Age-related changes in effective connectivity within and between the task-positive and task-negative networks during spatial and temporal context retrieval

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Abstract

Compared to young adults, older adults exhibit impairments in remembering the spatial and temporal contextual details associated with an event. During episodic memory (EM) retrieval, certain regions of the brain exhibit increases in activation (task-positive network, TPN), while others exhibit decreases in activation (task-negative network, TNN), compared to baseline. Studies have revealed that older adults exhibit impairments activating regions of the TPN, and deactivating regions of TNN compared to young adults, indicating that both of these age-related changes may contribute to deficits in context retrieval with age. Yet little is known about the relative changes in connectivity within and between regions of these two networks across different context retrieval tasks, in either age group, and how these changes may relate to memory performance. The goal of this thesis was to assess age-related effective connectivity changes in a simple item recognition task and in harder spatial context and temporal context tasks within and between the TPN and TNN, using structural equation modeling. Older adults performed as well as young in item recognition, but worse on both spatial and temporal context. The connectivity results revealed that there were no within-group task differences in the TPN, although there were between-group differences in this network: older adults displayed less connectivity between right lateral PFC and posterior visual areas, which may reflect less efficient selection of goal-relevant information from posterior visual areas. However, older adults exhibited greater connectivity of left lateral PFC with both right lateral PFC and medial premotor cortex, perhaps reflecting compensatory processes. Both groups exhibited within-group task differences effective connectivity in the TNN and between the TNN and TPN. While young adults exhibited decreased connectivity within the TNN and more negative connectivity the TNN and TPN in context versus item recognition, older adults displayed the opposite pattern: more positive connectivity within TNN and between regions of TNN and TPN in context tasks. Finally, older adults exhibited markedly reduced connectivity in TNN in the item recognition task, compared to young adults; however this difference was attenuated in the temporal context task, and eliminated in the spatial context task. Thus while young adults respond to increasing retrieval load by down-regulating subjective recollection processes in the TNN, older adults may rely on them to a greater extent as retrieval demands increase.

Résumé

Comparées à de jeunes adultes, les personnes âgées ont de la difficulté à se rappeler des détails spatiaux et temporels d'événements passés. Durant le rappel, certaines régions du cerveau augmentent leur niveau d'activité (réseau positif, RP), alors que d'autres diminuent leur niveau d'activité (réseau négatif, RN). Des études ont démontré que les personnes âgées n'activent pas les régions du RP, et ne désactivent pas les régions du RN autant que les jeunes adultes, indiquant que des changements dans les deux réseaux pourraient expliquer les troubles mnémoniques des personnes âgées. Cependant, très peu est connu sur les changements de connectivité se produisant dans différentes tâches de mémoire, dans les deux groupes d'âge. Le but de cette thèse était d'examiner les changements de connectivité dans le RP, le RN, et entre les deux réseaux, lors de tâche de mémoire d'item, de contexte spatial et de contexte temporel, en utilisant la modélisation par équation structurelle (MES). Les personnes âgées ont performé aussi bien que les jeunes de la tâche de mémoire d'item, mais moins bien dans les tâches de mémoire de contexte spatial et temporel. Les résultats de MES démontre que dans le RN, il n'y avait pas de changements de connectivité dus à la tâche, mais il y en avait qui était dû à l'âge : les personnes âgées avaient moins de connectivité entre le cortex préfrontal (CP) et le cortex fusiforme, indiquant un trouble avec la sélection d'information durant le rappel. Par contre, les personnes âgées avaient plus de connectivité entre le CP gauche et le CP droit, et entre le CP gauche et le cortex prémoteur, ce qui pourrait être un moyen de compensation. Les deux groupes ont démontré des changements de connectivité dus à la tâche dans le RN, en entre le RN et le RP. Alors que les jeunes adultes ont démontré moins de connectivité dans

le RN en entre le RN et le RP durant les tâches de mémoire contextuelle comparées à la tâche de mémoire d’item, les personnes âgées ont démontré des changements opposés : ils avaient plus de connectivité dans le RN et entre le RN et le RP dans les tâches de mémoire contextuelle. En conclusion, alors que les jeunes adultes se rappellent de mémoires plus détaillées en atténuant les mécanismes cognitifs du RP, les personnes âgées semblent s’en servir davantage pour se rappeler de mémoires plus détaillées.

Contents

List of abbreviations

BA - Brodmann area
CVLT - California verbal learning task
DLPFC- dorsolateral prefrontal cortex
EM – episodic memory
HC – Hippocampus
fMRI – functional magnetic resonance imaging
MTL – medial temporal lobes
PET – positron emission tomography
PFC – prefrontal cortex
PLS – partial least squares
PPC – posterior parietal cortex
SEM – structural equation modelling
SPM – statistical parametric mapping
TPN – task positive network
TNN – task negative network
VLPFC – ventrolateral prefrontal cortex

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Introduction

Overview

Healthy aging is associated with both structural and functional changes in brain regions involved in mediating episodic memory (EM) functions (Greenwood, 2007; Persson et al., 2006). However, healthy older adults do not exhibit behavioural deficits on all EM tasks. For example, older adults perform as well as young on forced-choice old/new item recognition tasks (Rajah et al., 2010; Schacter et al., 1991). On the other hand, older adults are impaired in tasks requiring the recall of the association between different features of an event, such as the association between an item and its spatial and temporal context (spatial and temporal context memory, respectively; Spencer & Raz, 1995).

Neuroimaging studies have revealed that young adults recruit regions spanning all four major lobes of the brain, the frontal, parietal, temporal and occipital lobes, during tasks of EM retrieval (Spaniol et al., 2009), indicating that memory processes rely on whole-brain networks . However, most studies of EM focus on region-specific changes in activation by using univariate statistical techniques such as statistical parametric mapping (SPM). These studies are often designed to test only a specific area's contribution to EM, such as the prefrontal cortex (PFC; e.g., Nolde, Johnson, & D'Esposito, 1998; Rajah & McIntosh, 2006), or the medial temporal lobes (MTL; e.g., Kirwan & Stark, 2004; Weis et al., 2004). This approach is useful, in that observing the relative contribution of one area in one task versus another, informs us about an area's functional specialization. Similarly, observing an age-related deficit in a specific brain region indicates that this functional specialization may be altered with age.

A study conducted in our lab illustrates this point. Functional magnetic resonance imaging (fMRI) data from 21 young and 21 older adults performing recognition, spatial context and temporal context retrieval tasks were collected. Older adults performed as well as young on the recognition task, but performed worse on both the spatial and temporal context tasks. Furthermore, there was a decreasing linear trend in accuracy scores across the recognition, spatial context, and temporal context tasks in both groups. Univariate SPM was conducted on the fMRI data to answer a specific question about age-related changes in PFC recruitment during context memory retrieval: is the age-related behavioural impairment in spatial and temporal context tasks due to common or distinct age-related changes in PFC activation (Rajah et al., 2010)? The SPM results revealed an age-related deficit common to spatial and temporal context tasks within PFC, specifically in the right dorsolateral (DLPFC) and left medial anterior PFC region. The right DLPFC deficit was interpreted as impaired cognitive control processing such as monitoring, and the anterior PFC deficit was interpreted as a failure to inhibit the task-negative network (TNN; see next paragraph for definition), also known as the default-mode network, in older adults. Furthermore, activity-behaviour correlations indicated that older adults partly compensated for these deficits by recruiting contralateral left DLPFC and right anterior PFC (Rajah et al., 2010).

The goal of this thesis is to investigate this dataset further, by examining whole-brain networks involved in the three EM retrieval tasks and their age-related change. The brain areas in which age-related changes were observed in the univariate analysis are part of whole-brain networks involved in memory retrieval. For example, the medial PFC is part of the TNN, a set of regions which also includes posterior cingulate, bilateral lateral temporal cortex and bilateral inferior parietal cortex, and which is thought to be involved in internally focused attention and which consistently exhibit decreased activation during cognitively demanding tasks, (Buckner et al., 2008; M.D. Fox et al., 2005; Toro et al., 2008) such as context memory retrieval. On the other hand, the right DLPFC is thought to be part of the task-positive network (TPN), a set of regions also including bilateral superior parietal lobe, premotor cortex and supplementary eye fields, which consistently exhibit increased activation in a variety of cognitively demanding tasks, including context memory retrieval (Cabeza et al., 2000; M.D. Fox et al., 2005; Toro et al., 2008).

Several questions remain unanswered from the univariate analysis, which a network analysis could elucidate. For example, since the univariate analysis was confined to PFC, it remains unclear whether only the medial PFC and right DLPFC are compromised with age, or whether the entire networks to which they belong to (TNN and TPN, respectively) are compromised. Second, it remains unclear how these region-specific deficits in distinct networks are related to one-another. One possibility is that older adults exhibit a distinct impairment *within* the TPN and *within* TNN. Another possibility is that the interactions *between* these networks are compromised with age. To investigate these issues, I propose to look at age-related changes in the functional and effective connectivity within and between the TNN and the TPN in the item recognition, spatial context and temporal context retrieval tasks.

Two multivariate statistical techniques will be used in this thesis. First, mean-centered partial least squares (PLS; McIntosh et al., 2004) will be conducted on the fMRI data to identify whole-brain patterns of activity which distinguish between tasks and age groups. It is expected that two sets of regions will be identified from this analysis: regions exhibiting increased activity during EM retrieval (TPN regions), and others exhibiting decreased activity during EM retrieval (TNN regions), compared to baseline. Regions from this analysis will be entered into structural equation modeling (SEM; McIntosh & Gonzalez-Lima, 1994) analysis, to obtain effective connectivity measures for each task and group, separately for the TNN, for the TPN and for the interactions between the TPN and TNN.

First, within-group SEM analyses will be conducted to test the null hypothesis that overall, effective connectivity between the chosen regions does not differ between the recognition, spatial context and temporal context tasks within and between the TNN and TPN. Second, a between-group SEM analysis will be conducted to test the null hypothesis that overall, effective connectivity between the chosen regions does not differ between groups. Provided that the null hypotheses of no group and task differences are rejected, specific path coefficients between sets of two regions will be tested for task and group differences. This will allow direct examination of effective connectivity change within and between the TPN and TNN.

In the following sections of this introduction I will present: 1) an introduction to EM and its neural correlates, 2) an overview of the TPN and TNN 3) age-related changes in EM retrieval and its neural correlates 4) the specific hypotheses to be tested in this thesis.

Episodic memory

Episodic memory (EM) has been defined as a system which stores information about personally experienced episodes or events and the spatio-temporal relations among them (Tulving, 1972). Tulving conceptualized an episode as an event that is part of an ongoing series of events. He also proposed to distinguish between the focal element of an event and its setting; the latter refers to the spatial and temporal context, and the former, to something that occurs in this setting (content or item memory).

EM refers to the ability to encode, store and consciously retrieve previously experienced events (Tulving, 1984). Encoding is the process by which an event is converted into a hypothetical internal representation referred to as the memory trace, or engram. A necessary condition for an engram to be retrieved (brought into consciousness once more) is the presence of a retrieval cue. Retrieval cues can be externally or internally generated. According to Tulving, retrieval arises when information about the cue is synergistically combined with information of the stored engram by a process termed ecphory (Tulving, 1984). A successful retrieval operation is usually conceptualized to occur in a series of sequential steps including pre-retrieval orientation, retrieval effort and post-retrieval monitoring (Dobbins et al., 2003; Rugg & Wilding, 2000; Simons, 2009). Retrieval orientation refers to the type of processing which is applied to a retrieval cue (Rugg & Wilding, 2000). In other words, it refers to the type of mnemonic information which is sought after, and is closely related to the notion of agenda- or goal-driven remembering (Mitchell & Johnson, 2009). Retrieval effort refers to the difficulty of the retrieval attempt (how hard the search operation is, and the level of processing consequently deployed), and is operationalized to be inversely related to retrieval accuracy (Rugg & Wilding, 2000). Finally, following the retrieval attempt, the retrieved content is thought to be held in working-memory, to be evaluated or monitored for task relevancy (R. N. Henson et al., 1999; Rugg & Wilding, 2000).

EM retrieval has been assessed using a variety of tasks and paradigms. EM retrieval is often sub-divided into different categories, which often take the form of a dichotomy (Tulving, 1972). Examples include verbal versus pictorial EM retrieval, item recognition versus free recall, "remember" versus "know" retrieval judgements and item recognition versus context retrieval. These sub-categories are not meant to refer to completely distinct forms of memories, mediated by different systems in the brain. Instead, the pool of processes mediating EM retrieval is generally assumed to be the same across all of these tasks; what varies is the extent to which any particular process is thought to be recruited in a particular sub-category of EM (M. R. Johnson & Johnson, 2009). For example, the remember-know paradigm dichotomizes memory retrieval according to the subjective experience through which information is recovered (Tulving, 1985). In this remember-know procedure, for every event that a subject recalls, she/he is asked whether the memory is rich in contextual detail (remember), or whether it is based on a non-specific sense of familiarity (know). "Remember", but not "know" responses, are thought to be accompanied by autonoetic awareness, a sense of reliving the event or mental time-travel (Tulving, 1985). Another type of EM retrieval paradigm dichotomizes the retrieval of content information from its source or spatio-temporal context. Retrieval of context information such as where an event occurred or when it occurred is thought to rely to a greater extent on strategic and organisational retrieval processes compared to simple retrieval of content (M. K. Johnson et al., 1993).

The neural correlates of EM retrieval

The concept of functional localization, that a particular cognitive process such as EM retrieval can be localized to a distinct area of the brain, has largely been abandoned by the field of neuroscience. Rather, circumscribed areas of cortex appear to be *specialized* in a particular aspect of information processing (Friston, 2004; Sporns, 2011). Modern conceptions of cognition suggest that it arises through the integration of the signal across a distributed network of such specialized regions (Bressler, 1995; Friston, 2004; McIntosh, 2000; Mesulam, 1990; Sporns, 2011). In this section, the specialization of cortical regions in EM retrieval is considered, and the next section examines the integration of these signals.

Evidence from both lesion and neuroimaging studies have indicated that widespread areas of cortex are involved in EM retrieval, and that these areas are specialized in different aspects of EM retrieval. All theories of EM formation and retrieval afford a central role to the MTL which includes the hippocampus (HC), entorhinal cortex, parahippocampal cortex and perirhinal cortex (Damasio, 1989; Fuster, 2009; Moscovitch, 1992; Paller, 2002; Squire, 1992). These regions, and especially the HC, are thought to be the “raw” memory structures (Moscovitch, 1992), in that they are necessary for memory formation and also appear to be critical for memory retrieval. This is primarily supported by the observation that lesions to this area cause anterograde, as well as varying degrees of retrograde amnesia (Spiers et al., 2001). Neuroimaging studies have also consistently identified activations in the MTL region during studies of EM (for reviews, see Diana et al., 2007; Eichenbaum et al., 2007; R. Henson, 2005). At retrieval, the MTL region is thought to be important in reactivating the memory trace, through interactions with cortical regions (Moscovitch, 1992). Recent research has led to clues about the specialization of regions within MTL. Since the perirhinal cortex receives the majority of its inputs from unimodal visual areas, while the parahippocampal cortex receives input mainly from association areas, it has recently been suggested that these areas process item and context information, respectively (Diana et al., 2007). These inputs are thought to converge in the HC, which binds them together and helps encoding and retrieval of the association between item and context (Diana et al., 2007). Both lesion and neuroimaging studies have provided evidence supporting this proposal (Diana et al., 2007; Eichenbaum et al., 2007).

The PFC, on the other hand, is thought to be important in the strategic and organizational aspects of EM retrieval (Moscovitch, 1992). This is supported by the observation that lesions to the PFC do not cause amnesia; PFC patients are relatively unimpaired in simple tests of item recognition (Kesner et al., 1994). Rather they are impaired in tasks which require the use of specific strategies or organization of information, such as the ordering of items according to their temporal recency (Kesner et al., 1994; Milner & Petrides, 1984). Neuroimaging studies have also implicated the PFC in various control processes during retrieval tasks. For example, DLPFC has been implicated in the monitoring/evaluation of retrieved information (Dobbins et al., 2004; Mitchell et al., 2004; Petrides et al., 1993) and retrieval orientation (Dobbins et al., 2003; Ranganath et al., 2007). On the other hand, the VLPFC has been involved in selection and inhibition of goal-relevant memory signals from posterior cortical areas, and in semantic encoding and retrieval strategies (Kostopoulos & Petrides, 2008; Kuhl & Wagner, 2009; Petrides, 2005; Raposo et al., 2009).

Finally, selective attention during EM retrieval has been associated with the lateral posterior parietal cortex (Cabeza, 2008; Cabeza et al., 2008; Ciaramelli et al., 2008; Kim, 2010a). Specifically, dorsal parietal cortex has been shown to be involved in top-down attention processes guided by retrieval goals, in close interaction with DLPFC (Ciaramelli et al., 2008). On the other hand, the inferior parietal lobe is involved in bottom-up capture of attention from retrieval content, possibly by close interaction with MTL (Ciaramelli et al., 2008). This proposal has also recently been supported by lesion evidence (Ciaramelli et al., 2010).

Interactions between neural elements in EM

As previously mentioned, cognitive processes such as EM retrieval are thought to arise through the *interactions* between anatomically distinct regions of cortex. This section considers evidence that the regions described in the previous section interact during EM retrieval. These interactions have mainly been assessed using measures of functional connectivity and effective connectivity. The former simply refers to the correlations of activity between different regions, while the latter allows for a measure of the directional influence that regions have on each other, through a model of causal interactions (Friston et al., 1993; McIntosh & Gonzalez-Lima, 1994).

