reuter-Lorenz & Cappell, 2008).

Alternatively, the lack of significantly different activation between the two semantic relationship conditions could be explained by the fact that our stimuli and task did not capture sufficient differences between taxonomic and thematic conditions to yield a difference in neurofunctional activation. For instance, we did not control our stimuli for animate versus inanimate items, which have been shown to influence processing (Sachs, Weis, Krings, et al., 2008), nor did we control for motor or visual features **(Geng & Schnur, 2016)**. Overall, it is thought that semantic judgment tasks tap both the semantic and multiple demand networks extensively, as they require internal and external representations to be integrated (Noonan et al., 2013). The thematic condition in our task appears to be more demanding than the taxonomic one. Our task's thematic condition was based on associations developed, so that when a word was named, participants were requested to produce the first semantically related word that came to mind. However, this definition of semantic association has been criticized because associated concepts may not sufficiently capture thematically related concepts (Estes et al., 2011). Moreover, many thematically related words are not associated, such as *milk* and *cat* (Estes et al., 2011), making semantic judgment more challenging, as the Likert difficulty scores also showed. Indeed, it has been claimed that word co-occurrence statistics and association norms do not efficiently isolate thematic relationships or may be ad hoc relationships that are developed for a specific situation but may not be part of long-term semantic memory (Mirman et al., 2017).

Overall, younger and older participants' behavioral performance was similar, when older adults' inherently longer RTs are considered. For both age groups, cognitively stimulating activities were found to be important for overall performance. Although we did not find a double dissociation, that is, significant activation in the ATLs during the taxonomic condition and in the TPJ during the thematic condition, we observed activation patterns that could support both hypotheses. Regarding the younger participants, our findings support single-hub theory more, with the ATLs potentially acting as a single hub and the TPJ modulated by task demands. In older participants, activations were found to be more condition-specific, and more in favor of the double-hub theory. Older participants engaged the ATLs less than the younger ones, but activation in the ATLs was significantly correlated with improved performance. On the other hand, older participants engaged the TPJ more during the low-demand condition and less during the high-demand condition, unlike the younger ones. Activation in the TPJ is thought to be correlated with task demands (Lambon Ralph et al., 2017), suggesting that the TPJ is involved in semantic control (Davey et al., 2015; Noonan 2013). The only condition where older adults performed worse than the younger ones was the thematic high-demand condition, at which all participants tended to be less successful. We observed activation adjustments in the older participants' semantic hubs, while they performed at an equal level with younger ones in almost all conditions. Although older adults have different activation patterns in the semantic hubs compared with younger participants, the more they resembled the "younger" pattern, the better their performance was in the most difficult condition, namely thematic high-demand.

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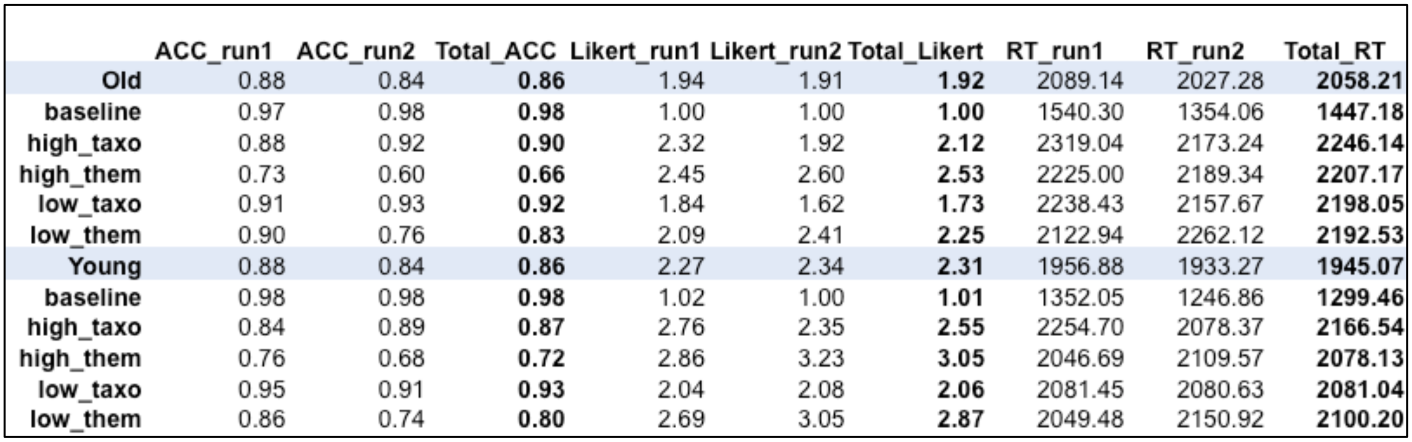
Appendix- Supplementary material

Tableau 13. – Table S1: Differences between groups in demographic, neuropsychological et behavioral variables

	Variables	Mean_Y	SD_Y	Mean_O	SD_O	t-value	df	p
Demographics	Edu_years	17.36	1.55	17.28	2.22	0.17	76	0.85
	Freq_french	3.37	0.46	3.45	0.47	-0.69	76	0.48
	Freq_english	2.15	0.75	1.07	0.81	6.11	76	0.001***
	Edinburgh	88.15	8.85	92.21	9.33	-1.96	76	0.06
	Activity_life	3.51	0.52	3.36	0.6	1.18	75	0.24
Neuropsy	MoCA	28.28	1.17	28.33	1.42	-0.17	76	0.86
	WAIS-III	17.03	4.05	17.41	3.39	-0.45	76	0.65
	PPPT	49.85	2.16	50.95	1.21	-2.78	76	0.02*
Behavioral performance	ACC_TAX	0.90	0.07	0.91	0.05	-0.96	76	0.33
	ACC_THEM	0.76	0.06	0.75	0.04	0.91	76	0.36
	ACC_base	0.86	0.03	0.86	0.04	0.83	76	0.9
	ACC_task	0.83	0.05	0.83	0.04	-0.12	76	0.9
	RT_TAX	2110.87	233.75	2232.5	270.08	-2.12	76	0.04*
	RT_THEM	2076.29	265.5	2209.89	326.83	-1.98	76	0.04*
	RT_base	1302.9	254.58	1439.95	277.53	-2.27	76	0.03*
	RT_task	2093.58	238.12	2221.19	293.31	-2.1	76	0.04*
	Composite_TAX	68.47	16.49	67.59	15.57	-1.88	76	0.06
	Composite_THEM	61.95	22.95	59.77	23.59	-2.2	76	0.06
	Composite_base	82.69	8.61	80.8	8.98	-2.18	76	0.06

	Composite_task	65.21	19.72	63.68	19.58	-2.37	76	0.06

Tableau 14. – Table S2: Mean behavioral data for both group of participants, with breakdown by



	ACC_run1	ACC_run2	Total_ACC	Likert_run1	Likert_run2	Total_Likert	RT_run1	RT_run2	Total_RT
Old	0.88	0.84	**0.86**	1.94	1.91	**1.92**	2089.14	2027.28	**2058.21**
baseline	0.97	0.98	**0.98**	1.00	1.00	**1.00**	1540.30	1354.06	**1447.18**
high_taxo	0.88	0.92	**0.90**	2.32	1.92	**2.12**	2319.04	2173.24	**2246.14**
high_them	0.73	0.60	**0.66**	2.45	2.60	**2.53**	2225.00	2189.34	**2207.17**
low_taxo	0.91	0.93	**0.92**	1.84	1.62	**1.73**	2238.43	2157.67	**2198.05**
low_them	0.90	0.76	**0.83**	2.09	2.41	**2.25**	2122.94	2262.12	**2192.53**
Young	0.88	0.84	**0.86**	2.27	2.34	**2.31**	1956.88	1933.27	**1945.07**
baseline	0.98	0.98	**0.98**	1.02	1.00	**1.01**	1352.05	1246.86	**1299.46**
high_taxo	0.84	0.89	**0.87**	2.76	2.35	**2.55**	2254.70	2078.37	**2166.54**
high_them	0.76	0.68	**0.72**	2.86	3.23	**3.05**	2046.69	2109.57	**2078.13**
low_taxo	0.95	0.91	**0.93**	2.04	2.08	**2.06**	2081.45	2080.63	**2081.04**
low_them	0.86	0.74	**0.80**	2.69	3.05	**2.87**	2049.48	2150.92	**2100.20**

session (Run 1 versus Run 2)

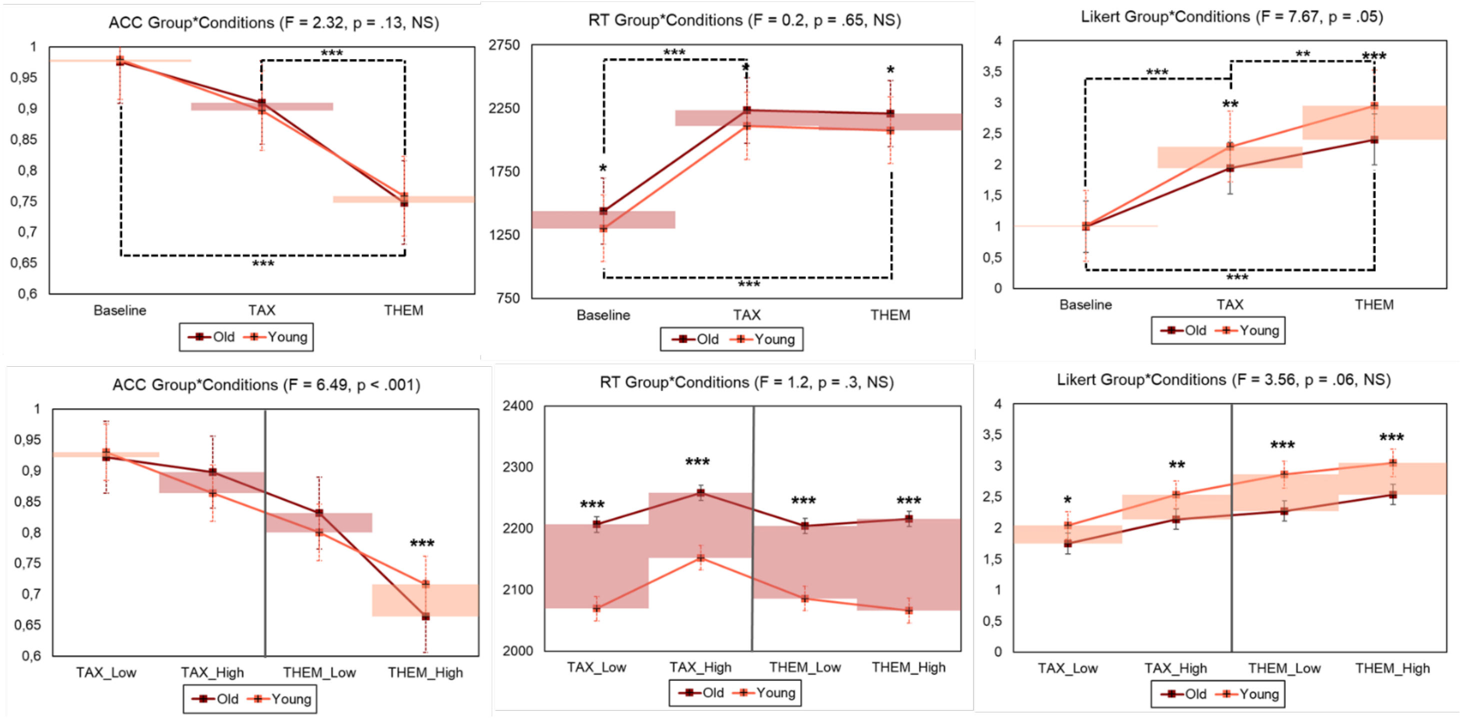


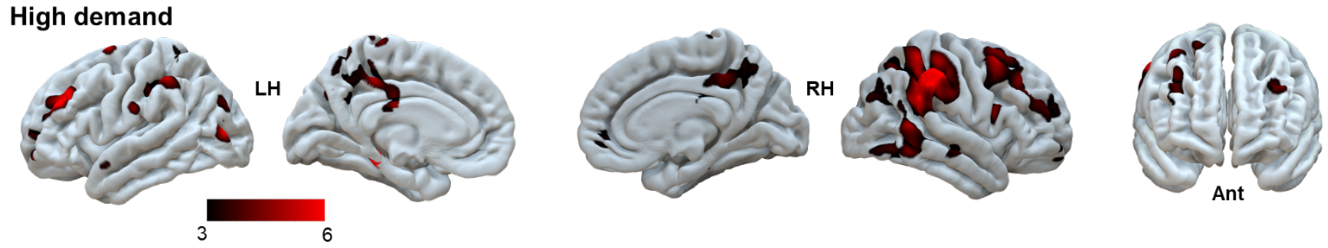
Figure 20. – Figure S1: Details of measures and scales related to semantic judgment, according to conditions

Note: NS = not significant (p > .05); * = significant at p < .05; ** = significant at p < .01; *** = significant at p < .001.

Tableau 15. – Table S3: fMRI activation clusters at a p < .001 uncorrected threshold (t > 3.14, k >5) for the contrast of All conditions of the task minus Baseline

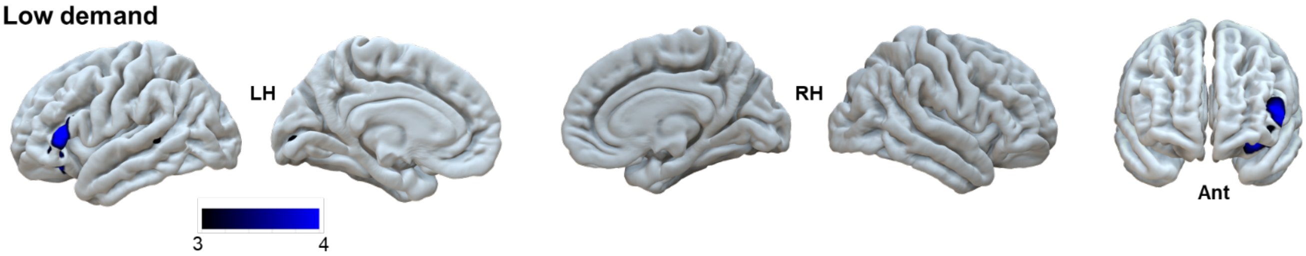
Clusters	Volume	Peak	PeakXYZ	Peak Structure	Structure	Hem
1	34415	12.1	-53.6×-49.6×32.2	**SupraMarginal_L**	Parietal	LH
2	9785	11.8	0.2×-85.0×32.2	**Cuneus_L**	Parietal	LH
3	20466	10.6	51.1×-54.7×35.2	**Angular_R**	Parietal	RH
4	7427	9.8	23.8×28.6×55.8	**Frontal_Sup_R**	Frontal	RH
5	909	9.7	-30.0×-42.9×-6.9	**ParaHippocampal_L**	Temporal	LH
6	3576	9.7	65.8×-22.3×-12.8	**Temporal_Mid_R**	Temporal	RH
7	3225	7.6	53.3×40.4×-7.6	**Frontal_Inf_Orb_R**	Frontal	RH
8	1070	7.1	-50.7×16.8×-12.8	**Temporal_Pole_Sup_L**	Temporal	LH
9	957	6.8	-41.8×19.8×44.0	**Frontal_Mid_L**	Frontal	LH
10	928	6.7	-11.6×28.6×61.7	**Frontal_Sup_Medial_L**	Frontal	LH
11	949	4.9	12.0×-61.4×-4.7	Lingual_R	Temporal	RH
12	2024	4.9	-6.4×-51.8×35.2	Precuneus_L	Parietal	LH
13	1861	4.6	-2.8×-16.4×77.2	Paracentral_Lobule_L	Frontal	LH
14	2846	4.5	-23.4×58.9×20.4	Frontal_Sup_L	Frontal	LH
15	334	4.4	-56.6×5.0×-24.6	Temporal_Mid_L	Temporal	LH
16	352	4.4	-62.5×-57.7×-1.0	Temporal_Mid_L	Temporal	LH
17	540	4.2	3.1×-85.0×-16.5	Cerebelum	Cerebelum	
18	278	4.0	-35.9×-15.6×20.4	Insula_L	Insula	LH
19	99	3.7	27.5×-79.1×-28.3	Cerebelum_Crus1_R	Cerebelum	RH
20	288	3.7	36.3×-7.5×17.5	Insula_R	Insula	RH
21	132	3.6	-14.6×-58.4×-6.9	Lingual_L	Occipital	LH
22	315	3.6	27.5×-42.9×-6.9	Lingual_R	Occipital	RH
23	224	3.5	6.1×53.0×22.6	Frontal_Sup_Medial_R	Frontal	RH
24	97	3.2	59.9×19.8×2.0	Frontal_Inf_Tri_R	Frontal	RH
25	58	3.2	-6.4×53.0×10.1	Frontal_Sup_Medial_L	Frontal	LH