A few studies have focused primarily on the interactions of MTL with other regions in EM retrieval. Kohler and colleagues (1998) compared effective connectivity in an object retrieval versus spatial retrieval task. They found that interactions between MTL and dorsal regions (supramarginal gyrus and parieto-occipital sulcus) were positive during spatial retrieval but negative in object retrieval. In contrast, interactions between MTL and ventral regions (fusiform gyrus and superior temporal sulcus) were negative in the spatial task and positive in the object task. In another study, McCormick and colleagues (2010) compared MTL interactions between encoding and retrieval of face stimuli. They found a stronger influence from supramarignal gyrus to MTL at retrieval, and a stronger influence from MTL to supramarginal gyrus at encoding. They interpreted their findings to mean that at retrieval, there was greater bottom-up attention to memory contents in the MTL.

Other studies have focused primarily on the interactions between PFC and the rest of the brain. Grady and colleagues (Grady et al., 2001) examined the connectivity of right anterior PFC during retrieval of words which had either been semantically or perceptually encoded. Right anterior PFC was similarly connected to a network of regions in both conditions, which included bilateral VLPFC, bilateral DLPFC, regions of the visual stream, and parietal regions. Additionally, activity in this network of regions was related to retrieval accuracy for words which had been semantically encoded.

In another study, Rajah and colleagues (Rajah et al., 1999) analysed effective connectivity differences in a frontotemporal model across face perception, face encoding and old/new face recognition tasks. Compared with the other two tasks, face recognition was associated with a positive loop in the right ventral visual stream from occipital, to fusiform to VLPFC, and back to fusiform gyrus. Additionally, there was a positive input from right fusiform to right MTL, which the authors hypothesized may have initiated the retrieval process, assuming retrieval was initiated by the face cue.

Overall, these results demonstrate that the interactions between MTL, PFC, PPC and sensory areas are important in EM retrieval. Additionally, they demonstrate that the nature of these interactions depend on the retrieved content and exact operations involved in the retrieval operation (McIntosh, 1999).

The neural correlates of context memory retrieval

In the last section, the roles of MTL, PFC, PPC and the interactions between them in EM retrieval were described. Here, the relative involvement of these regions in spatial context versus temporal context versus item recognition is presented. No study has examined functional or effective connectivity during spatial or temporal context retrieval; hence, the discussion is limited to region-specific changes based on univariate methods of analysis.

A few studies have directly assessed the relative contributions of spatial and temporal context memory in MTL. In two of these studies left (Kukolja et al., 2009), and right (Cansino et al., 2002) HC activity was greater for correctly versus incorrectly remembered spatial context judgements. In another study (Ekstrom & Bookheimer, 2007), both HC and parahippomapal gyrus were significantly activated by spatial context and temporal recency, although the magnitude of activation in both regions was greater in the spatial task. Similarly, Dobbins (2003) reported greater activation in left parahippocampal gyrus and HC in a direct comparison of spatial context versus temporal recency. The greater activation in HC and parahippocampal gyrus in spatial context versus temporal recency and in context versus recognition tasks has been interpreted under the dual-process model of memory. Specifically, it is assumed that a correct spatial context memory judgement must be made by recollecting specific details about the event (remember), while recency and item recognition judgments can be made without explicit recollection, but instead based on relative feelings of familiarity (know) about which event occurred first/second (Dobbins et al., 2003).

Studies contrasting item and context memory in the PFC have revealed laterality differences. Studies comparing spatial context retrieval with recognition tasks have reported mostly left-lateralized PFC activations (Mitchell et al., 2004; Rugg et al., 1999; Slotnick et al., 2003). For example, Rugg and colleagues (1999) reported greater activation in left VLPFC, DLPFC and anterior PFC in a spatial source versus item recognition contrast. On the other hand, studies comparing recency judgements with item recognition have reported right-lateralized DLPFC and anterior PFC activations (Cabeza et al., 2000; Rajah & McIntosh, 2006). Recently, some studies have directly compared spatial context retrieval with recency judgements. Consistent with prior studies, left versus right-lateralized PFC activation were reported for the spatial and temporal tasks respectively (Dobbins et al., 2003; Mitchell et al., 2004). Just as in the MTL literature, these lateralization differences have been attributed to differential recruitment of cognitive control processes involved in recollection versus familiarity. For example, it has been suggested that right PFC is involved in heuristic evaluation processes operating on information such as fluency, familiarity and recency (Nolde, Johnson, & Raye, 1998). Meanwhile, left PFC is thought to play a role in more systematic, recollection-based judgements (Nolde, Johnson, & Raye, 1998). In the current dataset, the SPM results revealed left and right prefrontal activations for spatial and temporal tasks respectively, although right (but not left) prefrontal activation was correlated with performance on both tasks (Rajah et al., 2010). Laterality differences were attributed to monitoring processes related to increased difficulty in the temporal, versus the spatial task.

A recent meta-analysis found that both the lateral superior and inferior posterior parietal cortex were activated to a greater in context tasks versus item recognition tasks (Ciaramelli et al., 2008). The greater activation in inferior parietal cortex was attributed to the fact that item recalled with their context should elicit greater bottom-up saliency, since more details are recalled. The greater activation in superior PPC was attributed to the greater need for attention to cognitive control process in context versus item recognition tasks. Very little information exists regarding the contributions of PPC to spatial versus temporal context retrieval, but one study reported greater left PPC activation in spatial context, and greater right PPC activation in temporal context (Dobbins et al., 2003).

Another perspective on the neural correlates of EM retrieval

In the previous sections, the contribution of various cortical regions to EM retrieval in general, and to context retrieval in particular, was described. However, fMRI studies have revealed that these various areas and especially those in PFC and PPC are activated not only in EM retrieval, but also in a variety of other tasks and paradigms (Cabeza & Nyberg, 2000; Toro et al., 2008). Indeed, meta-analyses have revealed remarkable similarity in the networks of regions coactivated across tasks thought to probe different cognitive domains such as memory encoding, memory retrieval, working-memory, attention and skill learning, to name only a few (Cabeza & Nyberg, 2000; Toro et al., 2008). This network of regions showing activity increases in a variety of cognitively demanding tasks has come to be known as the TPN (M.D. Fox et al., 2005). On the other hand, a different set of regions consistently exhibit decreases in activation during EM retrieval and a variety of other paradigms has been named the TNN (M.D. Fox et al., 2005).

Furthermore, it has been observed that not only are these regions coactivated during a variety of tasks, they are also coactivated in the absence of a cognitive task, when subjects are “at rest” (M.D. Fox et al., 2005). Much has been learned about the TPN and TNN by studying this “spontaneous activity”, which refers to intrinsic activity not generated by any stimulus or task. Biswal (1995) first demonstrated that spontaneous neural activity is not simply random noise, but is rather organized into distinct resting-state networks that exhibit striking resemblance to task-related networks (M.D. Fox et al., 2005; Greicius et al., 2003; Smith et al., 2009; Vincent et al., 2008). Indeed, a consistent finding is that regions which are co-activated during the performance of cognitive tasks tend to also be correlated at rest, in the absence of cognitive tasks (M. D. Fox & Raichle, 2007; Smith et al., 2009). In fact, this relationship is so strong and consistent that the organisation of *resting-state* networks is now being used as evidence to refine our understanding of *task-related* cognitive networks (e.g., Vincent et al., 2006).

The precise significance of the relationship between resting-state and task-related networks is still a matter of speculation (Deco et al., 2011; M. D. Fox & Raichle, 2007; Morcom & Fletcher, 2007; Raichle, 2009, 2010; Raichle & Snyder, 2007; Smith et al., 2009), and is beyond the scope of this thesis. Still, it is my belief that consideration of the different areas thought to be involved in EM retrieval within the context of these task-independent, intrinsically generated whole-brain networks can provide additional insight into our understanding the neural mechanisms giving rise to EM retrieval. The following sections summarize the converging evidence from task-related and resting-state literatures for the existence and organisation of the TNN and TPN and the role of these networks in memory retrieval.

The task-negative network as a core brain network

The TNN was first identified by meta-analyses of regions which were commonly deactivated across EM retrieval (Nyberg et al., 1996) and perceptual tasks (Shulman et al., 1997) compared to low-level control conditions. Areas including the posterior cingulate cortex (PCC), inferior parietal lobe, medial PFC, and inferior lateral temporal gyrus were found to be commonly deactivated during the performance of these tasks. Using quantitative positron emission tomography, Raichle et al. (2001) demonstrated that these regions are in their baseline state at rest, and that activity in these regions may be suspended during the performance of cognitive tasks.

The finding that these areas were similarly modulated by task-demand suggested that the may form a network, and this was largely confirmed by Greicius et al (2003). They identified regions that were maximally activated (VLPFC and DLPFC) and deactivated (ventral medial PFC and PCC) during a working memory task. They next examined the functional connectivity of these regions during a passive resting state condition, in which subjects were simply asked to close their eyes and not think of anything in particular and during a passive visual task. The PCC seed analysis recovered an almost identical set of regions as that found by Shulman (1997) in his meta-analysis, and the connectivity map was nearly identical in the rest and passive visual condition. Furthermore, they demonstrated that activity in PCC was inversely correlated with both the VLPFC and DLPFC at rest. These results demonstrated that regions in the TNN are functionally connected at rest, and exhibit similar modulation in activity during task performance, strongly suggesting that they form a cohesive network (Greicius et al., 2003).

The Sluman et al., and Greicius et al. studies demonstrate that neural networks such as the TNN network can be identified using very different methodologies. The first is task-related modulation of activity: like the Sulman study, others have identified the TNN through meta-analyses of task-related differences in activation (Kim, 2010a, 2010b; Toro et al., 2008). Second, like the Greicius study, the TNN can be identified by correlating activity of a seed region (typically medial PFC or PCC) to activity in the rest of the brain, either at rest (Andrews-Hanna, Reidler, Sepulcre, et al., 2010; M.D. Fox et al., 2005; Vincent et al., 2006), or during task-performance (Grady et al., 2010; Spreng & Grady, 2010). Finally, the TNN has also been identified as a component in independent component analyses (Damoiseaux et al., 2006; Greicius et al., 2004). The range of methods with which the TNN has been identified and the striking similarity in results between methods (Greicius et al., 2003; Toro et al., 2008) point to the robustness of the TNN as a core brain network.

The exact role of the TNN in cognition is unknown, but recent investigations suggest that it plays a role in self-referential cognitive processes, and internally focused attention (Andrews-Hanna, Reidler, Huang, et al., 2010; Andrews-Hanna, Reidler, Sepulcre, et al., 2010; Buckner et al., 2008; Mason et al., 2007; van Buuren et al., 2010). For example, recent meta-analyses have suggested that regions in this network are similarly *activated* in spatial navigation, theory of mind, autobiographical memory and prospective memory (Schacter & Addis, 2007; Spreng & Grady, 2010; Spreng et al., 2009). These processes share in common that attention is focused away from the external world and directed towards internal cognition (Buckner et al., 2008). Another study found that increased activity in regions of TNN positively correlates with self-reported rates of occurrence of stimulus-independent thoughts (Mason et al., 2007). The proposition that this network supports internally focused cognition is also an interesting explanation as to why the TNN needs to be deactivated during the performance of attentionally-demanding cognitive tasks; it is likely that during these tasks, attention needs to be driven away from distracting internally focused thoughts about the past or future and instead fully devoted to the task at hand for maximal performance (e.g., Daselaar et al., 2009; Vannini et al., 2010). Additionally, the extent of deactivation in TNN has been found to be proportional to the difficulty of the task being performed (McKiernan et al., 2003), and connectivity within regions of this network is also reduced with cognitive load (Fransson, 2006) further supporting this notion.

The task-positive network as a core brain network

The notion of a TPN refers to the fact that a specific set of lateral frontal, lateral parietal and visual areas are consistently activated during the performance of attention-demanding tasks (M.D. Fox et al., 2005). For example, Cabeza and Nyberg (2000) performed a meta-analysis of 275 PET and fMRI studies and found that lateral prefrontal and parietal regions were consistently activated across a broad range of tasks involving attention, spatial perception and imagery, working memory, episodic encoding, episodic retrieval and skill learning. These regions have also been shown to be functionally related at rest. For example, Fox et al. (2005) used seed analysis of resting state fMRI data using three regions of the TPN as seeds: the intra-parietal sulcus, the frontal eye fields and the middle temporal region. They also performed a seed analysis using three TNN regions: the medial PFC, PCC and lateral parietal cortex. They then performed a conjunction analysis, to identify regions that were consistently identified in at least 5 of the 6 seed analyses. The results yielded two anti-correlated networks: the first, which Fox et al. referred to as the TPN, contained peaks in bilateral DLPFC, bilateral intraparietal sulcus, bilateral premotor cortex and bilateral occipital and middle temporal regions. The second, which they referred to as the TNN, contained peaks in medial PFC, PCC, retrosplenial cortex, inferior temporal cortex and the MTL. These results are important, in that they clearly identify two separate neural networks, the TPN and the TNN, and demonstrate that they are intrinsically represented in the brain in the absence of any task or behavioural. They also demonstrate, similarly to Greicius et al. (2003), that these networks are anti-correlated at rest.

Investigators have attributed a role for the TPN, and especially the DLPFC and the region surrounding the intra-parietal sulcus in top-down modulation of attention, cognitive control processes and the processing of externally presented information (Cabeza et al., 2000; Corbetta & Shulman, 2002; Vincent et al., 2008). As the difficulty of a task increases, these regions are often recruited to a greater degree. For example, regions in lateral PFC and PPC are recruited to a greater degree with increased load in working memory tasks (Callicott et al., 1999). Similarly, these regions are recruited to a greater extent in context memory tasks, compared to simple item recognition, which is thought to reflect the greater reliance on strategic cognitive control processes in the former tasks (Mitchell & Johnson, 2009). This is in contrast to regions in the TNN, which as previously mentioned exhibit greater deactivation as a task becomes harder (McKiernan et al., 2003). The TPN and TNN therefore appear to act in opposition during the performance of cognitive tasks; activity in regions of the former increase as a task becomes more effortful, while activity in regions of the latter decreases. Supporting this notion, the degree of anti-correlation between TPN and TNN during cognitively demanding tasks predicts performance (Hampson et al., 2010; Kelly et al., 2008).

In summary, converging evidence from studies of resting-state correlations and task-related co-activations support the existence of the TPN and TNN. These networks appear to act in opposition both at rest and during the performance of cognitively demanding tasks, and have been suggested to subserve distinct cognitive processes. In the next section, the role these networks play in memory retrieval is examined.

The TNN and TPN in EM retrieval

The TNN is generally assumed to play a pivotal role in the retrieval of memories. Indeed, the first paper to clearly identify the TNN as a coherent network (through resting-state correlations) suggested a role for this network in memory retrieval (Greicius et al., 2003). Other investigators have also suggested that successful retrieval is mediated primarily by the TNN (Buckner & Carroll, 2007; Kim et al., 2010; Schacter & Addis, 2007). However, there is also a large body of literature indicating that regions of the TPN, especially lateral PFC and lateral parietal lobe are involved in memory retrieval (Cabeza, 2008; Ciaramelli et al., 2010; Dobbins & Han, 2006, 2009; Dobbins et al., 2003; Dobbins & Wagner, 2005; Mitchell et al., 2004; Rajah et al., 2010; Rajah & McIntosh, 2006; Wagner et al., 2005). This discrepancy in results can primarily be attributed to the different tasks used to assess memory retrieval. To clearly understand the role of the TPN and TNN in EM retrieval, their role across a variety of EM retrieval tasks must be examined and compared. This section summarizes the involvement of the TNN and TPN in EM retrieval, by considering their relative involvement in 1) episodic versus autobiographical retrieval, 2) Remember versus know judgments and 3) objective versus subjective recollection.

Episodic memory versus Autobiographical memory

To understand exactly which types of retrieval tasks lead to activation in the TNN, our definition of EM must be refined. To study EM, many investigators have used protocols where they present a series of stimuli (typically words, faces or objects) and later ask subjects to remember some aspect of these stimuli. This was thought to recruit the same cognitive processes as autobiographical memory (Tulving, 1983), which refers to events from one's past, outside the laboratory. However, evidence from neuroimaging studies has revealed that there are profound differences in the neural correlates or EM retrieval (henceforth used to refer to the retrieval of laboratory stimuli) and autobiographical retrieval. The two operations are now thought to differ in terms of personal relevance, time elapsed between encoding and retrieval, and the methods used to probe these memories (Gilboa, 2004). Several meta-analyses have revealed that autobiographical memory recruits a set of regions strikingly similar to the TNN including medial PFC, bilateral angular gyrus, bilateral inferior lateral temporal gyrus, posterior cingulate and the MTL (Gilboa, 2004; McDermott et al., 2009; Svoboda et al., 2006). On the other hand, EM retrieval recruits an almost completely non-overlapping network of regions (McDermott et al., 2009), and most of these, including lateral DLPFC, VLPFC, dorsal PPC belong to the TPN.