Tableau 16. – Table S4: fMRI activation clusters at a p < .001 uncorrected threshold (t > 3.14, k >5) for the High demand minus Baseline contrast



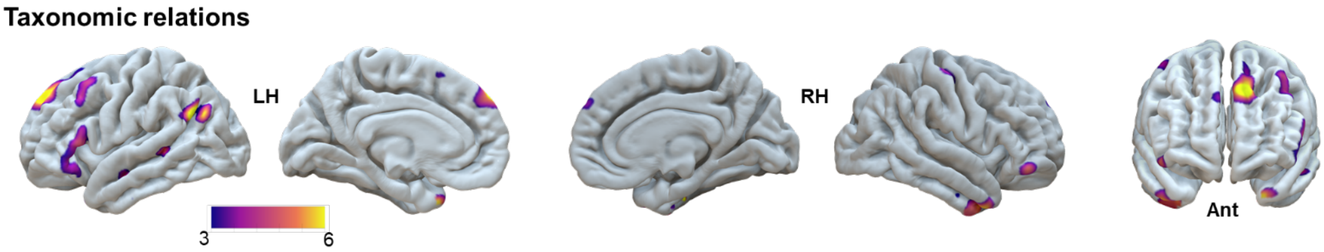
Clusters	Volume	Peak	PeakXYZ	Peak Structure	Structure	Hem
1	91468	9.6	54.0×-34.1×47.0	**Parietal_Inf_R**	Parietal	RH
2	52376	6.2	50.3×10.9×13.8	**Precentral_R**	Frontal	RH
3	6659	5.8	-35.9×35.3×32.2	**Frontal_Mid_L**	Frontal	LH
4	1772	5.4	-44.8×-85.0×7.9	**Occipital_Mid_L**	Occipital	LH
5	206	5.2	-27.1×-40.0×-9.8	**ParaHippocampal_L**	Temporal	LH
6	222	5.1	-6.4×-0.9×41.1	**Cingulum_Mid_L**	Frontal	LH
7	5664	5.1	-41.8×-31.1×35.2	**Parietal_Inf_L**	Parietal	LH
8	30456	5.1	172.0×80.1×79.0	**Temporal_Inf_R**	Temporal	RH
9	778	5.0	-20.5×2.1×68.4	**Frontal_Sup_L**	Frontal	LH
10	507	4.9	-8.7×38.2×-3.9	Cingulum_Ant_L	Frontal	LH
11	1358	4.8	-35.9×8.0×4.9	Insula_L	Insula	LH
12	613	4.7	-65.4×-16.4×26.3	Postcentral_L	Parietal	LH
13	149	4.7	33.4×-34.1×-15.7	Fusiform_R	Temporal	RH
14	1433	4.4	27.5×-45.9×-16.5	Fusiform_R	Temporal	RH
15	1191	4.4	-35.9×-79.1×34.4	Occipital_Mid_L	Occipital	LH
16	975	4.4	57.0×5.0×-15.7	Temporal_Pole_Mid_R	Temporal	RH
17	265	4.3	32.6×10.9×4.9	Putamen_R	Putamen	RH
18	348	4.3	-44.8×-54.7×-37.1	Cerebelum_Crus1_L	Cerebelum	LH
19	1116	4.3	-24.1×61.8×7.9	Frontal_Sup_L	Frontal	LH
20	533	4.3	-21.2×-67.3×-27.5	Cerebelum_Crus1_L	Cerebelum	LH
21	127	4.3	-18.2×10.9×16.7	Caudate_L	Caudate	LH
22	610	4.2	-56.6×2.1×-13.5	Temporal_Mid_L	Temporal	LH
23	979	4.2	-41.8×-22.3×2.0	Temporal_Sup_L	Temporal	LH
24	80	4.1	-35.9×2.1×13.8	Insula_L	Insula	LH
25	592	4.0	-2.8×8.0×41.1	Cingulum_Mid_L	Frontal	LH
26	128	4.0	-50.7×-16.4×16.7	Postcentral_L	Postcentral	LH
27	302	4.0	6.1×35.3×41.1	Frontal_Sup_Medial_R	Frontal	RH
28	140	3.8	9.0×-0.9×71.3	Supp_Motor_Area_R	Frontal	RH
29	61	3.8	-50.7×-51.8×25.6	Angular_L	Parietal	LH
30	119	3.7	-5.7×32.3×17.5	Cingulum_Ant_L	Cingulum	LH
31	79	3.7	3.1×32.3×17.5	Cingulum_Ant_R	Cingulum	RH
32	93	3.7	-45.5×-73.2×-9.8	Occipital_Inf_L	Occipital	LH

Tableau 17. – Table S5: fMRI activation clusters at a p < .001 uncorrected threshold (t > 3.14, k >5) for the Low demand minus Baseline contrast



Clusters	Volume	Peak	PeakXYZ	Peak Structure	Structure	Hem
1	9916	5.6	-33.0×35.3×-9.8	**Frontal_Inf_Tri_L**	Frontal	LH
2	406	4.9	-23.8×32.3×-9.8	**Frontal_Inf_Orb_L**	Frontal	LH
3	131	3.4	-45.5×-42.9×-15.7	Temporal_Inf_L	Temporal	LH
4	542	3.3	-56.6×-42.9×4.9	Temporal_Mid_L	Temporal	LH
5	67	3.1	20.8×-79.1×4.9	Calcarine_R	Occipital	RH
6	101	3.1	-57.3×-63.6×2.0	Temporal_Mid_L	Temporal	LH

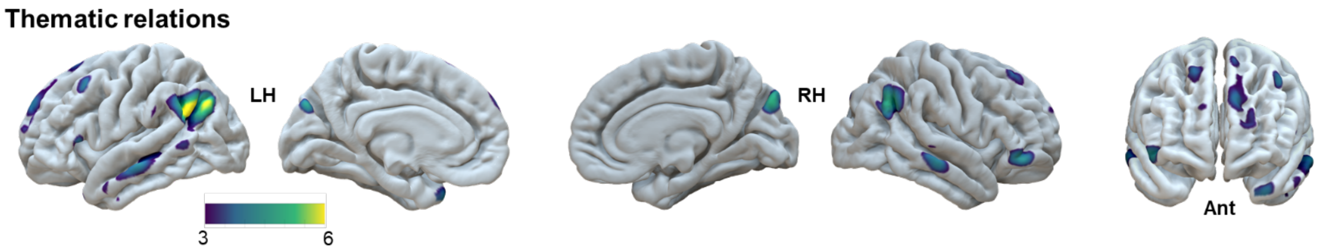
Tableau 18. – Table S6: fMRI activation clusters at a p < .001 uncorrected threshold (t > 3.14, k >5) for the Taxonomic relations minus Baseline contrast



Clusters	Volume	Peak	PeakXYZ	Peak Structure	Structure	Hem

1	6479	6.1	-51.4×-61.4×26.3	**Angular_L**	Parietal	LH
2	9221	6.1	-11.6×53.0×41.1	**Frontal_Sup_L**	Frontal	LH
3	1281	5.7	-35.9×15.3×-30.5	**Temporal_Pole_L**	Temporal	LH
4	1849	5.4	-45.5×-40.0×2.0	**SupraMarginal_L**	Parietal	LH
5	1197	5.3	54.0×40.4×-9.8	**Frontal_Inf_Orb_R**	Frontal	RH
6	3832	5.3	45.2×8.0×-37.1	**Temporal_Pole_R**	Temporal	RH
7	606	5.2	39.3×-19.3×52.9	**Postcentral_R**	Parietal	RH
8	1281	4.7	-53.6×-9.7×-18.7	Temporal_Mid_L	Temporal	LH
9	1281	4.5	-50.7×-42.9×3.46	Temporal_Mid_L	Temporal	LH
10	674	3.2	-15.3×8.0×26.3	Caudate_L	Caudate	LH
11	5227	3.1	-53.6×22.7×7.9	Frontal_Inf_Tri_L	Frontal	LH
12	87	3.1	51.1×-9.7×-27.5	Temporal_Inf_R	Temporal	RH
13	2835	3.1	-38.9×13.9×47.0	Frontal_Mid_L	Frontal	LH
14	732	3.1	6.8×55.2×34.4	Frontal_Sup_Medial_R	Frontal	RH

Tableau 19. – Table S7: fMRI activation clusters at a p < .001 uncorrected threshold (t > 3.14, k >5) for the Thematic relations minus Baseline contrast



Clusters	Volume	Peak	PeakXYZ	Peak Structure	Structure	Hem
1	14848	7.8	-51.4×-58.4×26.3	**Angular_L**	Parietal	LH
2	5517	6.0	0.2×-85.0×32.2	**Occipital_Sup_R**	Occipital	RH
3	6067	5.7	57.0×-63.6×23.4	**Angular_R**	Temporal	RH
4	2609	5.6	54.0×40.4×-9.8	**Frontal_Inf_Orb_R**	Frontal	RH
5	2196	5.2	-54.4×20.5×2.0	**Frontal_Inf_Tri_L**	Frontal	LH
6	5513	5.1	-65.4×-22.3×-12.8	**Temporal_Mid_L**	Temporal	LH

7	1265	5.0	-41.8×17.6×44.0	**Frontal_Mid_L**	Frontal	LH
8	2175	5.0	65.8×-22.3×-12.8	**Temporal_Mid_R**	Temporal	RH
9	1517	5.0	-0.2×-84.0×32.2	**Occipital_Sup_L**	Occipital	LH
10	1843	5.0	14.9×35.3×55.8	**Frontal_Sup_R**	Frontal	RH
11	906	4.8	-9.4×22.7×64.7	Supp_Motor_Area_L	Frontal	LH
12	3308	4.6	-14.6×58.9×31.5	Frontal_Sup_L	Frontal	LH
13	482	4.6	12.0×-61.4×-3.9	Lingual_R	Occipital	RH
14	45	4.4	-35.9×16.8×-30.5	Temporal_Pole_Mid_L	Temporal	LH
15	176	4.0	-56.6×5.0×-24.6	Temporal_Mid_L	Temporal	LH
16	312	3.9	-62.5×-55.5×2.0	Temporal_Mid_L	Temporal	LH
17	366	3.8	-50.7×43.4×-6.9	Frontal_Inf_Orb_L	Frontal	LH
18	751	3.6	12.0×61.8×26.3	Frontal_Sup_Medial_R	Frontal	RH
19	55	3.5	65.8×-16.4×26.3	SupraMarginal_R	Parietal	RH
20	117	3.5	-12.3×-48.8×32.2	Cingulum_Post_L	Parietal	LH
21	113	3.5	57.0×-25.2×8.6	Temporal_Sup_R	Temporal	RH
22	65	3.5	-15.3×-55.5×-6.9	Lingual_L	Occipital	LH
23	89	3.4	62.9×-28.2×41.1	SupraMarginal_R	Parietal	RH
24	47	3.3	57.0×23.5×-1.0	Frontal_Inf_Tri_R	Frontal	RH
25	62	3.3	-5.7×55.9×13.8	Frontal_Sup_Medial_L	Frontal	LH
26	35	3.2	-44.8×-34.1×10.8	Temporal_Sup_L	Temporal	LH
27	68	3.2	42.2×20.5×44.0	Frontal_Mid_R	Frontal	RH

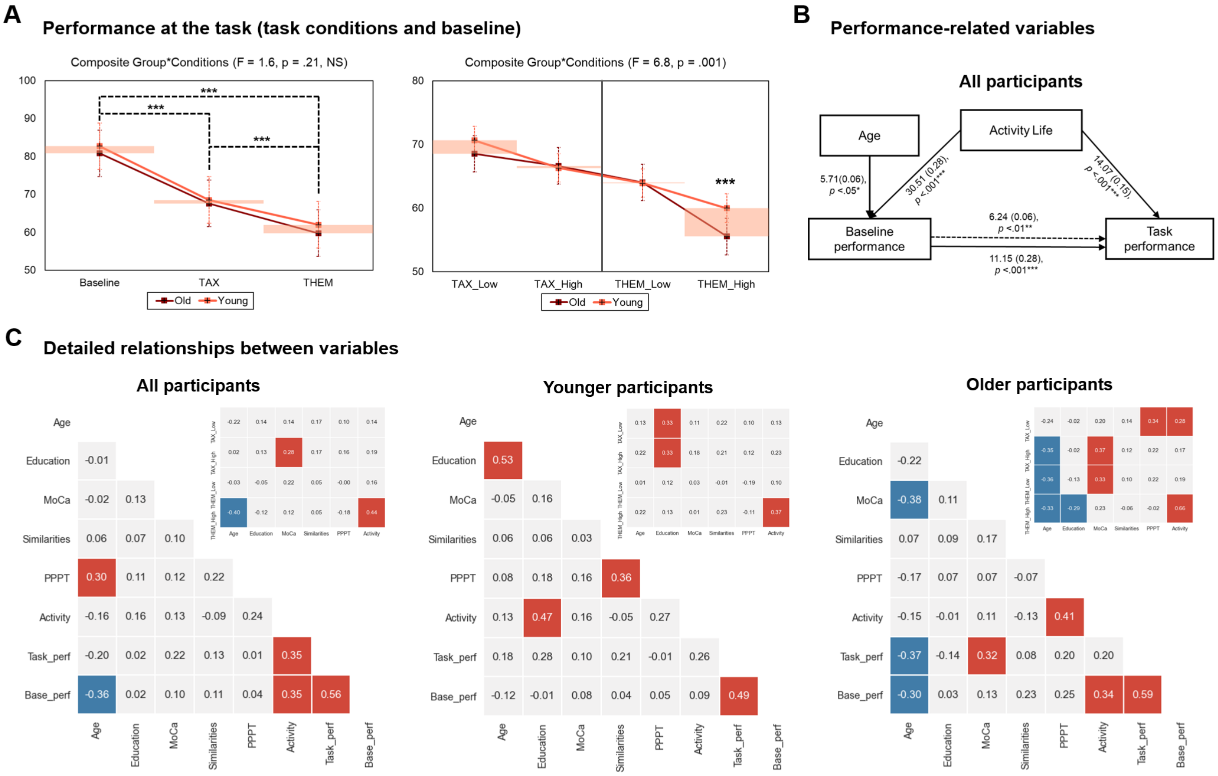


Figure 21. – Figure S2. Performance-related variables and relationships between variables