Remember versus know

Do all types of EM retrieval (retrieval of laboratory stimuli) lead to activation in the TPN? Evidence from the remember-know paradigm suggests that this is not the case. As discussed earlier, events given a remember response are thought to be rich in contextual details and accompanied by a sense of reliving the event. On the other hand, “know” judgements are harder than “remember” judgements, as operationalized by longer reaction times in the former (Dewhurst et al., 2006), and are assumed to require greater use of controlled retrieval processes such as iterative search, post-retrieval monitoring and response selection (Kim, 2010a), which are thought to be mediated especially by lateral PFC regions (Dobbins & Han, 2006, 2009; Dobbins et al., 2003; Dobbins & Wagner, 2005). A recent meta-analysis found that events given a "remember" response were associated with activation almost exclusively in the TNN, while events given a "know" judgement were associated almost exclusively with TPN regions (Kim, 2010a). Commenting on these results, Kim mentions that: "Self-referential processing is a strong component of recollection, but at best a weak component of familiarity memory. Thus, an association between default-mode network activity and recollection fits well with the view that this network supports self- referential processing". The association of "know" responses with TPN was attributed to the greater need for cognitive control processing for these events.

Objective versus subjective recollection

Events given a "remember" judgement in the remember-know paradigm are often referred to as subjective recollection, since the judgement can be based on *any* contextual experience that is re-experienced by a subject (it is inherently a subjective judgement). In contrast, in tests of objective recollection (such as spatial or temporal context memory), memory for a *specific* (objective) association between an item and its context is probed. For this reason, objective memory is thought to be more demanding than subjective recollection (Spaniol et al., 2009). A recent meta-analysis (Spaniol et al., 2009) compared the activations of objective versus subjective recollection. Objective recollection was associated more with TPN regions such as ventrolateral, dorsolateral and anterior PFC, supramarginal gyrus and superior PPC. On the other hand, subjective recollection was associated more with TNN regions such as medial PFC, angular gyurs, posterior cingulate and HC. Importantly, however, when considered individually, objective and subjective recollection were associated with both TPN and TNN regions, demonstrating that these distinctions are a matter of degree rather than being absolute.

In sum, the role of TNN and TPN in EM retrieval is roughly consistent with its role in other cognitive domains. The TNN is involved mainly in retrieval tasks putting a greater emphasis on self-referential processing such as autobiographical memory and subjective recollection. On the other hand, the TPN is associated with "difficult" retrieval judgements such as "know" versus "remember" judgements, objective versus subjective recollection and context versus item judgements, which may all require additional use of cognitive control processes.

Age-related changes in EM retrieval

Deficits in memory retrieval are among the most commonly reported complaints in aging (Park & Gutchess, 2005). However, older adults are not impaired on all tasks of EM retrieval; for example, they usually perform as well as young on item recognition tests, but perform worse on associative memory tasks such as context memory retrieval (Spencer & Raz, 1995). Several theories have been proposed to account for these deficits, some of which are specific to EM, and others which extend across cognitive domains.

Associative binding deficit theory

One theory postulates that older adults have a specific deficit in binding together the different features that make up a complex memory (Chalfonte & Johnson, 1996; Naveh-Benjamin, 2000). This theory is supported by the disproportionate deficit of older adults in associative versus item memory (Chalfonte & Johnson, 1996; Naveh-Benjamin, 2000; Spencer & Raz, 1995), and also by the relatively lower levels of recollection experienced by older adults (Mantyla, 1993; Parkin & Walter, 1992), which by definition involves remembering bound features in memory. Since in young adults, binding of features is thought to rely on the HC, this theory of age-related memory deficits would predict age-related changes in this region. Indeed, several studies have found age-related reduction of activity in the HC, both at encoding and retrieval (Daselaar et al., 2003; Davis et al., 2008; Dennis & Cabeza, 2008; Kukolja et al., 2009).

Furthermore, age-related changes in hippocampal connectivity during EM tasks have also been reported (Grady et al., 2003; Tsukiura et al., 2011). For example, in a face-name retrieval task, Tsukiura (2011) and colleagues found that older adults displayed less connectivity between HC and anterior temporal lobe, which they suggested contributed to older adult's poorer performance.

Resource deficit theories

Another theory, the resource deficit theory, suggests that older adults have less resources available to them to perform cognitive tasks such as EM encoding and retrieval (F. I. Craik, 1983). Support for this hypothesis comes from the observation that dividing the attention of young subjects at encoding (and thereby reducing their available resources) results in similar deficits to those observed in older adults (F. I. Craik, 1983). Specifically, it is suggested that older adults have difficulties spontaneously engaging organisational and strategic processes at encoding and retrieval (F. I. Craik, 1983). The word "spontaneously" is used since there is substantial evidence that part of this deficit can be eliminated by providing specific strategies to older adults at encoding, retrieval, or both (F. I. Craik, 1983; Naveh-Benjamin et al., 2007). However, while providing strategies to older adults improves their performance, they do not reach the same level as young adults (Naveh-Benjamin et al., 2007).

Since in young adults, organisational and strategic processes have been attributed to TPN regions in the PFC, such theories would predict age-related changes in this region during cognitively demanding tasks such as EM encoding and retrieval. Indeed, several studies have found reductions in PFC activity with aging, which are often interpreted as reflecting impaired functioning in these areas and the cognitive process they subserve (Rajah & D'Esposito, 2005; Spreng et al., 2010). However, *increases* in PFC activation are another common finding, across tasks and cognitive domains (Rajah & D'Esposito, 2005; Spreng et al., 2010). One possibility is that older adults compensate for the reduced resources mediated by the particular PFC regions recruited by young adults by recruiting additional resources mediating by other PFC regions (Cabeza, 2002). Indeed, recruitment of additional PFC regions by older adults is often interpreted as being compensatory, particularly when it is found that these increases are correlated with accuracy. Often, these increases in activation are seen in the region contralateral to that used in young adults, which has led to the hemispheric asymmetry reduction in older adults (HAROLD) model (Cabeza, 2002).

For example, Cabeza and colleagues (Cabeza et al., 1997) found that encoding and retrieval of word pairs was lateralized in left and right VLPFC, respectively, in young adults, but bilateral in older adults. A comparison of effective connectivity between encoding and retrieval mirrored the activation results. Age-related changes in the connectivity of bilateral VLPFC were observed during encoding and recall of paired associates. In the young, left BA 47 positively interacted with the rest of the brain, whereas in recall, it was right BA 47 which positively interacted with other areas. On the other hand, in older adults, interactions were mixed (both positive and negative) during encoding, and bilaterally positive during recall. The authors argued that older adults' bilateral use of VLPFC at retrieval was compensatory in nature, perhaps reflecting additional semantic retrieval operations.

A model related to HAROLD, and part of the family of resource-deficit theories, states that older adults need additional resources to perform tasks that young adults perform using fewer resources (Reuter-Lorenz & Cappell, 2008). However, because they use up their resources faster than young adults, they reach their point of resource limitation (the crunch) faster than young adults. Hence, this model predicts that over-activation in older adults will only be compensatory at lower task demand.

While the models discussed so far have hypothesized that PFC over-activation is compensatory, others have hypothesized that increased activity in PFC regions in older adults reflects a decreased signal-to-noise ratio in a noisier, less effective system (e.g., Li & Lindenberger, 1999; Morcom et al., 2007). An examination of the literature provides support for both of these perspectives (Rajah

& D'Esposito, 2005). One factor influencing the behavioural correlate of over-activation seems to be the precise PFC region involved. For example, the results from two meta-analyses, one quantitative (Spreng et al., 2010) and the other qualitative (Rajah & D'Esposito, 2005), converge to suggest that left DLPFC over-activation is generally compensatory, while right DLPFC over-activation is not. Another factor seems to be the difficulty of the task (Spreng et al., 2010); over-activation may only be compensatory at lower task demands (Reuter-Lorenz & Cappell, 2008).

Inhibition deficit theories

The inhibition deficit theory postulates that older adults are less able than young adults to prevent irrelevant information from entering working memory (Hasher & Zacks, 1988). This results in increased attention being paid to information irrelevant to the current goal, to the detriment of goal-related information. This “mental clutter” is thought to be detrimental to encoding since less attention is focused on the relevant information to be encoded (Hasher & Zacks, 1988). It is also thought to be detrimental at retrieval because of greater competition among related ideas and memories (Hasher & Zacks, 1988).

From the discussion of the interrelationship between the parietal lobe and attention during memory operations in young adults, a logical assumption would be that attention deficits in older adults arise from parietal deficits. This is largely not the case; in fact, the parietal region is probably the region of the brain where the least age-related changes are observed (Spreng et al., 2010). Dennis and Cabeza (2008) suggested that to identify the neural mechanisms of inhibition deficit, it is crucial to distinguish between the regions exerting the inhibition (in which less activity would be predicted in older adults), and the regions being inhibited (in which more activity would be predicted in older adults). They suggested the VLPFC as an example of the former, and cited a study (Jonides et al., 2000) which found decreased activity in this region in older versus young adults during an interference control working memory task. As an example of a region being inhibited, they cited a study (Gazzaley et al., 2005) showing increased activity in fusiform gyrus in older versus young adults when asked to remember scenes and increased activity in place-specific regions when asked to remember faces (i.e., increased activation in stimulus-specific regions irrelevant to the current task). However, other regions that need to be inhibited may include those in the TNN such as medial PFC, which as previously discussed, are thought to mediate internally focused attention such as autobiographical memories and daydreaming. In fact, in their original description of the inhibition deficit theory, Hasher and Zacks (1988) identify three sets of irrelevant information: irrelevant environmental details, personalistic memories or concerns, and off-goal interpretations. Thus at least some of the irrelevant information failing to be inhibited in older adults may include the autobiographical memories and daydreams mediated thought to be mediated by the TNN (Grady et al., 2006).

Neuroimaging studies have provided evidence for failure to inhibit the TNN during externally-driven cognitive tasks. Older adults typically display less deactivation of TNN during attention-demanding tasks compared to young adults (Grady et al., 2010; Koch et al., 2010; Miller et al., 2008; Park et al., 2010; Persson et al., 2006) and also exhibit reduced connectivity within this network (Andrews-Hanna et al., 2007; Damoiseaux et al., 2008; Grady et al., 2010; Sambataro et al., 2010). Importantly, both the reduced deactivation in TNN regions and reduced connectivity between them compared to young adults has been linked to age-related declines in task performance (Andrews-Hanna et al., 2007; Damoiseaux et al., 2008; Miller et al., 2008). For example, in one study (Andrews-Hanna et al., 2007), older adults displayed a dramatic reduction in connectivity between the medial PFC and posterior cingulate (young, $r = 0.43$, old, $r = 0$). The correlation between these two regions was also positively related to three composite measures of function (executive function, memory and processing speed). In another study (Grady et al., 2010), young and older subjects performed four different tasks: stimulus detection, perceptual matching, attention cueing and working memory. Across these tasks, older compared to young adults exhibited 1) reduced deactivation in TNN regions, 2) reduced connectivity between TNN regions, and 3) increased activation in regions of the TPN, including VLPFC, DLPFC and ventral PPC. The authors suggested that older adults compensated for TNN inefficiency by over-recruiting regions involved in the TPN.

This section has described theories of age-related reductions in EM, and their neural correlates. The next section discusses age-related changes specific to spatial and temporal context memory.

Age-related changes in activation in older adults during context memory retrieval

A few studies have assessed age-related changes in spatial and temporal context memory retrieval. Five such studies are considered here. In the first study of age-related changes in context memory retrieval, Cabeza and colleagues (2000) compared memory for temporal recency with item recognition. Young, but not older adults activated right anterior PFC and right posterior parietal cortex to a greater extent in the recency versus the item recognition task. In a similar study of item recognition and recency retrieval, Rajah and McIntosh (2008) found that older adults over-activated right parahippocampal, right parietal, left precuneus and right DLPFC and anterior PFC during both item recognition and recency retrieval, compared to item recognition. In older adults, activation in right PFC and left precuneus positively correlated with improved performance in the recognition task, while activation in right parahippocamapal and parietal cortex was related to poorer retrieval performance. The authors concluded that older adults compensated for MTL and parietal deficits by recruiting precuneus and PFC. In another study, Duarte and colleagues (2008) compared the retrieval of spatial and temporal context in young and older adults. They found an age-related change common to both context tasks in medial and right lateral PFC. In another study, Kukolja and colleagues (2009) report that young but not older adults show increased activation in left HC for correctly versus incorrectly remembered spatial source judgements. Finally, in the dataset used in the present thesis (Rajah et al., 2010), it was found that older adults exhibited a deficit common to spatial and temporal context retrieval in right DLPFC and medial PFC. Older adults failed to activate right DLPFC and deactivate medial PFC as much as young adults. Older adults partially compensated for these deficits by recruiting left DLPFC in the spatial context task and right anterior PFC in the temporal context task. Hence, overall, age-related changes during context memory retrieval have been observed mostly in MTL and PFC.

Goals and hypotheses

The goal of this thesis is to broaden our understanding of age-related changes in the neural correlates of context memory retrieval in two largely unexplored domains: 1) the contribution of regions exhibiting deactivations to this deficit and 2) age-related changes in connectivity during these tasks.

First, until very recently, regions exhibiting deactivations have not been the focus of studies examining the neural correlates of EM retrieval. To my knowledge, no theory of EM retrieval considers deactivations, and the vast majority of the context memory literature is focused on region-specific changes in MTL, and in TPN regions in lateral PFC, or more recently, in PPC. Similarly, studies of age-related changes in EM retrieval have tended to focus on the MTL and PFC. Based on evidence of age-related deficits in deactivating regions of the TNN in other tasks and cognitive domains, and based on the SPM results of the current dataset demonstrating an age-related failure in deactivating the medial PFC during context retrieval, I suggest that a full understanding of the neural correlates of impaired context memory in older adults also requires an examination of age-related changes in regions exhibiting decreases in activation (compared to baseline) during these tasks. Second, to my knowledge no study has assessed connectivity differences during spatial or temporal context memory retrieval in young or older adults. Furthermore, to my knowledge, no study has examined age-related changes in effective connectivity within the TNN in *any task*. This is unfortunate, given the additional information which connectivity methods can provide over traditional univariate methods of analysis (McIntosh & Gonzalez-Lima, 1994).

First, between-group mean-centered PLS will be conducted to identify whole-brain patterns of activations which distinguish between the three retrieval tasks and age groups. I hypothesize that two sets of regions can be identified: some regions, part of the TPN, like the right DLPFC which exhibit increased activity during EM retrieval, and others, part of the TNN like medial PFC, which exhibit decreased activity during EM retrieval. Regions will be selected from this analysis to construct two models, one consisting of TNN regions and the other of TPN regions. Effective connectivity within and between these networks will then be tested for differences based on task or age group.

Within-group SEM analyses will be conducted to determine whether effective connectivity changes in the three EM tasks within the TPN, within the TNN and between these networks. I hypothesize that young adults will exhibit 1) increased positive connectivity between regions of the TPN during context retrieval versus item recognition, reflecting increased reliance on strategic retrieval processes in these tasks (Mitchell & Johnson, 2009), 2) decreased connectivity between regions of the TNN during context versus item recognition, reflecting the need for greater suppression of internally generated and self-referential processes in these tasks (Fransson, 2006) and 3) increased negative connectivity between regions of the TPN and TNN, reflecting greater opposition between these two networks in harder, more effortful tasks (Hampson et al., 2010). Since the temporal context task was harder than the spatial context task, it is possible that these three connectivity patterns (greater positive connectivity within the TPN, and decreased connectivity within TNN, and between the TPN and TNN) will be expressed to an even greater extent in this task.

Next, between-group SEM analyses will be conducted to determine whether there are age-related differences in effective connectivity in the three EM tasks within the TPN, within the TNN and between these networks. I hypothesize that older adults will display significantly different effective connectivity patterns compared to young in all networks and in all tasks (rejection of the null hypothesis). Within the TPN, it is probable that older adults will display both more and less connectivity between different nodes of this network, compared to young, consistent with both the under- and over-activation observed in the literature. It is possible that older adults will display less connectivity between regions of the same hemisphere, but increased connectivity between regions of different hemisphere, which would be consistent with HAROLD (Cabeza, 2002). Within the TNN, I hypothesize that older adults will display decreased connectivity, compared to young adults, consistent with other studies (Andrews-Hanna et al., 2007; Grady et al., 2010). Finally, I also hypothesize that due to altered function of the TPN and TNN with age, older adults will display less negative connectivity between the two networks, indicating that the intrinsic opposition which exists between these two networks in young adults (M.D. Fox et al., 2005) is impaired with age (Grady et al., 2006).

Methods

Subjects

2 additional young adults and 3 additional old adults were recruited for the current study, yielding a total of 24 young (age range, 20-34, mean = 23.92) and 25 older (age range, 60-80, mean = 66.76) adults. Volunteers were right-handed and fluent in English. They were administered a battery of neuropsychological tests which included the Language and Social Background Questionnaire (Bialystok et al., 2007; Bialystok et al., 2005), the Mini-Mental Status Exam (Folstein et al., 1975),the Beck Depression Inventory (Beck, 1987; Beck et al., 1961), the Geriatric Depression Scale (Brink et al., 1982), the Cognitive Assessment Scale for the Older Adults (Geneau & Gjedde, 1996), the California Verbal Learning Task (CVLT) long-form free recall, CVLT long-form category assisted free recall and CVLT long-term recognition (Delis et al., 1988; Delis et al., 1987). Independent samples T-tests will be conducted to assess any age differences on these measures. Exclusion criteria for the elderly sample included family history of Alzheimer's disease, the diagnosis of diabetes, the presence of cataracts or glaucoma, high cholesterol levels left untreated in the past 2 years, and high or low blow pressure left untreated in the past 2 years. All participants signed a consent form, and the

study was approved by the ethics boards of the Douglas Hospital, the Montreal Neurological Institute and McGill University.

Behavioural Methods

Subjects were told that they would be participating in a memory study for non-famous, age-variant human faces. During encoding, subjects were presented with twelve face stimuli, one at a time, for 2s, either on the left or right of the computer screen. They were asked to rate each face as being pleasant (button 1) or neutral (button 2). They were also asked to intentionally encode the stimuli for an upcoming item recognition, spatial context or temporal context retrieval task. The encoding phase was identical across all tasks, but subjects were informed of which retrieval task would follow. Faces were presented in black and white, were cropped from the neck upwards and were rated as pleasant or neutral by two independent raters (Rajah et al., 2008).

After each encoding list, a one minute distraction task followed, in which subjects were asked to alphabetize a series of two simultaneously presented words. This was followed by an item recognition, spatial context or temporal context retrieval task. In all three tasks, two faces were simultaneously presented on the top and bottom of the computer screen. In the recognition task, one of these was 'old' (had been previously seen by the subject) and the other was new. Depending on the retrieval cue, the subject was asked to respond to the face that was 'old' or new. In the spatial context memory task, two 'old' faces were presented, one of which had appeared on the left side of the screen at encoding and the other on the right. Subjects were asked to respond to the face that had been presented on the left/right, depending on the retrieval cue. In the temporal context memory task, subjects were presented with two 'old' faces and, depending on the retrieval cue, asked to respond to the one that had been presented most/least recently. Hence, a two alternative forced-choice decision was made in all three retrieval tasks. Stimuli were presented in such a way that spatial information could not inform a temporal judgement and vice versa. They were also oriented vertically to avoid masking effects.

The experiment consisted of 8 runs within a single scanning session. Each run consisted of 3 encoding lists (one per task), each followed by a break and retrieval phase. Thus in total, there were 24 lists, 8 per task. This yielded a total of 96 encoding events, and 48 retrieval events for each task. Each run lasted 11 minutes and 20 seconds, and there was a brief break in between runs. Furthermore, the run order was counterbalanced across subjects.

A group (2) X task (3) mixed ANOVA will be performed to assess main effects and group by task interactions in reaction time and accuracy. Post-hoc tests will be conducted to clarify the results.

fMRI methods

Data acquisition

Structural and functional images were acquired using a 3 T Siemens Trio scanner at the Montreal Neurological Institute. T1-weighted image volumes were acquired at the start of the experiment using a 9.35 min gradient-echo (GRE) ADNI (Alzheimer's Disease Neuroimaging Initiative) sequence (TR 2300 msec, TE 2.94 msec, flip angle 30^0, 160 1 mm sagittal slices, 1 X 1 X 1.2 mm voxels, field of view – FOV = 256 mm^2). BOLD images were acquired using a fast echo-planar imaging (EPI) pulse sequence (TR = 2000 msec, TE = 30 msec, FOV = 256 mm^2, matrix size = 64 X 64, in-plane resolution = 4 X 4 mm, 340 whole brain acquisitions/11:20 min run) while subjects performed the aforementioned behavioural tasks. Each whole brain acquisition consisted of thirty-two oblique slices of 4.0 mm thickness, .0 mm slice gap, acquired along the anterior-posterior commissural plane. 20 sec of gradient RF pulses preceded each experimental run to establish steady-state tissue magnetization and minimize startle- related movement during acquisition.

Functional image processing and analysis

Images were converted to ANALYZE format and subsequently pre-processed in SPM2 software (http://www.fil.ion.ucl.ac.uk/spm/software/spm2/). Images from the first 10 sec of each run were discarded to control for field inhomogeneities. Functional images were spatially realigned to the first image, spatially normalized to the MNI EPI-template available in SPM2, and smoothed using 10mm full-width half maximum (FWHM) isotropic Gaussian kernel. The smoothed images were used in the partial least squares (PLS) analysis, performed using the PLSGUI software (http://www.rotman-baycrest.on.ca/index.php?section=84). For all my analyses, only correctly recalled retrieval events were included.

Mean-centered partial least squares

PLS is similar to independent component analysis (ICA), in that both techniques attempt to identify "components", distributed sets of voxels which represent core features in the data. However, PLS differs fundamentally from ICA, and is in fact more similar to canonical correlation, in that it does not "blindly" identify components (Huettel et al., 2009), but rather does so in relation to another set of variables. This other set of variables can be behavioural measures (e.g., accuracy, reaction time etc.), activity in a seed region of interest, or in the present case, the experimental design. The following description of PLS is based on the paper by McIntosh and colleagues (2004).

The fMRI data for both groups was stored in a between-group data matrix or "datamat". The rows of the datamat represent observations, that is, each subject's data for each condition. In the present study, there were 49 subjects (24 young and 25 older adults), and 3 tasks, for a total of 147 rows. Data for each age group were stacked one above the other, and tasks were stacked within each age group. The columns in the datamat represent the variables, that is, the signal from each voxel at each time lag. Each time lag contains data for a 2 second period, with the first time lag coinciding with event onset. The signal was zeroed at event onset, and expressed as a percentage deviation from this baseline in subsequent time lags. For this thesis, I included 8 time lags, thereby considering activation spanning 16s after event onset, to encapsulate the entire breadth of the hemodynamic response function (HRF).

The between group datamat was then subjected to singular value decomposition (SVD). SVD derives the optimal, in the least-squares sense, effects in the data, and re-expresses the datamat as three matrices: the singular image and the task saliences, which together form a latent variable (LV) and their singular values. The task saliences reflect the relationship between the singular image and the experimental design. A singular image is a graphical representation of voxel saliences, which are the weighted contribution of each voxel, at each time point, which were maximally related to the task saliences for that LV. "Brain scores" reflect the degree to which each subject expresses the pattern identified by the seed saliences. They are calculated by multiplying each voxel's salience by the BOLD signal in that voxel, and summing over all voxels for that participant. Brain scores are helpful in identifying at which time lags the brain-experimental design effect identified by the LV was most expressed.

Singular values are used to infer the statistical significance of each LV. The singular value obtained for each LV is compared to 500 other singular values obtained through permutation testing. In each permutation, sampling without replacement is used to reassign the order of conditions for each subject. ST-PLS is recalculated for each of these samples, and a new singular value is obtained each time, for every LV. If the singular value obtained from the real data for a particular LV exceeds the one obtained from 95% ($p < 0.05$) of the permutations, then it is deemed significant.

A second independent step is conducted to assess the reliability of each voxel's contribution to an LV. This is done by estimating the standard error of the voxel saliences through 100 bootstrap samples. Sampling with replacement is used to select a new sample of subjects for each of the bootstrap. ST-PLS is recalculated for each sample. From these 100 samples, it is now possible to calculate the standard error for each voxel salience. This procedure is analogous to a Z-score. For the present thesis, I considered voxels to be reliable if their bootstrap ratio was equal to or larger than 3.5 ($p < 0.0005$).

Structural Equation Modelling

Effective connectivity is a means of estimating the influence that brain regions have on each other, through a model of causal relationships between these areas (McIntosh & Gonzalez-Lima, 1994). SEM is a statistical technique used to measure these causal relations. Please note that the technique used in this thesis should more appropriately be referred to as path analysis, and not SEM, in the sense that there are no latent variables included in the model; activity in all regions is assumed to be directly measured. The term SEM is used to be consistent with the fMRI literature. SEM of fMRI data has been used towards two applications. The first is to compare two competing anatomical models to see which one explains more of the variance (has a better “fit”; Bullmore et al., 2000). The second is to describe only one anatomical model, and test whether the effective connections within this model change as a function of task or group (McIntosh & Gonzalez-Lima, 1994). The present thesis will utilize the latter application. A correlation matrix of the activity in the chosen ROIs from the ST-PLS analysis was calculated by averaging the fMRI signal between lags 2-4 and used as input for SEM. These lags were chosen because they represented the time at which both activations and deactivations were maximally expressed. LISREL software (http://www.ssicentral.com/lisrel/index.html) was used to conduct SEM. The following description of SEM is based on the article by McIntosh & Gonzalez-Lima (1994).

An anatomical model linking the regions was constructed based on primate neuroanatomy. The correlation matrix of activity between regions was then decomposed, within the context of this anatomical model, yielding a functional model of path coefficients. In the functional model, every anatomical connection is assigned such a path coefficient. A path coefficient is the expected change in the activity of one region given a unit change in the region influencing it with all other regions in the model left unchanged. For example, if the path coefficient from region A to region B is 0.3, then a unit increase in A is expected to lead to a 0.3 increase in B.

The solution in SEM is obtained through techniques of iterative estimation. The most commonly used method, and the method which will be used in this thesis is maximum likelihood estimation. This method selects values for the path coefficients that are the most likely (i.e., explain the most variance) given the correlation matrix through an iterative procedure. Importantly, this procedure allows for a pre-defined residual value or unexplained variance for each region in the model. The residual term is important, because it is unlikely that activity in any one region is entirely predicted by activity in the other region is the model. The residual term represents the combined influences of regions not included in the model, and the influence of a brain region upon itself. Unlike multiple regression, SEM incorporates the residuals into the calculation of the parameters, reinforcing the statistical power of this method. In the present thesis, the residual for each region in the model was set to 0.35, based on the estimations of McIntosh and colleagues (McIntosh et al., 1994).

The ability of a model to adequately explain the correlation matrix is assessed through the chi-square goodness of fit statistic. In cases of bad model fit, modification indices are suggested by LISREL. Modification indices are provided for all possible path coefficients which were omitted for the model, and represent the degree to which model fit would be improved by their inclusion, as assessed through a chi-square diff test with one degree of freedom. The anatomical model was modified by adding the path coefficients which would most improve model fit. The chi-square statistic is also used to determine whether there are differences in effective connectivity within a model as a function of task or age group. An omnibus test using the stacked model option in LISREL was performed to this end.

A null model in which path coefficients are set to be equal between tasks/age groups was compared to an alternate model in which path coefficients are allowed to differ. The two models are then compared by subtracting their chi-square values and degrees of freedom, yielding a chi-square diff. If the alternate model has a significantly lower chi-square value than the null model, then age group/task can be said to have a significant impact on effective connectivity within the model.

Provided a significant omnibus test (rejection of the null model), individual path coefficients were assessed for significance using a hierarchical model. A null model with all connections set to be equal was compared to an alternate model in which a path coefficient was allowed to vary, in a stepwise manner. If a path coefficient was not significantly different between conditions, it was set to be fixed as the analysis moved to the next path coefficient. On the other hand, if it was significant, it was left free to vary as the analysis moved on to the next path. Hence, this procedure allows testing of each individual path coefficient for significance. No correction for multiple comparisons was applied for individual path coefficient testing. The inferential nature of the results comes from the omnibus test; the path coefficient testing is provided for descriptive purposes only (McIntosh et al., 1996).

Since the order in which path coefficients are freed affects which ones emerge as significant, the path coefficients were freed twice, with the order of paths freed the second time being exactly opposite to that in the first. Only path coefficients which emerged as significant in both iterations are reported. However, a situation which sometimes occurred is that a path coefficient between area A and B was significant, and the path from B to A was not in the first iteration, and the opposite results (significant B-A path, non-significant A-B) path) occurred in the second iteration. In such cases, both path coefficients were freed simultaneously, and either both paths were deemed significant (given a significant chi-square diff) or both were deemed non-significant.

For the present thesis, separate omnibus tests were performed to test for task and groups difference in the TPN and TNN networks. Within-network path coefficients values were then fixed to the values obtained from these analyses and a third omnibus test was performed to test for between-network connections. The reasons for using 3 omnibus tests for the within-network connections and between-network connections, instead of using a single omnibus test for all connections at once were twofold: First, this allowed testing the hypothesis that there may be connectivity differences within only one network, and not the other. Second, had all the path coefficients been estimated at once, the number of path coefficients to be estimated would have been larger than the sample size, and the path coefficients would have been unreliable.

Two omnibus tests probing task differences were conducted, within each network: 1) spatial and temporal context versus item recognition, and 2) spatial versus temporal context. Three omnibus tests probing group differences were conducted within each network, one for each task.

Results

Neuropsychological Results

Results are shown in table 1. The independent samples T-test for CASE score was significant, $t(39) = 2.796$, $p < 0.01$. However, both group means were above the 94 score cut-off for individuals with 15+ years of education. The independent samples T-test for LFCVLT was also significant, $t(45) = 3.184$, $p < 0.005$. This is consistent with studies indicating older adults have a deficit in free recall (F. I. M. Craik & Salthouse, 2000). There were no other significant differences between the groups on neuropsychological tests.

Behavioural Results

Reaction time and accuracy results are shown in table 2. A group (2) X task (3) mixed ANOVA revealed a significant interaction $F(2,94) = 10.42$, $p < 0.001$.

Post-hoc T-tests revealed the interaction was due to there being a smaller, yet still significant difference in reaction time during the item recognition task t(47) = 3.465, $p = 0.001$, than during both the spatial, t(47) = 4.850, $p < 0.001$, and temporal ,t(41) = 4.089, $p < 0.001$, context tasks in both age groups.

A group (2) X task (3) mixed ANOVA revealed a significant interaction F(2,94) = 12,085 $p <0.001$, in accuracy scores. Post-hoc T-tests revealed the interaction was due to there being no difference in recognition accuracy between the two groups, t(47) = 0.452, $p = 0.654$, but a significant difference in spatial accuracy, t(47) = 5.187, $p = 0.001$ and temporal accuracy, t(47) = 4.118, $p < 0.001$. A post hoc linear trend analysis was run to determine if there was a linear decrease in accuracy across recognition, spatial and temporal tasks. The analysis revealed that there was a linear trend X group interaction, F(1,47) = 19.552, $p < 0.001$. The interaction was due to their being a smaller, albeit still significant linear trend in young, F(1,23) = 43.920, $p < 0.001$ than in older adults, F(1,24) = 190.269, $p < 0.001$.

Mean-centered PLS

Since the ST-PLS was run on 6 conditions (2 groups X 3 tasks), 6 LVs were identified, two of which were significant ($p<0.05$). The first LV ($p<0.001$; percent cross-block covariance accounted for = 42.35%), identified a task main effect: positive saliences reflected regions that both groups recruited to a greater extent in spatial and temporal context tasks, versus the recognition task, while negative saliences reflected the opposite effect (see figure 1d for singular image, figure 1c for design saliences and table 3 for a complete list of saliences). The temporal brain score plots (figure 1a and 1b) revealed that this effect was maximally expressed in time lags 3 and 4 (6-10 sec after event onset).

Positive saliences included many areas of the TPN and of the ventral visual stream including bilateral DLPFC, left VLPFC, premotor cortex, left parietal cortex, dorsal precuneus, right visual cortex and right fusiform gyrus. Inspection of the HRF in all these positive salience peaks indicated that these areas were all activated in all tasks and groups, with the extent of activation being larger in the context tasks versus the recognition tasks (see figure 2a and 2b for HRF of a representative region exhibiting activations). On the other hand, negative saliences included many areas of the TNN, including vental and dorsal medial PFC, anterior and posterior cingulate, bilateral lateral temporal cortex and bilateral inferior parietal cortex. Inspection of the HRF in these negative salience peaks indicated that all these areas exhibited a negative HRF, in both age groups, with the extent of deactivation being greater in the context tasks versus the recognition tasks (see figure 2c and 2d for the HRF of a representative region exhibiting a deactivation). Thus this LV primarily differentiated between areas that were activated and deactivated during the retrieval tasks; positive saliences reflected areas which activated to a greater extent in the context tasks versus the recognition tasks, while negative saliences reflected areas which were deactivated to a greater extent in the context tasks versus the recognition tasks.

The second LV ($p<0.005$; percent cross-block covariance accounted for = 25.30%) identified regions which in young adults, were more activated in the spatial versus the temporal context task, and in which in old adults, were more activated in the spatial versus both the recognition and temporal context task (see figure 3c for design saliences). Negative saliences represented this effect (see table 2 for a complete list of saliences and figure 3d for singular image). No regions exhibiting the opposite pattern (positive saliences) were observed. Negative saliences included dorsal anterior cingulate, cerebellum, right VLPFC and right HC. This affect was maximally expressed at time lags 2 and 3 (see figure 3a and 3b for temporal brain score plots).

Region selection for SEM

Regions were selected according to how reliably (high absolute value of bootstrap ratio) they were identified by the PLS analysis, and their theoretical relevance to EM retrieval in young and older adults. The precuneus (LV1) fit these criteria, but was not included because model fit decreased dramatically upon its inclusion. The HC was not very reliable, but was included nonetheless on theoretical grounds. All regions which were included in the TPN model exhibited a positive HRF during memory retrieval. All regions included in the TNN model exhibited a negative HRF during memory retrieval. Hence even though the HC is sometimes considered as part of the TNN, it was included as part of TPN on these grounds, and is henceforth referred to as a TPN region. See Gimbel & Brewer (2011) for further evidence that the HC dissociates from the rest of the TNN in EM retrieval. Regions included in the TPN were: Right BA37, right BA47, left BA9/44, right BA46/45, medial BA6/8, left BA7/40 and right HC. Regions included in the TNN were: BA 31, bilateral BA40, right BA 21, BA 24 and medial PFC (BA 9).The correlation matrix of activity in these regions is illustrated in figures 4 (young adults) and 5 (older adults). The anatomical model, based on anatomical findings (Mesulam et al., 1977; Pandya et al., 1981; Petrides & Pandya, 1984, 1999, 2009; Schmahmann & Pandya, 2006; Ungerleider et al., 1989; Webster et al., 1991) and modification indices is illustrated in figure 6.