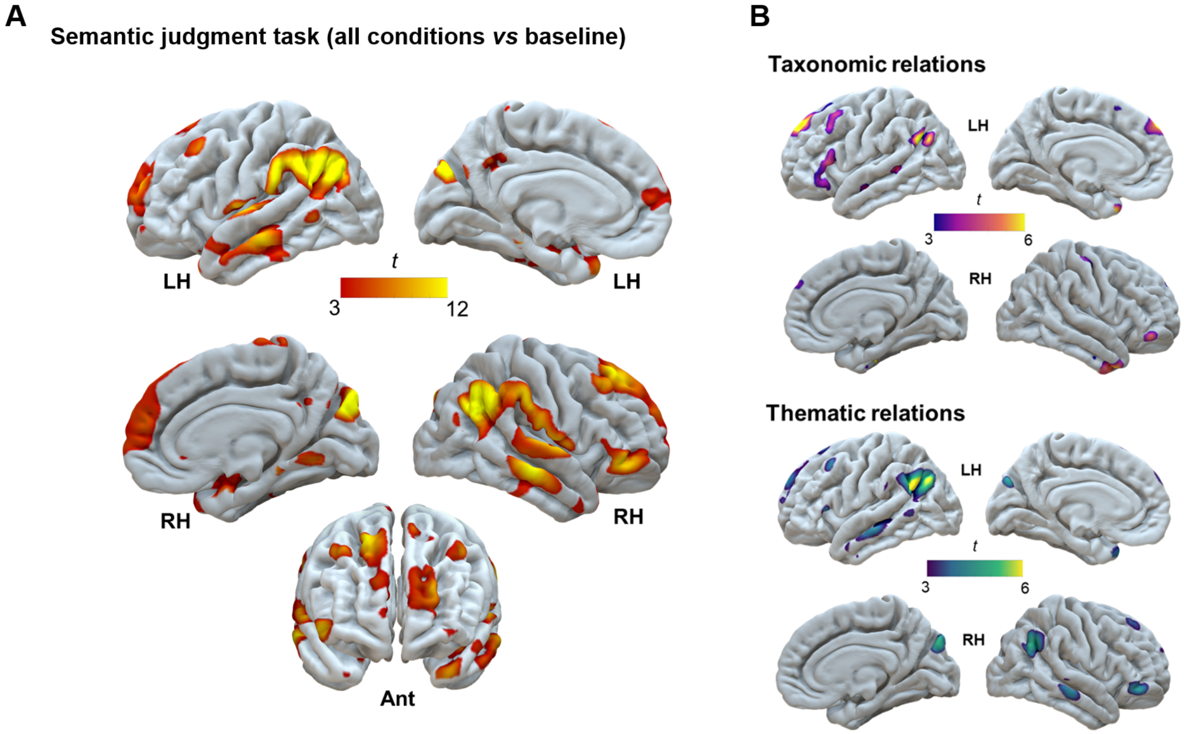


Figure 22. – Figure S3. Semantic judgment task activations (taxonomic versus thematic relations)

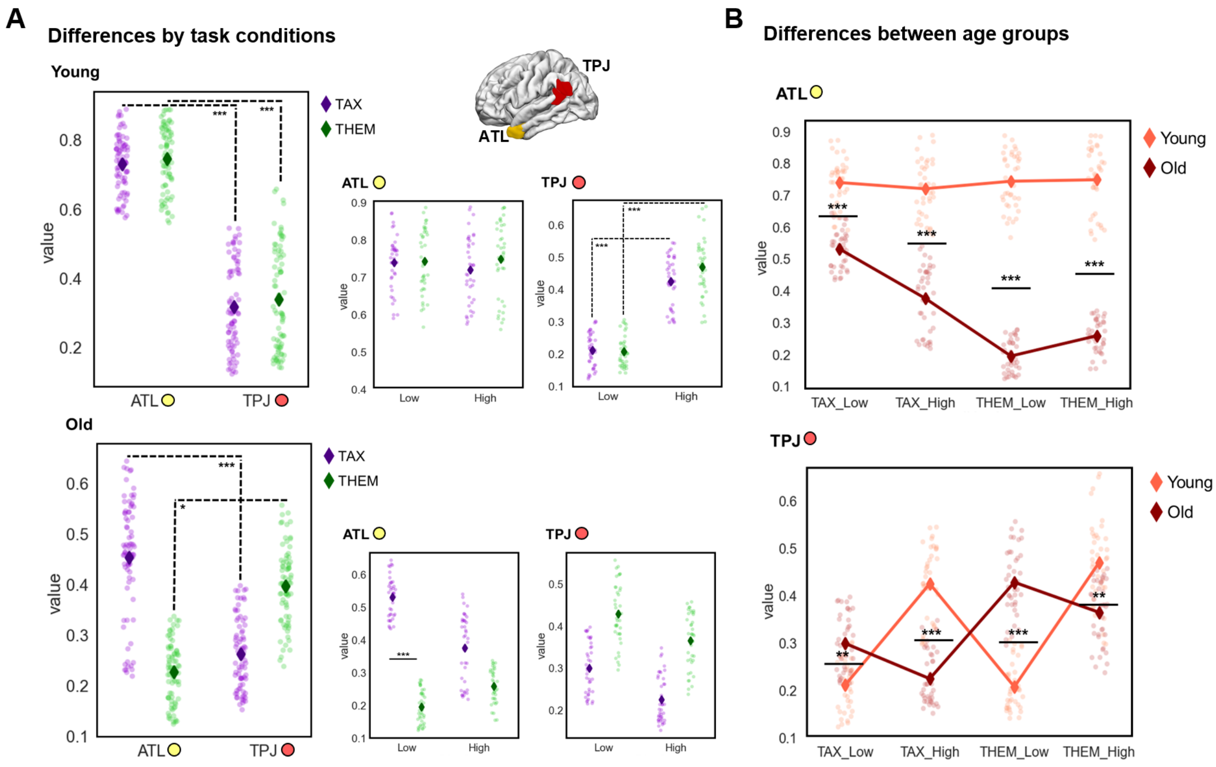


Figure 23. – Figure S4. Differences by task conditions and by age groups

Tableau 20. – Table S8. Bonferonni corrected post-hoc t-tests for repeated measures analysis of variance

Cond.	Dem.	ROI	Age Group		Cond.	Dem.	ROI	Age Group	Mean Diff.	SE	df	t	p_{bonf}
Tax	Low	ATL	Older	-	Tax	Low	ATL	Y	-0.209	0.015	76	-13.57	< .00001
				-	Tax	Low	TPJ	O	0.232	0.014	76	17.05	< .00001
				-	Tax	Low	TPJ	Y	0.320	0.014	76	22.50	< .00001
				-	Tax	High	ATL	O	0.155	0.019	76	8.09	< .00001
				-	Tax	High	ATL	Y	-0.189	0.019	76	-9.95	< .00001
				-	Tax	High	TPJ	O	0.306	0.014	76	22.44	< .00001

	-	Tax	High	TPJ	Y	0.106	0.015	76	6.90	< .00001
	-	Them	Low	ATL	O	0.336	0.017	76	19.73	< .00001
	-	Them	Low	ATL	Y	-0.213	0.016	76	-13.47	< .00001
	-	Them	Low	TPJ	O	0.103	0.014	76	7.24	< .00001
	-	Them	Low	TPJ	Y	0.323	0.015	76	22.11	< .00001
	-	Them	High	ATL	O	0.273	0.015	76	17.92	< .00001
	-	Them	High	ATL	Y	-0.217	0.017	76	-13.04	< .00001
	-	Them	High	TPJ	O	0.166	0.018	76	9.19	< .00001
	-	Them	High	TPJ	Y	0.061	0.017	76	3.70	0.04902
Younger	-	Tax	Low	TPJ	O	0.440	0.014	76	30.97	< .00001
	-	Tax	Low	TPJ	Y	0.528	0.014	76	38.89	< .00001
	-	Tax	High	ATL	O	0.364	0.019	76	19.15	< .00001
	-	Tax	High	ATL	Y	0.020	0.019	76	1.03	1
	-	Tax	High	TPJ	O	0.515	0.015	76	33.63	< .00001
	-	Tax	High	TPJ	Y	0.314	0.014	76	23.03	< .00001
	-	Them	Low	ATL	O	0.545	0.016	76	34.53	< .00001
	-	Them	Low	ATL	Y	-0.004	0.017	76	-0.24	1
	-	Them	Low	TPJ	O	0.311	0.015	76	21.28	< .00001
	-	Them	Low	TPJ	Y	0.532	0.014	76	37.52	< .00001
	-	Them	High	ATL	O	0.481	0.017	76	28.89	< .00001
	-	Them	High	ATL	Y	-0.009	0.015	76	-0.57	1
	-	Them	High	TPJ	O	0.375	0.017	76	22.64	< .00001
	-	Them	High	TPJ	Y	0.270	0.018	76	14.93	< .00001