SEM results

In the following sections, SEM results are presented, first for the TPN, then for the TNN, and finally for the connections between regions of TPN and TNN. Provided a significant omnibus model for task or age-group differences, individual path coefficients were tested for significance. In the first iteration (forward, F), path coefficients were freed in a random manner (but reciprocal paths were always estimated one after the other). In the second iteration, path coefficients were freed in the opposite order (backward, B). To ease the reading of the results section, chi-square values and significance levels of path coefficients are not reported in the text; they are instead reported in tables 7-10 in case the reader wishes to consult them. In these tables, chi-square diff values for significant path coefficients are reported for both iterations. As mentioned in the methods section, some reciprocal paths were freed simultaneously; these paths can be identified by the fact that they have DF = 2. All path coefficients for young adults are presented in table 5, and those of older adults in table 6. Chi-square values and significance levels for task and group differences in path coefficients are reported in tables 7-10.

TPN-within group results in young and older adults

In young adults, the omnibus test revealed that there were no significant task differences in connectivity, either between the context task versus the recognition tasks, $X^2_{diff}(24) = 18.44; P > 0.05$, or between the spatial and temporal context tasks, $X^2_{diff}(24) = 14.36; P > 0.05$ in TPN. Similarly, in older adults the omnibus test revealed that there were no significant task differences in connectivity, either between the context task versus the recognition tasks, $X^2_{diff}(24) = 26.23; P > 0.05$, or between the spatial and temporal context tasks, $X^2_{diff}(24) = 19.81; P > 0.05$ in the TPN.

TPN- Between group results

Because neither the young nor the older adults displayed task differences within the TPN, a single between-group comparison was made in the TPN between young and older adults (across all tasks). The omnibus results of this analysis revealed a highly significant age difference within the TPN, $X^2_{diff}(24) = 123.85; P < 0.001$. Hierarchical analyses revealed this was due to significant differences in path coefficients in the reciprocal connections between BA37 and BA46/45, between BA 47 and medial BA6/8, between BA6/8 and left BA9/44 and between right BA46/45 to left BA46/45. These differences are illustrated graphically in figure 7. Chi-square values and significance levels are reported in table 7. The reciprocal influences between BA 37 and right BA46/45 and between BA 47 and medial BA6/8 were stronger (more positive) in young adults, while the path coefficients between BA6/8 and left BA9/44 and the reciprocal influences between BA9/44 and right BA46/45 were stronger in older adults.

TNN – within group results in young adults

In young, the omnibus test revealed that there were significant connectivity differences between the context and recognition tasks $X^2_{diff}(14) = 34.54; P < 0.01$.

The hierarchical analysis revealed that this was due to there being significant differences in the reciprocal connections between bilateral BA 40, and in the reciprocal connections between BA 24 and right BA 21. These differences are illustrated graphically in figure 8 a) and b). Chi-square values and significance levels are reported in table 8 a). For all these connections, positive influence was reduced in the context tasks, compared to the recognition task. On the other hand, there were no significant differences in the TNN between the spatial and temporal context tasks, $X^2_{diff}(14) = 6.17; P > 0.05$.

TNN-within group results in older adults

In older adults, the omnibus test revealed that there were very significant connectivity differences between the context and recognition tasks, $X^2_{diff}(14) = 42.54; P < 0.001$. The hierarchical analysis revealed that this was due to there being significant differences in the reciprocal connections between bilateral BA 40, the reciprocal connections between BA 31 and BA 24, the reciprocal connections between BA 24 and BA 21 and in the connection from BA 24 and BA 9. These differences are illustrated graphically in figure 8 c) and d). Chi-square values and significance levels are reported in table 8 b). For all of these connections, the influences changed from being negative in the recognition task to being positive in the context tasks.

In older adults, the omnibus test between the spatial and temporal context tasks was also significant, $X^2_{diff}(14) = 30.42; P < 0.01$. The hierarchical analysis revealed that this was due to there being significant differences in the reciprocal connections between BA 31 and right BA 40, between BA 24 and BA 9, and between BA 9 and left BA 40. Chi-square values and significance levels are reported in table 8 c). The reciprocal influences from BA31 to right BA40 changed from being negative in the spatial task to being positive in the temporal task, the ones from BA24 to BA9 changed from positive in the spatial task to negative in the temporal task, and the ones between BA9 and left BA40 were stronger in the spatial compared to the temporal task.

TNN – between-group differences

The within-group results in young adults revealed a significant difference in the TNN between the recognition and context tasks, but no difference between the spatial and temporal context tasks. The within-group results in older adults revealed significant differences in the TNN both between the context tasks versus the recognition tasks, and between the spatial and temporal context tasks. Therefore, three between-group analyses were performed for the TNN: 1) Young recognition versus Old recognition, 2) Young context (spatial and temporal) versus old spatial, and 3) Young context versus old temporal.

The between-group comparison in TNN for the recognition task was highly significant, $X^2_{diff}(14) = 115.80$; $P < 0.001$. The reciprocal connections between BA 24 and BA 9, between BA 24 and BA 21, between bilateral BA 40, and the connection from BA 24 and BA 31 were all significantly different between age groups. These differences are illustrated in figure 9 a) and b). Chi-square values and significance levels are reported in table 9 a). For all these connections, the influences were negative in older adults, and positive in young adults.

The between-group comparison in TNN between the young context tasks and the old spatial task was not significant, $X^2_{diff}(24) = 6.69$; $P > 0.05$. However, the between-group comparison in TNN between the young context tasks and the old temporal task was significant, $X^2_{diff}(14) = 37.45$; $P < 0.001$. This was due to age differences in the reciprocal connections between BA 9 and left BA 24 and between BA 9 and left BA 40. These differences are illustrated in figure 9 c) and d). Chi-square values and significance levels are reported in table 9 b). For all these connections, the influences were stronger (more positive) in young adults.

TPN-TNN – within group results in young adults

In young adults, the omnibus test for the connections between the TPN and TNN was significant when comparing the context tasks to the recognition task, $X^2_{diff}(24) = 41.49$, $P < 0.05$. The hierarchical analysis revealed that this was due to there being a significant difference in six path coefficients: the reciprocal connection between left BA7/40 and left BA40, the connection from right BA46/45 to medial BA9, the reciprocal connections between right BA 40 and HC, and the connection from HC to right BA 21. These differences are illustrated in figure 10 a) and b). Chi-square values and significance levels are reported in table 10 a). For four of these connections, the influence changed from being positive in the recognition task to being negative in the context tasks (right BA46/45 to BA9, reciprocal connections between HC and right BA40 and left BA 40 to left BA 7/40). The influence from left BA7/40 to left BA 40 was reduced in the context versus the recognition tasks. The only connection that became stronger in the context versus the recognition task is the influence from HC to right BA 21.

The omnibus test comparing the path coefficients between the TPN and TNN was not significant, $X^2_{\mathrm{diff}}(24) = 19.54; P > 0.05$ when comparing the spatial to the temporal context task.

TPN-TNN – within group differences in older adults

The omnibus test for the connections between the TPN and TNN was significant when comparing the context tasks to the recognition task, $X^2_{\mathrm{diff}}(24) = 39.31; P < 0.05$. There were significant path coefficient differences in the connection from left BA9/44 to BA 24, from left BA7/40 to left BA 40 and in the reciprocal connections between right BA 47 and BA 21. These differences are illustrated in figure 10 c) and d). Chi-square values and significance levels are reported in table 10 b). For all these connections, there was a trend for increased positive influences in the context versus the recognition task: the influence from left BA9/44 to BA 24 became less negative, while the reciprocal influences between BA 47 and BA 21, and the influence between left BA7/40 to left BA 40 became more positive in the context tasks. The omnibus test for between-network connections in the spatial versus the temporal context task was not significant, $X^2_{\mathrm{diff}}(24) = 32.70; P > 0.05$

TPN-TNN – between-group differences

Both the within-group results in young adults and older adults revealed significant between-network connectivity differences between the context tasks versus the recognition tasks, but no differences between the spatial and temporal tasks. Thus, two between group analyses were conducted: 1) recognition young versus recognition old and 2) context young versus context old.

The between group difference in the recognition task was not significant, $X^2_{diff}(24) = 30.3; P > 0.05$. However, the between group difference in the context tasks was significant, $X^2_{diff}(14) = 67.12; P < 0.001$. There were significant differences in the connection from medial and medial BA6/8 to BA 9, in the reciprocal connections between left BA7/40 and left BA 40 and in the connection from BA7/40 to left BA 31. These differences are illustrated in figure 11. Chi-square values and significance levels are reported in table 10 c). For four of these five connections, the influences were positive in older adults, but negative in older adults. The other significant connection, the influence from left BA7/40 to left BA 40 was weaker in young adults.

Discussion

The TPN is a network of regions that increase their activity during cognitively demanding cognitive tasks (M.D. Fox et al., 2005). At retrieval, this network is thought to be important in controlled retrieval processes such as monitoring and top-down attention (Sestieri et al., 2011). The TNN is a network of regions that decrease their activity during cognitively demanding cognitive tasks (M.D. Fox et al., 2005). This network has been associated with high-confidence, and self-referential retrieval judgments, and with retrieval success (Cabeza, 2008; Cabeza et al., 2008; Kim, 2010a; Kim et al., 2010; Svoboda et al., 2006). A previous analysis of this dataset using univariate statistics had revealed two types of age-related deficits in the PFC: older adults failed to activate certain regions of TPN such as DLPFC as much as young adults, and failed to deactivate regions of

TNN such as medial PFC as much as young adults (Rajah et al., 2010), suggesting that an age-related change in both networks may account for context deficits. In the current thesis, age-related changes in effective connectivity were assessed *within* the TNN and the TPN, respectively, and *between* regions of the TPN and TNN. I hypothesized that older adults would display 1) reduced intra-hemispheric connectivity and increased inter-hemisphere connectivity in the TPN, 2) reduced connectivity throughout the TNN and 3) weaker negative connectivity (anticorrelation) between the TNN and TPN.

The behavioural results revealed that there was a linear decrease in performance across the item recognition, spatial context and temporal context tasks common to both age groups. Furthermore, older adults performed as well as young adults on item recognition, but worse on spatial and temporal context tasks, consistent with prior findings.

The between group PLS analysis identified two significant LVs. The first LV reflected a task main effect. Positive saliences reflected TPN region such as bilateral lateral PFC, left lateral parietal cortex and premotor cortex: these regions all exhibited a positive deviation in activity from baseline, and were activated to a greater extent during retrieval in the two context tasks versus the item recognition task. In contrast, negative salience reflected TNN regions, which were *deactivated* in all tasks; and were more deactivated during context retrieval versus item recognition tasks. The second LV revealed a set of regions including right HC, dorsal anterior cingulate and right VLPFC which were activated to a greater extent in the spatial compared to the temporal context task. This effect was present in both groups, but was stronger for the older adults.

A representative set of regions from the two LVs were selected to construct a TPN and TNN model. All regions included in the TPN model exhibited increased activation during EM retrieval, while all regions in the TNN model exhibited decreased activation during EM retrieval, compared to baseline. Interactions within and between these networks were tested for within-group task differences and between-group differences.

Connectivity changes in the task-positive network

All the regions included in the TPN, including HC, bilateral lateral PFC, premotor cortex, dorsal PPC and fusiform gyrus have commonly been reported in studies of EM retrieval (Spaniol et al., 2009). During EM retrieval, the HC is thought to be critical in reactivating the memory trace, in concert with TPN regions of lateral PFC and lateral PPC that are thought to mediate controlled retrieval processes such as selection of goal/relevant memory signals from posterior visual areas, monitoring/evaluation of retrieved information, and top-down attention (Cabeza, 2008; Cabeza et al., 2008; Cabeza & Nyberg, 2000; Ciaramelli et al., 2008; Diana et al., 2007; Eichenbaum et al., 2007; M. R. Johnson & Johnson, 2009; Kostopoulos & Petrides, 2008; Mitchell et al., 2004; Moscovitch, 1992; Petrides, 2005; Petrides et al., 1993; Rajah & McIntosh, 2006). The within-group SEM results revealed that there were no significant effective connectivity differences in the TPN between the three retrieval tasks, in either age group. These results indicate that a common pool of processes was recruited across the item recognition and context tasks in the TPN. Indeed, it is unlikely that context tasks recruit qualitatively different cognitive processes compared to item recognition (Mitchell & Johnson, 2009). However, the activation results from the PLS results indicate that nodes of this network were recruited to a greater extent in context tasks versus item recognition, consistent with prior studies (Mitchell & Johnson, 2009). Thus, it appears that while a common network was recruited across all retrieval tasks, indicating the recruitment of qualitatively similar processes, these processes were recruited to a greater extent in context tasks, as reflected by greater activation in these tasks.

Although no within-group differences were found in the TPN in either age group, between-group differences were identified. One of the most striking age-related differences was in the reciprocal influences between fusiform gyrus (BA37) and right lateral PFC (BA45/46): influences were large and positive in young adults, but close to null in older adults. Age-related reductions in activity in posterior visual areas have been reported across a large number of studies and are thought to reflect the age-related impairment in visual processing, and in reflective attention to perceptual features (Dennis & Cabeza, 2008; Goh et al., 2010; Mitchell et al., 2010; Spreng et al., 2010). The results of the current study demonstrate that the connectivity of posterior visual areas may also be impaired. In young adults, the strong positive interactions between lateral PFC and fusiform gyrus during EM retrieval likely reflect selection of goal-relevant memory signals (Cadoret et al., 2001; Dobbins & Wagner, 2005; Kostopoulos & Petrides, 2003, 2008) from face processing regions, a process that may be impaired in older adults.

We also observed age-related increases in connectivity between left lateral PFC (BA 9/44) and both right BA45/46 and medial premotor cortex (BA 6/8). Recruitment of left lateral PFC, and especially of left DLPFC in older adults has been associated with compensatory processes across many tasks and cognitive domains (Rajah & D'Esposito, 2005; Spreng et al., 2010); thus in the current study, the age-related increase in connectivity of this region with other TPN regions may reflect compensatory processes in older adults. Increased connectivity with contralateral PFC in older adults is particularly interesting, given the ample evidence that older adults recruit more bilateral regions of PFC compared to young adults, in which activation is more lateralized (Cabeza, 2002). Thus, taken together, these results indicate that across tasks, older adults exhibited both increases and decreases in connectivity compared to young adults, across different nodes of the TPN network; older adults may have compensated for the reduced connectivity between right lateral PFC and fusiform gyrus with increased connectivity of left lateral PFC with medial premotor cortex and contralateral PFC.

Connectivity change in TNN and between the TNN and TPN

Young adults

All regions included in the TNN model, including posterior and anterior cingulate, bilateral inferior parietal lobe, right lateral temporal cortex and medial PFC exhibited decreased activation during all three EM retrieval tasks compared to baseline, in both age groups. Additionally, TNN regions were deactivated to a greater extent in context tasks versus the item recognition task.

The SEM analysis revealed significant differences in effective connectivity within the TNN, and between the TNN and TPN networks in the context tasks versus the item recognition task. These task differences in connectivity were largely driven by task-related connectivity changes in bilateral inferior parietal lobe (BA 40). Indeed, the connectivity between left and right BA 40, from left BA 7/40 to left BA 40 and between right BA40 and HC was reduced in context tasks. The inferior parietal lobe has been involved in retrieval success, in high-confidence versus low-confidence retrieval, in self-referential retrieval and in bottom-up attention to retrieved content (Cabeza, 2008; Cabeza et al., 2008; Ciaramelli et al., 2010; Ciaramelli et al., 2008; Kim, 2010a; Sajonz et al., 2010). The task-differences in connectivity of this region may be due to any of these factors. For example, it is likely that subjects were less confident in the context judgements than their item recognition judgements (as indexed by higher reaction time and lower accuracy in context tasks), which could account for the reduced connectivity of this region. Alternatively, it is possible that subjects used less of a self-referential strategy (e.g., remembering whether they judged the faces as pleasant or not at encoding) in context tasks. Consistent with this hypothesis, in context versus item recognition, there was also a greater negative influence of right BA 45/46 on medial PFC (BA 9), one of the region most consistently associated with self-referential processing (Gusnard et al., 2001; Sajonz et al., 2010), and in the retrieval of self-generated information (Dobbins & Wagner, 2005; Simons, Gilbert, et al., 2005; Simons, Owen, et al., 2005).

Age-related changes in TNN connectivity

During item recognition, there were marked between-group differences in connectivity within widespread regions of TNN: the reciprocal influences from medial PFC to anterior cingulate, between anterior cingulate and right middle temporal cortex, between bilateral inferior parietal lobes and from anterior cingulate to posterior cingulate were all weakly negative in older adults, but strongly positive in young adults. These results are consistent with other studies that have also found age-related reductions in connectivity in TNN in aging

(Andrews-Hanna et al., 2007; Grady et al., 2010; Sambataro et al., 2010). Reduced connectivity in TNN in aging is thought to reflect greater difficulty in older adults to down-regulate task- irrelevant processes, and the tendency of older adults to be more distracted (Grady et al., 2010; Grady et al., 2006). However, in the current study, this dramatic age-related change in connectivity did not negatively impact task performance: older adults performed extremely well (accuracy = 94%) in item recognition, as well as young adults.

The within-group results in older adults indicated that all the negative path coefficients in the item recognition task changed to being positive in the context tasks. Furthermore, between-group results reveal that the number of significant path coefficients between age groups was reduced in the temporal context tasks, and completely eliminated in the spatial context task. Thus, these results indicate that between-group connectivity in the TNN was more similar in the context tasks, which older adults performed less well than young, than in the item recognition task, in which both groups performed equally well. These results raise the possibility that reduced connectivity in TNN in older adults is actually beneficial, and essential for optimal task performance. Unfortunately, this possibility cannot be tested in the current thesis, due to an inability to test for connectivity-performance relationships with the methods used. Additionally, it is possible that the increased positive connectivity in TNN in older adults in context tasks may have been compensatory, reflecting a greater reliance on subjective recollection processes (see next section) in these tasks.

Age-related changes in TNN-TPN connectivity

Within-group results revealed significant differences in the connectivity between regions of TPN and TNN in context tasks, versus item recognition; older adults exhibited stronger (more positive) connectivity between right BA 21 and BA 47, and from left BA 7/40 to BA 40. Furthermore, between-group results revealed significant differences in TPN-TNN connectivity in context tasks: older adults had greater connectivity from BA 7/40 to both BA40 and BA 31 and from BA 6/8 to medial BA 9. The greater positive connectivity from TPN to TNN regions, and especially of BA7 with both BA 40 and BA 31 in older adults may indicate greater top-down attention to cognitive processes mediated by these regions (Cabeza, 2008), such as spontaneous thoughts and self-referential processing (Mason et al., 2007; Sajonz et al., 2010). Indeed, other studies have reported that older adults rely more on their thoughts and feelings during memory tasks compared to young adults, to the detriment of specific perceptual or contextual details (Hashtroudi et al., 1990; Kensinger, 2009). Because the encoding task was self-referential in nature, older adults may have primarily encoded these affective details, and used them to make their retrieval decision. Furthermore, it is possible that older adults depend on these affective thoughts and feelings to a greater extent as a task becomes harder, that is in context tasks versus the item recognition task, as a compensatory mechanism.

Limitations

This study has several limitations. First, with the methods used in the current thesis, it was impossible to assess the relationship between connectivity between two areas and performance. A selection of regions for the SEM based on a relation to performance (Grady et al., 2003), or the use of a method yielding correlation strength for individual subjects (Andrews-Hanna et al., 2007) would have been possible alternatives.

Another set of limitations results from the use of SEM; first, this method assumes that interactions between brain regions are linear, and instantaneous (Friston et al., 2003), two assumptions which are likely false. Other effective connective connectivity methods such as granger causality (Goebel et al., 2003) and dynamic causal modeling (Friston et al., 2003) would have been possible alternatives.

Finally, it is unclear the degree to which age-related differences in connectivity observed in this study are due to structural brain changes in gray and white matter, and also in vascular changes, instead of actual age-related changes in functional connectivity (Grady et al., 2003).

Conclusion

The goal of this thesis was to assess age-related changes in effective connectivity during item recognition, spatial context and temporal context tasks within and between the TPN and TNN, using SEM. In both groups, task differences in connectivity were only observed within TNN, and between regions of TPN and TNN, but not within TPN. Age differences, however, were apparent both within and between both the TPN and TNN. Within TPN, older adults displayed less connectivity between right lateral PFC and posterior visual areas, which may reflect less efficient selection of goal-relevant information from posterior visual areas. However, older adults exhibited greater connectivity of left lateral PFC with both right lateral PFC and medial premotor cortex, perhaps reflecting compensatory processes. Additionally, young adults exhibited decreased connectivity within the TNN and more negative connectivity between the TNN and TPN in context versus item recognition, while older adults displayed the opposite pattern; increases in positive connectivity within TNN and between TNN-TPN n context tasks. Finally, older adults exhibited markedly reduced connectivity in TNN in the item recognition task, compared to young adults; however this difference was attenuated in the temporal context task, and eliminated in the spatial context task. Thus while young adults respond to increasing retrieval load by down-regulating subjective recollection processes in the TNN, older adults may rely on them to a greater extent as retrieval demands increase.

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Table 1 - Group means for education and Neuropsychological Measures

Group		EDU	MMSE	BECK	GDS	CASE	LFCVLT	LCRCVLT	RGCVLT
Young adults	Mean	16.21	28.29	2.67	1.00	98.79*	13.64*	13.09	15.27
	S.E.	0.26	1.24	0.83	0.31	0.32	0.46	0.54	0.26
Older adults	Mean	15.16	29.48	4.60	1.24	97.45*	10.96*	11.61	15.00
	S.E.	0.48	0.17	0.88	0.323	0.35	0.67	0.71	0.30

Note: This table presents the group means and standard errors (S.E.) for education (EDU) in years, and other psychological measures taken. LSBQ = Language and social background questionnaire, LFCVLT = CVLT, long-form free recall; LCRCVLT = CVLT, long-form. Significant group differences ($p < 0.05$) are highlighted with asterisks.

Table 2: Mean Accuracy and Reaction Time Data with Standard error

		Recognition	**Spatial Context**	**Temporal Context**
Young Adults	Accuracy	0.94 (0.10)	0.90 (0.13)	0.81 (0.21)
	Reaction Time	1828 (67)	2246 (85)	2583 (79)
Older Adults	Accuracy	0.94 (0.01)	0.79 (0.18)	0.69 (0.21)
	Reaction Time	2200 (83)	3062 (143)	3319 (159)

Note: Accuracy values shown are the proportion correct per task type with SE. Reaction time values are shown in milliseconds per task type with SE.

Table 3: Local maxima for LV1 of the ST-bPLS analysis

Lag	BSR	Cluster size	X	Y	Z	Hem	Brodmann area (BA)
In both groups, regions activated to a greater degree in context vs recognition							
3	**9.18**	**2493**	**-4**	**10**	**51**	**Left**	**BA 6/8**
3	**8.44**		**-40**	**-40**	**46**	**Left**	**BA 40***
3	7.25	173	44	-48	-25	Right	Cerebellum
3	6.68	157	24	-97	1	Right	BA 17/18
3	6.32	257	-16	-97	-2	Left	Cerebellum
3	5.98	45	-28	23	-8	Left	BA 47
3	5.41	28	40	-72	33	Right	BA 19/39
3	4.30	21	51	32	17	Right	BA 45
4	**13.65**	**1387**	**44**	**-55**	**-17**	**Right**	**BA 37**
4	9.16	1560	0	-63	51	Left	BA 7
4	7.82	316	0	14	51	Left	BA 6/8
4	**7.52**	**232**	**-55**	**21**	**28**	**Left**	**BA 9/44**
4	**5.80**	**148**	**51**	**28**	**21**	**Right**	**BA 46/45**
4	4.78	25	32	3	59	Right	BA 6
4	4.48	14	-44	0	7	Left	BA 6
In both groups, regions deactivated to a greater degree in context vs recognition							
3	**-5.75**	**142**	**67**	**-42**	**24**	**Right**	**BA 40**
3	**-5.68**	**225**	**-20**	**56**	**30**	**Left**	**BA 9**
3	**-5.36**	**28**	**-4**	**27**	**-8**	**Left**	**BA 24/32**
3	**-5.28**	**23**	**48**	**6**	**-34**	**Right**	**BA 21**
3	-5.11	32	8	-74	4	Right	BA 18
3	-4.88	19	16	60	34	Right	BA 9
3	**-4.84**	**24**	**-63**	**-45**	**35**	**Left**	**BA 40**
4	-8.48	683	16	-92	30	Right	BA 19
4	-5.54	173	-4	51	1	Left	BA 10
4	-5.21	100	71	-46	6	Right	BA 21
4	-4.78	31	-59	-45	32	Left	BA 40
4	-4.48	72	32	-54	6	Right	BA 30
4	-4.45	63	-16	-10	30	Left	Caudate Nucleus
4	**-4.16**	**19**	**-24**	**-37**	**31**	**Left**	**BA 31**
4	-4.01	13	-40	-47	-1	Left	BA 21

Note: Temporal Lag represents the time interval (2 sec each) after event-onset, when a cluster of voxels exhibited a peak bootstrap ratio reflecting the identified effect. The bootstrap ratio threshold (BSR) was set to +/- 3.5 ($p < 0.0005$) for all areas. The spatial extent refers to the total number of voxels included in the voxel cluster (threshold =/>10). HEM refers to the cerebral hemisphere in which the activation occurred. The stereotaxic coordinates are reported in Talairach coordinates,in mm, and the Brodmann Areas (BA) were determined by reference to Talairach & Tournoux (1988). Regions in bold were chosen for the structural equation modelling analysis.

* This is the strongest sub-peak from the 2493 cluster size activation identified in BA6/8.

Table 4: Local maxima for LV2 of the mean-centered PLS analysis

Lag	BSR	Cluster size	X	Y	Z	Hem	Brodmann area (BA)
In both groups, regions activated more in the spatial task than in the recognition and temporal tasks							
2	-6.16	169	-40	-52	-21	Left	Cerebellum
2	-5.48	147	-40	-21	49	Left	BA 3
2	-5.44	96	-55	-15	19	Left	BA 43
2	-5.22	24	40	-1	59	Right	BA 6
2	-5.05	338	44	-48	-28	Right	Cerebellum
2	-4.78	180	4	21	32	Right	BA 32
2	-4.76	29	36	-89	-2	Right	BA 18
2	-4.47	31	0	-58	3	Left	Cerebellum
2	-4.38	34	-51	6	33	Left	BA 6
2	**-4.30**	**58**	**51**	**16**	**-1**	**Right**	**BA 47**
2	-4.13	20	36	55	16	Right	BA 10
2	**-3.95**	**3**	**28**	**-9**	**-23**	**Right**	**Hippocampus***
3	-5.39	58	-24	-36	-25	Left	Cerebellum
3	-5.28	36	24	-33	-29	Right	Cerebellum
3	-4.03	21	-8	-70	-3	Left	BA 18
3	-4.02	10	44	-78	1	Right	BA 19
3	-3.96	14	-24	-8	-10	Left	Amygdala
3	-3.94	15	40	-71	-13	Right	BA 19

Note: Temporal Lag represents the time interval (2 sec each) after event-onset, when a cluster of voxels exhibited a peak bootstrap ratio reflecting the identified effect. The bootstrap ratio threshold (BSR) was set to +/- 3.5 ($p < 0.0005$) for all areas. The spatial extent refers to the total number of voxels included in the voxel cluster (threshold =/>10). HEM refers to the cerebral hemisphere in which the activation occurred. The stereotaxic coordinates are reported in Talairach coordinates,in mm, and the Brodmann Areas (BA) were determined by reference to Talairach & Tournoux (1988). Regions in bold were chosen for the structural equation modelling analysis.
* At a bootstrap threshold of 3.5, this region had a cluster size of 3, however at a bootstrap threshold of 3, this regions had a cluster size of 18.

Table 5: Path coefficients in young adults

Young Recognition task													
	R37	R47	R46/45	L44/9	M6/8	L7/40	HC	M31	L40	R40	R21	M24	M9
R37		0.23	0.50				0.14				-.19		
R47	-.17		0.01		0.63		-.04				-.12		
R46/45	0.23	0.07		0.13	0.34		-.26					0.21	-.02
L46/45			-0.10		0.05	0.44						0.08	0.18
M6/8		0.31	-0.13	0.06		0.40							0.03
L7/40				0.17	0.38			0.09	0.08				
R-HC	0.25	0.15	-0.30					-0.01		0.22	0.44		
M31						-0.09	0.09		0.65	-.30		0.14	
L40						0.21		0.07		0.47			0.06
R40							0.12	-0.03	0.57				
R21	-.25	0.24					0.08					0.50	
M24			-0.09	-0.10				-0.07			0.13		0.33
M9			0.06	0.10	-0.20				0.36			0.39	

Young context task													
	R37	R47	R46/45	L44/9	M6/8	L7/40	HC	M31	L40	R40	R21	M24	M9
R37		0.23	0.50				0.14				0.01		
R47	-.17		0.01		0.63		-.04				0.11		
R46/45	0.23	0.07		0.13	0.34		-.26					0.02	-.11
L46/45			-0.10		0.05	0.44						0.12	0.06
M6/8		0.31	-0.13	0.06		0.40							-.07
L7/40				0.17	0.38			-0.04	-.15				
R-HC	0.25	0.15	-0.30					-0.19		-.08	0.35		
M31						-0.10	0.09		0.28	0.04		0.11	
L40						0.03		0.18		0.11			0.27
R40							-.10	0.05	0.20				
R21	-.20	0.05					0.45					0.06	
M24			-0.03	-0.08				0.13			-.06		0.29
M9			-0.14	0	-0.29				0.29			0.20	

Note: These tables present path coefficients in young adults for the item recognition and context tasks. Looking at the table horizontally indicates a region's input, while looking vertically indicates a region's output. Since connectivity did not differ between the spatial and temporal context tasks, the path coefficients for these two tasks is represented in a single table.

Table 6: Path coefficients in young adults

Older adults, Recognition task

	R37	R47	R46/45	L44/9	M6/8	L7/40	HC	M31	L40	R40	R21	M24	M9
R37		0.10	-0.01				0.24				-.06		
R47	0.10		0.24		0.07		0.04				-.11		
R46/45	-.01	0.13		0.33	0.10		-.15					-0.04	-.01
L46/45			0.14		0.30	0.18						0	0.06
M6/8		0.01	0.14	0.36		0.14							0.04
L7/40				0.33	0.20			0.21	0.06				
R-HC	0.23	0.03	-0.18					0.04		0.07	0.14		
M31						0.28	0.34		0.13	0.24		-0.34	
L40						-0.05		-0.07		-.14			0.03
R40							0.07	0.07	-.13				
R21	0.05	-.06					0.20					-0.18	
M24			-0.11	-0.45				-0.05			-.13		-.13
M9			-0.26	0.23	0.10				0.09			-0.21	

Older adults, Spatial task

	R37	R47	R46/45	L44/9	M6/8	L7/40	HC	M31	L40	R40	R21	M24	M9
R37		0.10	-0.01				0.24				-.03		
R47	0.10		0.24		0.07		0.04				0.18		
R46/45	-.01	0.13		0.33	0.10		-.15					-0.07	0.03
L46/45			0.14		0.30	0.18						0.04	0.03
M6/8		0.01	0.14	0.36		0.14							0.04
L7/40				0.33	0.20			0.09	0.08				
R-HC	0.23	0.03	-0.18					-0.08		0.11	0.30		
M31						0.34	0.16		0.23	-.07		0.20	
L40						0.33		-0.04		0.11			0.31
R40							-.18	-0.09	0.16				
R21	-.18	0.19					0.42					0.09	
M24			-0.14	-0.01				0.03			0.08		0.19
M9			0	-0.09	0.20				0.32			0.25	

Older adults, Temporal task

	R37	R47	R46/45	L44/9	M6/8	L7/40	HC	M31	L40	R40	R21	M24	M9
R37		0.10	-0.01				0.24				-.03		
R47	0.10		0.24		0.07		0.04				0.18		
R46/45	-.01	0.13		0.33	0.10		-.15					-0.07	0.03
L46/45			0.14		0.30	0.18						0.04	0.03
M6/8		0.01	0.14	0.36		0.14							0.04
L7/40				0.33	0.20			0.09	0.08				
R-HC	0.23	0.03	-0.18					-0.08		0.11	0.30		
M31						0.34	0.16		0.07	0.23		0.07	
L40						0.33		0.13		0.14			-.05
R40							-.18	0.22	0.12				
R21	-.18	0.19					0.42					0.11	
M24			-0.14	-0.01				0.20			0.14		-.21
M9			0	-0.09	0.20				0.06			-0.10	

Note: These tables present path coefficients in older adults for the item recognition and context tasks. Looking at the table horizontally indicates a region’s input, while looking vertically indicates a region’s output.

Table 7: Between-group differences in path coefficients in the TPN

From	To	DF	Chi-square diff	Significance
R46/45	R 37	1	F: $X^2_{diff}(1) = 39.5$ B: $X^2_{diff}(1) = 23.36$	$P < 0.001$ $P < 0.001$
R 37	R46/45	1	F: $X^2_{diff}(1) = 4.09$ B: $X^2_{diff}(1) = 18.07$	$P < 0.05$ $P < 0.001$
R 47	M6/8	1	F: $X^2_{diff}(1) = 23.5$ B: $X^2_{diff}(1) = 20.71$	$P < 0.001$ $P < 0.001$
M 6/8	R 47	1	F: $X^2_{diff}(1) = 9.16$ B: $X^2_{diff}(1) = 7.52$	$P < 0.01$ $P < 0.01$
M6/8 L9/44	L9/44 M6/8	2	F: $X^2_{diff}(2) = 7.26$ B: $X^2_{diff}(2) = 18.46$	$P < 0.05$ $P < 0.001$
L9/44 R46/45	R46/45 L9/44	2	F: $X^2_{diff}(2) = 12.76$ B: $X^2_{diff}(2) = 8.59$	$P < 0.01$ $P < 0.05$

Note: This table indicates the chi square diff values and significance levels for path coefficients that are significantly different in the TPN between young and older adults. Brain regions are identified by their Brodmann area. A degree of freedom (DF) of 1 indicates that a path was freed individually. A DF of 2 indicates that the two paths were freed simultaneously (see text for details). R = Right, L = Left, M = Medial, F= Forward, B= Backward.