TPJ	Older	-	Tax	Low	TPJ	Y	0.088	0.013	76	6.81	< .00001
		-	Tax	High	ATL	O	-0.077	0.019	76	-4.00	0.01757
		-	Tax	High	ATL	Y	-0.421	0.018	76	-23.28	< .00001
		-	Tax	High	TPJ	O	0.075	0.014	76	5.38	0.0001
		-	Tax	High	TPJ	Y	-0.126	0.014	76	-8.91	< .00001
		-	Them	Low	ATL	O	0.105	0.015	76	7.16	< .00001
		-	Them	Low	ATL	Y	-0.444	0.015	76	-30.31	< .00001
		-	Them	Low	TPJ	O	-0.129	0.013	76	-9.78	< .00001
		-	Them	Low	TPJ	Y	0.092	0.013	76	6.85	< .00001
		-	Them	High	ATL	O	0.041	0.015	76	2.73	0.95023
		-	Them	High	ATL	Y	-0.449	0.016	76	-28.78	< .00001
		-	Them	High	TPJ	O	-0.066	0.015	76	-4.37	0.00468
		-	Them	High	TPJ	Y	-0.170	0.015	76	-11.01	< .00001
	Younger	-	Tax	High	ATL	O	-0.165	0.018	76	-9.12	< .00001
		-	Tax	High	ATL	Y	-0.509	0.019	76	-26.57	< .00001
		-	Tax	High	TPJ	O	-0.014	0.014	76	-0.97	1
		-	Tax	High	TPJ	Y	-0.214	0.014	76	-15.45	< .00001
		-	Them	Low	ATL	O	0.017	0.015	76	1.13	1
		-	Them	Low	ATL	Y	-0.533	0.015	76	-36.39	< .00001
		-	Them	Low	TPJ	O	-0.217	0.013	76	-16.21	< .00001
		-	Them	Low	TPJ	Y	0.003	0.013	76	0.26	1
		-	Them	High	ATL	O	-0.047	0.016	76	-3.02	0.41273
		-	Them	High	ATL	Y	-0.537	0.015	76	-35.62	< .00001

			-	Them	High	TPJ	O	-0.154	0.015	76	-9.93	< .00001
			-	Them	High	TPJ	Y	-0.259	0.015	76	-17.25	< .00001
High	ATL	Older	-	Tax	High	ATL	Y	-0.344	0.022	76	-15.62	< .00001
			-	Tax	High	TPJ	O	0.151	0.021	76	7.16	< .00001
			-	Tax	High	TPJ	Y	-0.049	0.019	76	-2.61	1
			-	Them	Low	ATL	O	0.181	0.019	76	9.46	< .00001
			-	Them	Low	ATL	Y	-0.368	0.019	76	-19.03	< .00001
			-	Them	Low	TPJ	O	-0.052	0.018	76	-2.93	0.52933
			-	Them	Low	TPJ	Y	0.168	0.018	76	9.15	< .00001
			-	Them	High	ATL	O	0.118	0.020	76	5.87	0.00001
			-	Them	High	ATL	Y	-0.372	0.020	76	-18.57	< .00001
			-	Them	High	TPJ	O	0.011	0.020	76	0.55	1
			-	Them	High	TPJ	Y	-0.094	0.020	76	-4.70	0.00135
		Younger	-	Tax	High	TPJ	O	0.495	0.019	76	26.15	< .00001
			-	Tax	High	TPJ	Y	0.295	0.021	76	13.96	< .00001
			-	Them	Low	ATL	O	0.525	0.019	76	27.18	< .00001
			-	Them	Low	ATL	Y	-0.024	0.019	76	-1.24	1
			-	Them	Low	TPJ	O	0.292	0.018	76	15.86	< .00001
			-	Them	Low	TPJ	Y	0.512	0.018	76	28.70	< .00001
			-	Them	High	ATL	O	0.462	0.020	76	23.03	< .00001
			-	Them	High	ATL	Y	-0.028	0.020	76	-1.42	1
			-	Them	High	TPJ	O	0.355	0.020	76	17.79	< .00001
			-	Them	High	TPJ	Y	0.250	0.020	76	12.41	< .00001

		TPJ	Older	-	Tax	High	TPJ	Y	-0.201	0.015	76	-13.16	< .00001
				-	Them	Low	ATL	O	0.030	0.017	76	1.80	1
				-	Them	Low	ATL	Y	-0.519	0.016	76	-33.01	< .00001
				-	Them	Low	TPJ	O	-0.204	0.015	76	-14.02	< .00001
				-	Them	Low	TPJ	Y	0.017	0.015	76	1.18	1
				-	Them	High	ATL	O	-0.033	0.018	76	-1.86	1
				-	Them	High	ATL	Y	-0.523	0.017	76	-31.54	< .00001
				-	Them	High	TPJ	O	-0.140	0.016	76	-8.95	< .00001
				-	Them	High	TPJ	Y	-0.245	0.016	76	-14.86	< .00001
			Younger	-	Them	Low	ATL	O	0.231	0.016	76	14.68	< .00001
				-	Them	Low	ATL	Y	-0.318	0.017	76	-18.96	< .00001
				-	Them	Low	TPJ	O	-0.003	0.015	76	-0.21	1
				-	Them	Low	TPJ	Y	0.218	0.015	76	15.00	< .00001
				-	Them	High	ATL	O	0.167	0.017	76	10.07	< .00001
				-	Them	High	ATL	Y	-0.323	0.018	76	-17.98	< .00001
				-	Them	High	TPJ	O	0.060	0.016	76	3.67	0.0546
				-	Them	High	TPJ	Y	-0.044	0.016	76	-2.84	0.69643
Them	Low	ATL	Older	-	Them	Low	ATL	Y	-0.549	0.016	76	-33.93	< .00001
				-	Them	Low	TPJ	O	-0.234	0.015	76	-15.13	< .00001
				-	Them	Low	TPJ	Y	-0.013	0.015	76	-0.87	1
				-	Them	High	ATL	O	-0.064	0.016	76	-3.95	0.02054
				-	Them	High	ATL	Y	-0.554	0.017	76	-32.50	< .00001
				-	Them	High	TPJ	O	-0.170	0.015	76	-11.68	< .00001

			-	Them	High	TPJ	Y	-0.275	0.017	76	-16.25	< .00001
		Younger	-	Them	Low	TPJ	O	0.315	0.015	76	20.95	< .00001
			-	Them	Low	TPJ	Y	0.536	0.015	76	34.69	< .00001
			-	Them	High	ATL	O	0.485	0.017	76	28.49	< .00001
			-	Them	High	ATL	Y	-0.005	0.016	76	-0.29	1
			-	Them	High	TPJ	O	0.379	0.017	76	22.37	< .00001
			-	Them	High	TPJ	Y	0.274	0.015	76	18.79	< .00001
	TPJ	O	-	Them	Low	TPJ	Y	0.221	0.014	76	15.95	< .00001
			-	Them	High	ATL	O	0.170	0.017	76	9.82	< .00001
			-	Them	High	ATL	Y	-0.320	0.016	76	-20.03	< .00001
			-	Them	High	TPJ	O	0.063	0.015	76	4.29	0.00626
			-	Them	High	TPJ	Y	-0.041	0.016	76	-2.61	1
		Younger	-	Them	High	ATL	O	-0.051	0.016	76	-3.17	0.26553
			-	Them	High	ATL	Y	-0.541	0.017	76	-31.21	< .00001
			-	Them	High	TPJ	O	-0.157	0.016	76	-9.92	< .00001
			-	Them	High	TPJ	Y	-0.262	0.015	76	-17.72	< .00001
High	ATL	O	-	Them	High	ATL	Y	-0.490	0.018	76	-27.45	< .00001
			-	Them	High	TPJ	O	-0.107	0.019	76	-5.59	0.00004
			-	Them	High	TPJ	Y	-0.212	0.018	76	-11.91	< .00001
		Younger	-	Them	High	TPJ	O	0.383	0.018	76	21.60	< .00001
			-	Them	High	TPJ	Y	0.279	0.019	76	14.61	< .00001
	TPJ	Older	-	Them	High	TPJ	Y	-0.105	0.018	76	-5.94	< .00001

Clinical impact

The current research project contributes unique observations on language and aging, especially in the field of age-related neurofunctional reorganization when processing word-semantic relationships. It adds to the limited knowledge about cerebral dynamics contributing to the maintenance of semantic processing with age. From a methodological perspective, it tests the CRUNCH theory with a large number of participants and stimuli, ensuring enough power to test its predictions. The study of the ATLs and TPJ as hubs for semantic processing of words had never been studied before in the context of aging. In doing so, the exploration of the mechanisms of neurofunctional reorganization through a semantic judgment task, highlights the heterogeneity of age-related trajectories of changes in cerebral activation. It also highlights the importance of the interdependence between semantic processing and semantic/executive control, in agreement with literature on functional neuroimaging (Noonan et al., 2013, Wagner et al., 2001, Binder et al., 2009). In sum, this thesis provides a considerable contribution to the understanding of brain mechanisms associated with the maintenance of word semantic processing during normal aging. Preservation of such skills is particularly important for older adults, since it contributes to successful aging by allowing to support social interactions and quality of life (Nussbaum, 2000). By drawing a detailed portrait of the cerebral dynamics at the base of an optimal performance during the semantic processing of taxonomic or thematic relationships at low and high demand levels, this thesis could contribute to understanding the impact of neurological deficits (e.g., stroke) on semantic processing functions.