Table 8: Within-group differences in path coefficients in the TNN

A) Young adults, context versus recognition

From	To	DF	Chi-square diff	Significance
L40	R40	2	F: $X^2_{diff}(2) = 13.96$	$P < 0.001$
R40	L40		B: $X^2_{diff}(2) = 12.28$	$P < 0.01$
M24	R21	2	F: $X^2_{diff}(2) = 12.28$	$P < 0.01$
R21	M24		B: $X^2_{diff}(2) = 12.29$	$P < 0.01$

B) Older adults, context versus recognition

From	To	DF	Chi-square diff	Significance
L40	R40	2	F: $X^2_{diff}(2) = 10.21$	$P < 0.01$
R40	L40		B: $X^2_{diff}(2) = 10.21$	$P < 0.01$
M24	M31	1	F: $X^2_{diff}(1) = 11.35$	$P < 0.001$
			B: $X^2_{diff}(1) = 7.31$	$P < 0.01$
M31	M24	1	F: $X^2_{diff}(1) = 3.85$	$P < 0.05$
			B: $X^2_{diff}(1) = 5.06$,	$P < 0.05$
M24	R21	2	F: $X^2_{diff}(2) = 8.3$	$P < 0.05$
R21	M24		B: $X^2_{diff}(2) = 9.22$	$P < 0.01$
M24	M9	1	F: $X^2_{diff}(1) = 5.21$	$P < 0.05$
			B: $X^2_{diff}(1) = 5.29$	$P < 0.05$

C) Older adults, spatial versus temporal context

From	To	DF	Chi-square diff	Significance
M31	R40	2	F: $X^2_{diff}(2) = 8.36$	$P < 0.05$
R40	M31		B: $X^2_{diff}(2) = 8.41$	$P < 0.05$
M24	M9	2	F: $X^2_{diff}(2) = 12.31$	$P < 0.01$
			B: $X^2_{diff}(2) = 11.8$	$P < 0.01$
M9	L40	2	F: $X^2_{diff}(2) = 7.86$	$P < 0.05$
L40	M9		B: $X^2_{diff}(2) = 8.32$	$P < 0.05$

Note: These tables indicate chi square diff values and significance levels for path coefficients in the TNN for which within-group differences in young and older adults were identified. Brain regions are identified by their Brodmann area. A degree of freedom (DF) of 1 indicates that a path was freed individually. A DF of 2 indicates that the two paths were freed simultaneously (see text for details). R = Right, L = Left, M = Medial, F= Forward, B= Backward.

Table 9: Between-group differences in path coefficients in the TNN

A) Between-group differences in TNN the recognition task

From	To	DF	Chi-square diff	Significance
M9	M24	1	F: $X^{2}_{diff}(1) = 14.21$ B: $X^{2}_{diff}(1) = 8.71$	$P < 0.001$ $P < 0.01$
M24	M9	1	F: $X^{2}_{diff}(1) = 11.6$ B: $X^{2}_{diff}(1) = 23.75$	$P < 0.001$ $P < 0.001$
M24	R21	1	F: $X^{2}_{diff}(1) = 20.91$ B: $X^{2}_{diff}(1) = 10.72$	$P < 0.001$ $P < 0.01$
R21	M24	1	F: $X^{2}_{diff}(1) = 8$ B: $X^{2}_{diff}(1) = 11.24$	$P < 0.01$ $P < 0.001$
R40	L40	1	F: $X^{2}_{diff}(1) = 29.95$ B: $X^{2}_{diff}(1) = 12$	$P < 0.001$ $P < 0.001$
L40	R40	1	F: $X^{2}_{diff}(1) = 12.57$ B: $X^{2}_{diff}(1) = 30.94$,	$P < 0.001$ $P < 0.001$
M24	M31	1	F: $X^{2}_{diff}(1) = 6.54$ B: $X^{2}_{diff}(1) = 6.71$	$P < 0.05$ $P < 0.05$

B) Between-group differences in TNN in the temporal context task

From	To	DF	Chi-square diff	Significance
M9	M24	1	F: $X^{2}_{diff}(1) = 15.2$ B: $X^{2}_{diff}(1) = 7.93$	$P < 0.001$ $P < 0.01$
M24	M9	1	F: $X^{2}_{diff}(1) = 5.45$ B: $X^{2}_{diff}(1) = 10.73$	$P < 0.05$ $P < 0.01$
M9	L40	2	F: $X^{2}_{diff}(2) = 10.09$ B: $X^{2}_{diff}(2) = 12.08$	$P < 0.01$ $P < 0.001$

Note: These tables indicate chi square diff values and significance levels for path coefficients in the TNN for which between-group differences were identified. Brain regions are identified by their Brodmann area. A degree of freedom (DF) of 1 indicates that a path was freed individually. A DF of 2 indicates that the two paths were freed simultaneously (see text for details). R = Right, L = Left, M = Medial, F= Forward, B= Backward.

Table 10: Within- and between-group differences in path coefficients between regions of the TPN and TNN

A) Within-group differences in young adults in the recognition vs context tasks				
From	To	DF	Chi-square diff	Significance
L7/40	L40	2	F: $X^2_{diff}(2) = 8.61$ B: $X^2_{diff}(2) = 8.86$	$P < 0.05$ $P < 0.05$
R46/45	M9	1	F: $X^2_{diff}(1) = 6.26$ B: $X^2_{diff}(1) = 5.99$	$P < 0.05$ $P < 0.05$
R40	HC	2	F: $X^2_{diff}(2) = 10.89$ B: $X^2_{diff}(2) = 11.05$	$P < 0.01$ $P < 0.01$
HC	R21	1	F: $X^2_{diff}(1) = 5.03$ B: $X^2_{diff}(1) = 4.89$	$P < 0.05$ $P < 0.05$

B) Within-group differences in older adults in the recognition vs context tasks				
From	To	DF	Chi-square diff	Significance
L9/44	M24	1	F: $X^2_{diff}(1) = 8.88$ B: $X^2_{diff}(1) = 8.92$	$P < 0.01$ $P < 0.01$
L7/40	L40	1	F: $X^2_{diff}(1) = 6.53$ B: $X^2_{diff}(1) = 6.49$	$P < 0.05$ $P < 0.05$
R47	R21	2	F: $X^2_{diff}(2) = 8.69$ B: $X^2_{diff}(2) = 8.69$	$P < 0.05$ $P < 0.05$

C) Between-group differences in the context tasks				
From	To	DF	Chi-square diff	Significance
M6/8	M9	1	F: $X^2_{diff}(1) = 19.4$ B: $X^2_{diff}(1) = 18.43$	$P < 0.001$ $P < 0.001$
L40	L7/40	1	F: $X^2_{diff}(1) = 11.93$ B: $X^2_{diff}(1) = 6.41$	$P < 0.001$ $P < 0.05$
L7/40	L40	1	F: $X^2_{diff}(1) = 4.67$ B: $X^2_{diff}(1) = 12.79$	$P < 0.05$ $P < 0.001$
L7/40	M31	1	F: $X^2_{diff}(1) = 17.65$ B: $X^2_{diff}(1) = 16.02$	$P < 0.001$ $P < 0.001$

Note: These tables indicate chi square diff values and significance levels for path coefficients between regions of TPN and TNN for which within-group and between-group differences were identified. Brain regions are identified by their Brodmann area. A degree of freedom (DF) of 1 indicates that a path was freed individually. A DF of 2 indicates that the two paths were freed simultaneously (see text for details). R = Right, L = Left, M = Medial, F= Forward, B= Backward.

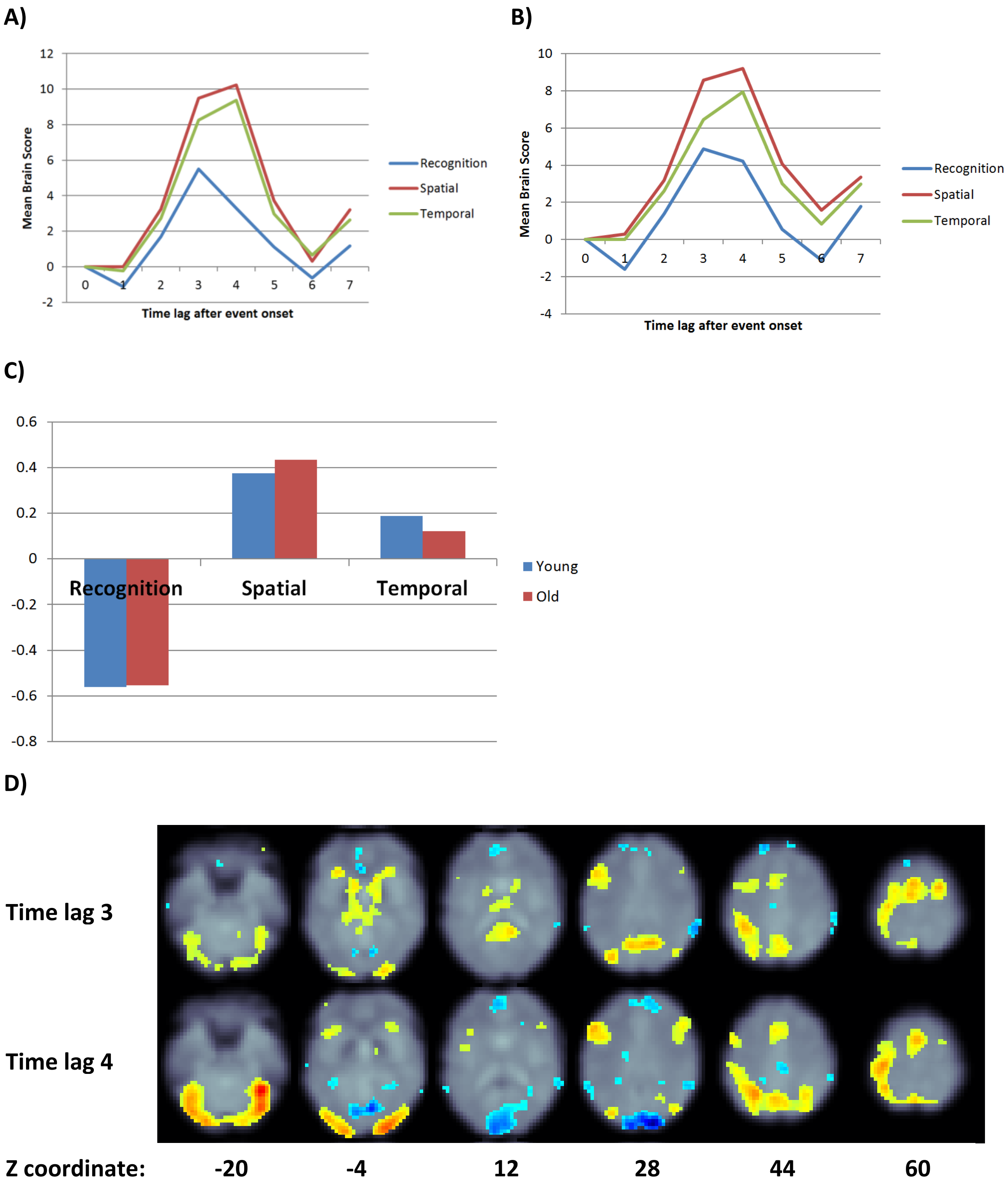


Figure 1) Latent Variable 1. A) Graph of the temporal brain scores in young and B) in older adults, showing that the effect was maximally represented at time lags 3-4. C) Design scores for each task. Blue bars = young adults, red bars = older adults. D) Singular image. Yellow/red voxels were positively related to the experimental effect found in C). Blue voxels were negatively related to the experimental effect found in C)

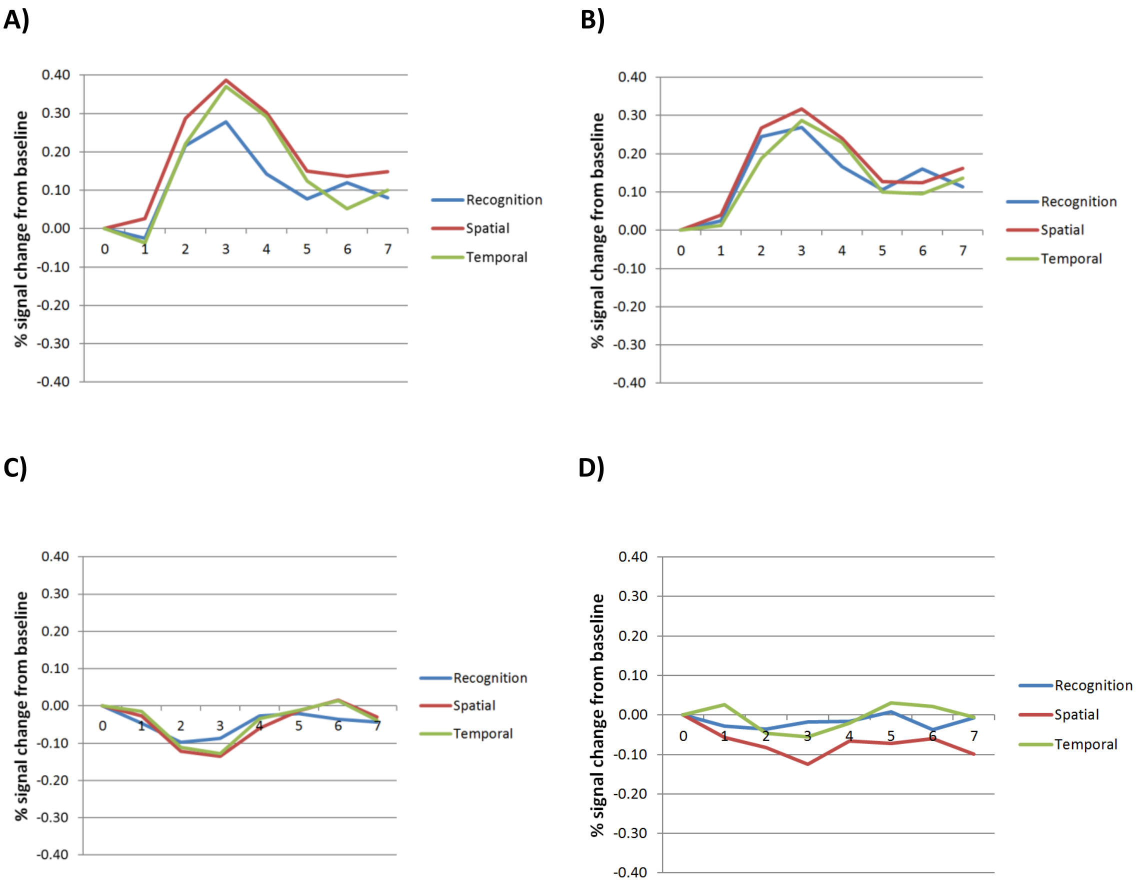


Figure 2) Hemodynamic response function (HRF) of representative regions in the TPN and TNN. A) HRF for the right Brodmann area 46/45 in young adults. B) HRF for the same region in older adults. C) HRF for Brodmann area 24 in young adults. C) HRF for the same region in older adults.