Conclusion

In this study, we aimed to test 1) the CRUNCH hypothesis and 2) the single and double-hub hypotheses about activation in their proposed respective semantic hubs (ATLs and TPJ), as well as the differential processing of taxonomic versus thematic relations, in relation to aging. We used a novel task that varied task demands (low versus high) in 39 younger and 39 older adults. Our participants, younger and older adults, were overall matched in regards to level of education and as shown in questionnaires assessing engagement in cognitively stimulating activities, MoCA and WAIS-III tests. The behavioral results confirmed that the task was successful in manipulating task demands, with error rates and RTs increasing with increasing task demands, namely in the high-demand condition. We found that engaging in cognitively stimulating activities impacted positively on both baseline RTs and accuracy. There was no statistical difference in accuracy between young and older participants regardless of the condition, so there was no age effect in accuracy. We found that higher scores on the WAIS-III and the PPTT tests were positively correlated with accuracy in older adults. This is in line with literature that shows that accuracy in semantic tasks is overall well-preserved in older adults considering their more extensive experience with word use and a larger vocabulary than younger ones (Balota et al., 2004; Kahlaoui et al., 2012; Kavé et al., 2009; Laver, 2009; Methqal et al., 2018; Verhaegen & Poncelet, 2013; Wingfield & Grossman, 2006). In terms of RTs, there was a statistically significant difference between young and older participants for all conditions, including the baseline, with older adults being slower to respond in general. This is in line with literature that shows that RTs of older adults are overall longer in comparison to younger ones (Balota et al., 2004). As such, the semantic memory task was successful in a) manipulating task difficulty across two levels of demands and b) demonstrating age-invariant behavioural performance for the older group (e.g., behavioral performance of the older equal to the younger), as requires to test the CRUNCH model (Fabiani, 2012; Schneider-Garces et al., 2010). Despite our behavioral findings, there was no statistically significant difference in activation however between the low and high-demand conditions. We did not obtain an interaction between age group and task demands either. Thus, the crucial tests of CRUNCH model, the fMRI group by difficulty interaction, was not consistent with the predictions of the model. In other words, we did not find the expected interaction between task demands and age group neither for RT or accuracy not for brain activation. Only the age group effect demonstrated significant activation in the bilateral occipital cortex and the cerebellum. Despite lack of task demand effects and only minimal age effects, at the neural level and independently of age, we found robust task-related activity. The semantic similarity judgment task activated a large bilateral fronto-temporo-parietal network. More specifically, ten distinct clusters of activation were observed when all task conditions were contrasted with the baseline, including the left supramarginal gyrus, the left cuneus, the right angular gyrus, the left middle frontal and superior gyri, the dorsolateral and medial superior frontal gyri. The activated regions correspond overall with regions reported to belong to the semantic network. Region of interest analyses demonstrated uncorrected significant effects of task demands within the left and right inferior frontal gyrus, the left posterior middle temporal gyrus, the posterior inferior temporal gyrus and the pre-frontal gyrus. In the pars triangularis and the pars orbitalis, lower activity was observed for the high task-demand level versus the lower task demand level. This demonstrates the task demand effect in these regions. We did not find any significant interactions between task demands and activation in the regions of interest. We found only minimal task demand effects and strong task-related effects. The co-activation of IFG and pMTG is frequently associated in the literature with high executive-semantic demands [153], for the controlled retrieval and management of semantic memory [49], [55], [156], [157]. In regards to age-related IFG activation, a meta-analysis on age-related changes in the neural networks supporting semantic cognition demonstrated reduced activation in the left IFG in older adults performing semantic tasks whereas IFG recruitment was enhanced in the right IFG, especially when their performance was not maintained, in comparison to their younger counterparts [22]. Within the current data, the lack of a significant difference in activation between the two levels of task demand conditions may be explained by the fact that our stimuli did not capture differences sufficient to yield a difference in neurofunctional activation. It is possible that the task was not sufficiently challenging for either younger or older particpants, such that it would not require the recruitment of additional neural resources, or that the difference between low and high task demands was not big enough to provoke an increase in activation in either younger or older adults. It is also possible that the task was already too demanding for both younger and older adults such that no additional activation was possible, as participants had maxed out their neural resources. Indeed, since the IFG is key to semantic processing as part of the semantic network, demonstrating robust activation across numerous semantic tasks, its spare capacity for additional recruitment may be limited, either in younger or older adults [23]. It is also possible that the CRUNCH model cannot easily be tested or falsified based on imaging methodologies, since whether activation increases or decreases, it can still be claimed to be compensation, whether successful or failed (e.g., that behavioral performance would be worse without the additional activation) [40]. To efficiently test CRUNCH it would be necessary to manipulate semantic memory task demands parametrically across 3-4 levels [40].

For our second objective, we aimed to assess how aging affects the processing of taxonomic versus thematic relationships and their respective hubs. Two theories have proposed predictions about the existence of hubs in charge of converging semantic information, the Single-hub and Dual-hub theories. The Single-hub or Controlled Semantic Cognition theory posits that the ATLs act as a hub for semantic processing and would subserve both types of relationships, whereas activation in the TPJ would vary as a function of task demands and semantic control requirements. The Dual-hub theory posits that two hubs would sub-serve differentially the two types of semantic relationships, the ATLs acting as a hub for taxonomic relationships and the TPJ performing this role for thematic ones. We used a novel task that varied type of semantic relation (taxonomic versus thematic) and task demands (low versus high) in 39 younger and 39 older adults. In regards to the semantic relation effect, the contrast of the taxonomic with the thematic condition directly did not find any robust activation at a corrected threshold. The taxonomic condition yielded interesting results when contrasted with the baseline one. Seven distinct clusters in the fronto-temporo-parietal cortex were activated across the two hemispheres, including the anterior temporal lobes (ATLs) and the left temporo-parietal junction (TPJ). Additionally, activation was significant in the left frontal syperior gyrus, the left angular gyrus (AG) and the inferior frontal gyrus (orbital part) on the right hemisphere. This finding could be partly in line with the dual-hub theory, that proposes that both the ATLs bilaterally and the TPJ act as semantic hubs. Though we did not find significant activation in the ATLs during the taxonomic condition and in the TPJ during the thematic condition by means of double dissociation, we found however that in the taxonomic condition among the seven significantly activated clusters, activation in the left superior frontal gyrus was significantly correlated with performance in the taxonomic condition for both age groups. Activation in the right middle temporal gyrus was also correlated with improved performance, but this was not significant in the older group. During the thematic condition, when contrasted with baseline, ten distinct clusters were activated, including the temporo-parietal junction (TPJ), whereas the ATLs were not robustly activated. More specifically, activated regions included bilaterally the angular gyrus, the middle temporal gyrus, the inferior frontal gyrus (triangular part) and the middle frontal gyrus. The activation of the left TPJ during the thematic condition could lend support to the dual-hub theory. Our findings could lend differing support to the two hypotheses, depending on age group. In younger adults, neither ATL nor TPJ activation varied as a function of type of semantic relationship. TPJ activation did, however, vary as a function of task demands, potentially supporting the CSC hypothesis, with the TPJ playing a role in regulating semantic control. In the older age group, the ATLs were recruited less than in the younger group. This could potentially be explained by the dedifferentiation hypothesis, referring to reduced neural efficiency, and the detrimental effect that aging may have on the recruitment of the ATLs as a semantic hub (Baltes & Lindenberger, 1997; Jiang et al., 2017; Park et al., 2004; Reuter-Lorenz & Lustig, 2005). Alternatively, it could support the CRUNCH (Compensation Related Utilization of Neural Circuits Hypothesis), whereby underactivation is seen in areas subserving “redundant” tasks and neural resources migrate to serve more urgent task requirements (Reuter-Lorenz & Cappell, 2008). In the low-demand condition, older adults recruited the TPJ more than younger ones, potentially demonstrating a compensation effect, that is, recruiting additional resources to meet task demands (Cabeza & Dennis, 2012; Reuter-Lorenz & Cappell, 2008). In the high-demand condition, however, when potentially they could have exhausted their resources, there was less activation in the TPJ than in the younger participants, which is somewhat in line with CRUNCH. Focusing on task complexity and demands regardless of age, CRUNCH proposes that both younger and older people can benefit from overactivation in these regions when task demands require additional resources (Reuter-Lorenz & Cappell, 2008). For older adults, however, the benefit of overactivation reaches a threshold above which the neural resources recruited are not adequate and performance declines (Reuter-Lorenz & Cappell, 2008).

In conclusion, although we did not find the expected double dissociation, we observed activation patterns that could support both hypotheses. Regarding the younger participants, our findings support single-hub theory more, with the ATLs potentially acting as a single hub and the TPJ modulated by task demands. In older participants, activations were found to be more condition-specific, and more in favor of the double-hub theory. Additional analyses are expected to elucidate the relation between task demands and type of semantic relation in light of age-related neurofunctional reorganization.

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Annexes

Annex 1: Stimuli

Run 1

Target	Option1	Option2	Correct answer
couvent	église	magasin	Option 1
relation	trahison	couple	Option 2
coccinelle	perdrix	abeille	Option 2
joue	pleure	bisou	Option 2
CKDHG	KDJUH	lgyhy	Option 1
compte	chiffre	équilibre	Option 1
démocratie	peuple	dictature	Option 1
poutre	cloison	fenêtre	Option 1
scalpel	scie	marteau	Option 1
enfant	jouet	sourire	Option 1
esprit	humour	fantôme	Option 2
pied	soulier	mesure	Option 1
tlfns	dgsnt	WZDFP	Option 1
côte	dune	mer	Option 2
temps	retard	montre	Option 2

spaghetti	potage	brioche	Option 1
larme	haleine	salive	Option 2
brousse	safari	paille	Option 1
pouvoir	royaume	politique	Option 2
défrisage	cheveux	coiffeur	Option 1
RTLPX	ylpzt	TJXRT	Option 2
amour	sentiment	cœur	Option 2
rue	boutique	trottoir	Option 2
air	pollution	tempête	Option 1
yeux	expression	regard	Option 2
chien	collier	niche	Option 2
beauté	ambiance	splendeur	Option 2
FSDX	VSDX	klpy	Option 1
dentiste	médecin	coiffeur	Option 1
bouteille	flasque	cadre	Option 1
ciment	acier	argile	Option 2
wqlfg	rqlfv	QWZMK	Option 1
oiseau	nid	arbre	Option 1
main	poignée	instrument	Option 1
machine	robot	industrie	Option 1
banane	chocolat	singe	Option 2
érable	olivier	cactus	Option 1
innovation	progrès	diversité	Option 1

TSBNM	TSBLG	lsbtm	Option 1
train	vitesse	rail	Option 2
puissance	courage	gaieté	Option 1
volcan	verger	colline	Option 2
théâtre	film	randonnée	Option 1
oignon	tulipe	potiron	Option 2
chaise	sofa	portail	Option 1
émeraude	rubis	fossile	Option 1
orgueil	innocence	mépris	Option 2
doigt	piano	bague	Option 2
motel	camping	chalet	Option 2
midi	zénith	repas	Option 2
mouton	vache	sanglier	Option 1
FSPZX	GTFSP	mnvzc	Option 1
cerise	raisin	pomme	Option 1
artère	gencive	tendon	Option 2
cheveu	peigne	pou	Option 1
QWRTY	ztylk	WRQWR	Option 2
jwpx	phcz	STRN	Option 2
hippopotame	éléphant	singe	Option 1
forêt	sapin	écureuil	Option 1
taureau	étalon	castor	Option 1
fauteuil	table	toit	Option 1

rêve	sommeil	espoir	Option 1
FDSHK	EVZXC	pwzlk	Option 1
llkkg	mmnnv	YYTTR	Option 1
carotte	biscotte	asperge	Option 2
wqhm	wqlx	KLVB	Option 1
sorcier	village	baguette	Option 2
force	muscle	combat	Option 1
justice	légalité	conviction	Option 1
xcvwh	blmvn	RTQSZ	Option 2
goût	mémoire	vue	Option 2
PZMVN	ldtyx	PZMBA	Option 2
fleur	couleur	printemps	Option 2
pianiste	peintre	médecin	Option 1
QWVXZ	QKLKV	rwqtr	Option 1

Run2

BGKF	HGFT	kjhf	Option 1
ouragan	pluie	cyclone	Option 2
cheval	équitation	galop	Option 1
lotion	baume	vernis	Option 1
gazelle	caribou	biche	Option 2
robe	chapeau	jupe	Option 2
musée	banque	château	Option 2

morue	saumon	moule	Option 1
monde	humanité	univers	Option 2
BGKF	HGFT	kjhf	Option 1
asphalte	béton	ivoire	Option 1
drapeau	patrie	hymne	Option 1
effort	récompense	sport	Option 2
guitare	cymbale	violon	Option 2
masque	théâtre	carnaval	Option 2
canoë	yacht	kayak	Option 2
kvlw	lytr	KSWT	Option 1
PTYMN	GPTYX	wqrxz	Option 1
HLDF	vbmn	SPRT	Option 2
cabinet	ministre	avocat	Option 2
règlement	discipline	solidarité	Option 1
porte	robinet	tiroir	Option 2
vent	froid	écharpe	Option 1
amitié	sympathie	méfiance	Option 1
bière	vin	limonade	Option 1
rocher	escalade	sirène	Option 1
gendarme	inspecteur	fleuriste	Option 1
rose	épine	romantisme	Option 1
classe	élève	chaise	Option 1
mode	magazine	vêtement	Option 2

connaissance	apprentissage	culture	Option 2
université	science	faculté	Option 2
KSVTR	LKSVG	lmnvf	Option 1
dos	massage	nageur	Option 1
mot	phrase	verbe	Option 1
liberté	droit	colombe	Option 1
rtypl	srtyn	OCVXZ	Option 1
KPLNV	KLNWZ	bdfgh	Option 1
xcvwh	mvwhd	WQKXM	Option 1
biberon	crayon	flacon	Option 2
GYTR	xvnm	YTZN	Option 2
feuille	automne	escargot	Option 1
cuisine	toilette	escalier	Option 1
ngws	jklp	PLNM	Option 1
ciel	nuage	paradis	Option 1
énergie	vitamine	soleil	Option 2
éclat	succès	soleil	Option 2
LSGHK	wrtvc	RTLPV	Option 2
football	ski	promenade	Option 1
armoire	rideau	lit	Option 2
vipère	araignée	python	Option 2
grotte	montagne	espace	Option 1
perfection	excellence	dignité	Option 1

ministre	soldat	président	Option 2
trésor	pirate	cachette	Option 1
GPZQM	nbcvr	HGFTM	Option 2
perroquet	oie	paon	Option 2
tgvhj	lknvm	ZAQVP	Option 1
vin	tisane	cognac	Option 2
KQNVM	KVMQN	stycn	Option 1
vache	fromage	herbe	Option 2
témoin	tribunal	crime	Option 2
livre	culture	fable	Option 1
crapaud	biche	lézard	Option 2
épaule	soutien	fusil	Option 1
étage	immeuble	palier	Option 1
étang	glacier	fleuve	Option 2
loi	égalité	justice	Option 2
luge	hochet	trottinette	Option 2
cycliste	écrivain	plongeur	Option 2
musique	inspiration	harmonie	Option 2
chef	tribu	cuisine	Option 2
piment	sucre	poivre	Option 2
coude	genou	cuisse	Option 1
maison	jardin	cocon	Option 1