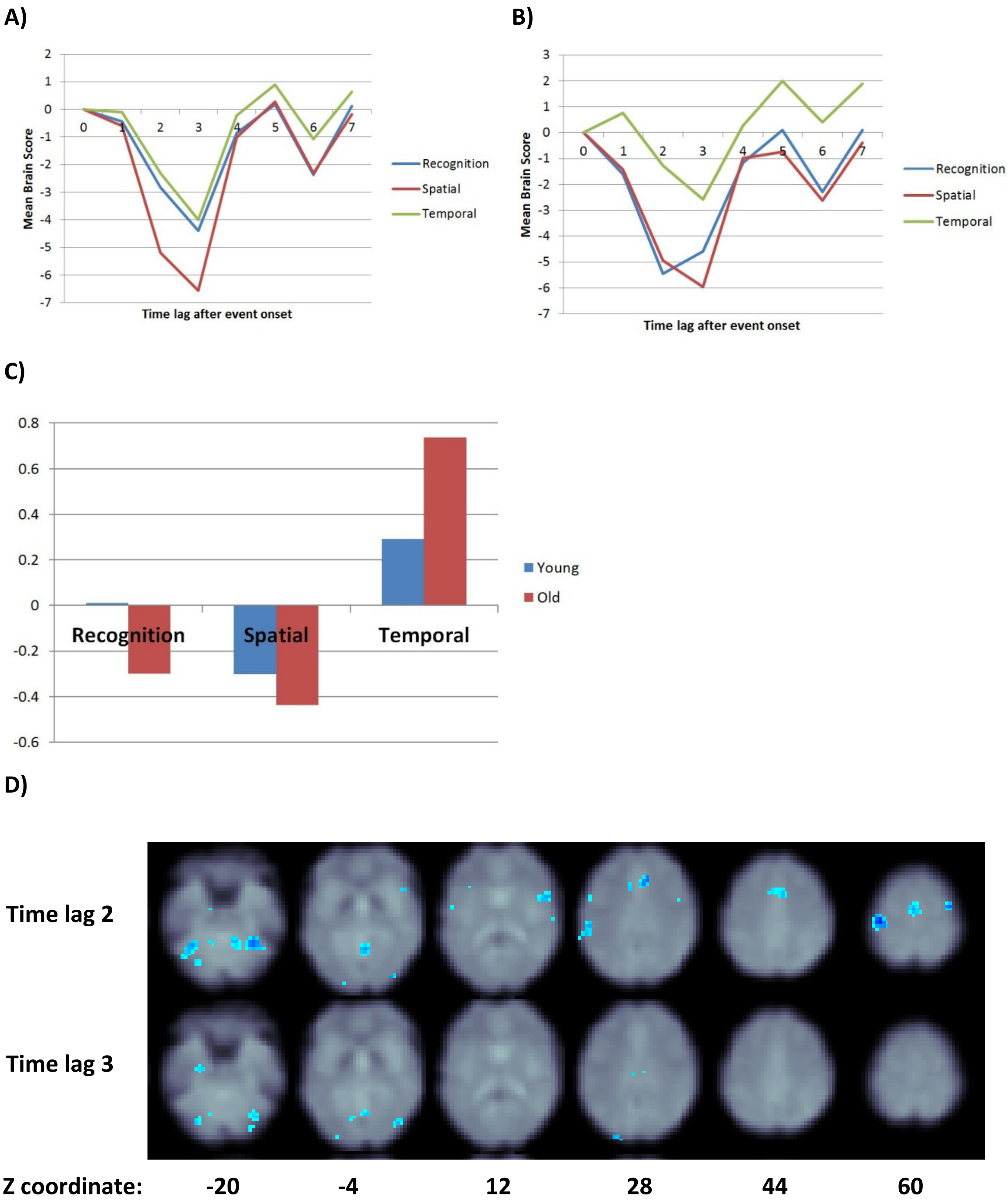
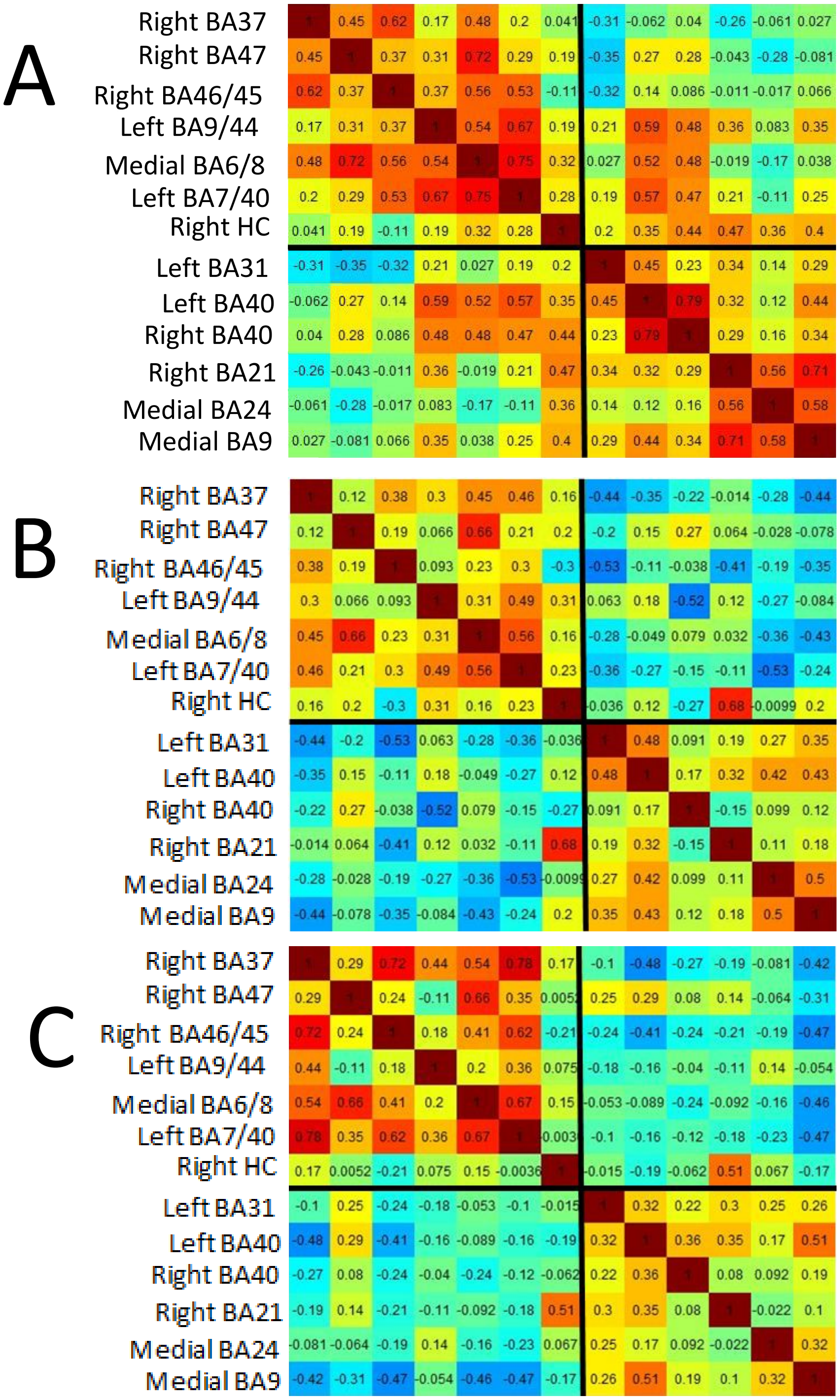


Figure 3) Latent Variable 2. A) Graph of the temporal brain scores in young and B) in older adults, showing that the effect was maximally represented at time lags 2-3. C) Design scores for each task. Blue bars = young adults, red bars = older adults. D) Singular image. Blue voxels were negatively related to the experimental effect found in C)



A

Right BA37	1	0.45	0.62	0.17	0.48	0.2	0.041	-0.31	-0.062	0.04	-0.26	-0.061	0.027
Right BA47	0.45	1	0.37	0.31	0.72	0.29	0.19	-0.35	0.27	0.28	-0.043	-0.28	-0.081
Right BA46/45	0.62	0.37	1	0.37	0.56	0.53	-0.11	-0.32	0.14	0.086	-0.011	-0.017	0.066
Left BA9/44	0.17	0.31	0.37	1	0.54	0.67	0.19	0.21	0.59	0.48	0.36	0.083	0.35
Medial BA6/8	0.48	0.72	0.56	0.54	1	0.75	0.32	0.027	0.52	0.48	-0.019	-0.17	0.038
Left BA7/40	0.2	0.29	0.53	0.67	0.75	1	0.28	0.19	0.57	0.47	0.21	-0.11	0.25
Right HC	0.041	0.19	-0.11	0.19	0.32	0.28	1	0.2	0.35	0.44	0.47	0.36	0.4
Left BA31	-0.31	-0.35	-0.32	0.21	0.027	0.19	0.2	1	0.45	0.23	0.34	0.14	0.29
Left BA40	-0.062	0.27	0.14	0.59	0.52	0.57	0.35	0.45	1	0.79	0.32	0.12	0.44
Right BA40	0.04	0.28	0.086	0.48	0.48	0.47	0.44	0.23	0.79	1	0.29	0.16	0.34
Right BA21	-0.26	-0.043	-0.011	0.36	-0.019	0.21	0.47	0.34	0.32	0.29	1	0.56	0.71
Medial BA24	-0.061	-0.28	-0.017	0.083	-0.17	-0.11	0.36	0.14	0.12	0.16	0.56	1	0.58
Medial BA9	0.027	-0.081	0.066	0.35	0.038	0.25	0.4	0.29	0.44	0.34	0.71	0.58	1

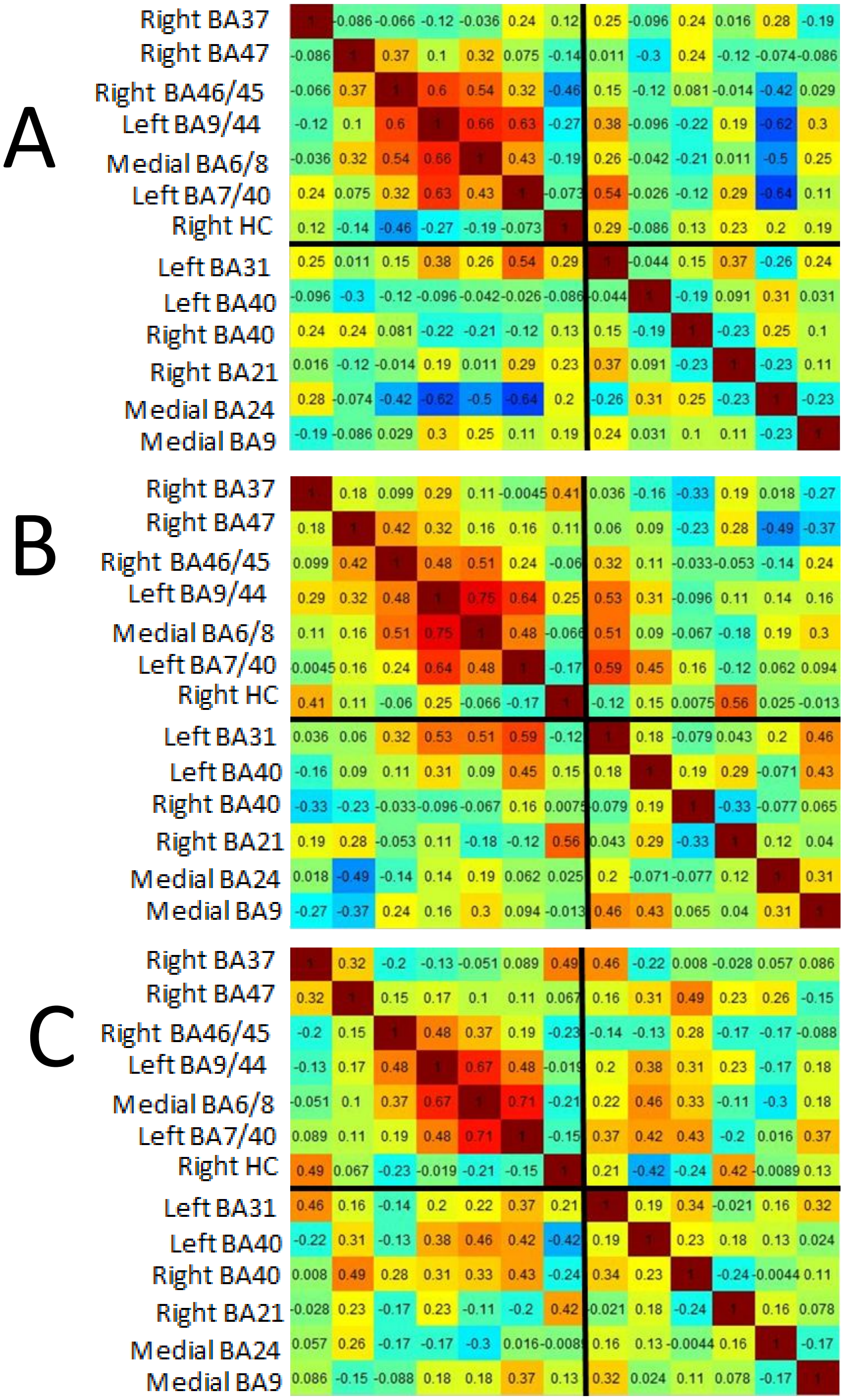
B

Right BA37	1	0.12	0.38	0.3	0.45	0.46	0.16	-0.44	-0.35	-0.22	-0.014	-0.28	-0.44
Right BA47	0.12	1	0.19	0.066	0.66	0.21	0.2	-0.2	0.15	0.27	0.064	-0.028	-0.078
Right BA46/45	0.38	0.19	1	0.093	0.23	0.3	-0.3	-0.53	-0.11	-0.038	-0.41	-0.19	-0.35
Left BA9/44	0.3	0.066	0.093	1	0.31	0.49	0.31	0.063	0.18	-0.52	0.12	-0.27	-0.084
Medial BA6/8	0.45	0.66	0.23	0.31	1	0.56	0.16	-0.28	-0.049	0.079	0.032	-0.36	-0.43
Left BA7/40	0.46	0.21	0.3	0.49	0.56	1	0.23	-0.36	-0.27	-0.15	-0.11	-0.53	-0.24
Right HC	0.16	0.2	-0.3	0.31	0.16	0.23	1	-0.036	0.12	-0.27	0.68	-0.0099	0.2
Left BA31	-0.44	-0.2	-0.53	0.063	-0.28	-0.36	-0.036	1	0.48	0.091	0.19	0.27	0.35
Left BA40	-0.35	0.15	-0.11	0.18	-0.049	-0.27	0.12	0.48	1	0.17	0.32	0.42	0.43
Right BA40	-0.22	0.27	-0.038	-0.52	0.079	-0.15	-0.27	0.091	0.17	1	-0.15	0.099	0.12
Right BA21	-0.014	0.064	-0.41	0.12	0.032	-0.11	0.68	0.19	0.32	-0.15	1	0.11	0.18
Medial BA24	-0.28	-0.028	-0.19	-0.27	-0.36	-0.53	-0.0099	0.27	0.42	0.099	0.11	1	0.5
Medial BA9	-0.44	-0.078	-0.35	-0.084	-0.43	-0.24	0.2	0.35	0.43	0.12	0.18	0.5	1

C

Right BA37	1	0.29	0.72	0.44	0.54	0.78	0.17	-0.1	-0.48	-0.27	-0.19	-0.081	-0.42
Right BA47	0.29	1	0.24	-0.11	0.66	0.35	0.005	0.25	0.29	0.08	0.14	-0.064	-0.31
Right BA46/45	0.72	0.24	1	0.18	0.41	0.62	-0.21	-0.24	-0.41	-0.24	-0.21	-0.19	-0.47
Left BA9/44	0.44	-0.11	0.18	1	0.2	0.36	0.075	-0.18	-0.16	-0.04	-0.11	0.14	-0.054
Medial BA6/8	0.54	0.66	0.41	0.2	1	0.67	0.15	-0.053	-0.089	-0.24	-0.092	-0.16	-0.46
Left BA7/40	0.78	0.35	0.62	0.36	0.67	1	-0.003	-0.1	-0.16	-0.12	-0.18	-0.23	-0.47
Right HC	0.17	0.0052	-0.21	0.075	0.15	-0.0036	1	-0.015	-0.19	-0.062	0.51	0.067	-0.17
Left BA31	-0.1	0.25	-0.24	-0.18	-0.053	-0.1	-0.015	1	0.32	0.22	0.3	0.25	0.26
Left BA40	-0.48	0.29	-0.41	-0.16	-0.089	-0.16	-0.19	0.32	1	0.36	0.35	0.17	0.51
Right BA40	-0.27	0.08	-0.24	-0.04	-0.24	-0.12	-0.062	0.22	0.36	1	0.08	0.092	0.19
Right BA21	-0.19	0.14	-0.21	-0.11	-0.092	-0.18	0.51	0.3	0.35	0.08	1	-0.022	0.1
Medial BA24	-0.081	-0.064	-0.19	0.14	-0.16	-0.23	0.067	0.25	0.17	0.092	-0.022	1	0.32
Medial BA9	-0.42	-0.31	-0.47	-0.054	-0.46	-0.47	-0.17	0.26	0.51	0.19	0.1	0.32	1

Figure 4): Correlations of activity between the regions of interest in the a) recognition, b) spatial context, and c) temporal context task in young adults. Black lines separate the correlation matrix into task positive network regions (top left), task negative network regions (bottom right) and interactions between the two networks (top right). HC = Hippocampus, BA = brodmann area.



A

Right BA37	1	-0.086	-0.066	-0.12	-0.036	0.24	0.12	0.25	-0.096	0.24	0.016	0.28	-0.19
Right BA47	-0.086	1	0.37	0.1	0.32	0.075	-0.14	0.011	-0.3	0.24	-0.12	-0.074	-0.086
Right BA46/45	-0.066	0.37	1	0.6	0.54	0.32	-0.46	0.15	-0.12	0.081	-0.014	-0.42	0.029
Left BA9/44	-0.12	0.1	0.6	1	0.66	0.63	-0.27	0.38	-0.096	-0.22	0.19	-0.62	0.3
Medial BA6/8	-0.036	0.32	0.54	0.66	1	0.43	-0.19	0.26	-0.042	-0.21	0.011	-0.5	0.25
Left BA7/40	0.24	0.075	0.32	0.63	0.43	1	-0.073	0.54	-0.026	-0.12	0.29	-0.64	0.11
Right HC	0.12	-0.14	-0.46	-0.27	-0.19	-0.073	1	0.29	-0.086	0.13	0.23	0.2	0.19
Left BA31	0.25	0.011	0.15	0.38	0.26	0.54	0.29	1	-0.044	0.15	0.37	-0.26	0.24
Left BA40	-0.096	-0.3	-0.12	-0.096	-0.042	-0.026	-0.086	-0.044	1	-0.19	0.091	0.31	0.031
Right BA40	0.24	0.24	0.081	-0.22	-0.21	-0.12	0.13	0.15	-0.19	1	-0.23	0.25	0.1
Right BA21	0.016	-0.12	-0.014	0.19	0.011	0.29	0.23	0.37	0.091	-0.23	1	-0.23	0.11
Medial BA24	0.28	-0.074	-0.42	-0.62	-0.5	-0.64	0.2	-0.26	0.31	0.25	-0.23	1	-0.23
Medial BA9	-0.19	-0.086	0.029	0.3	0.25	0.11	0.19	0.24	0.031	0.1	0.11	-0.23	1

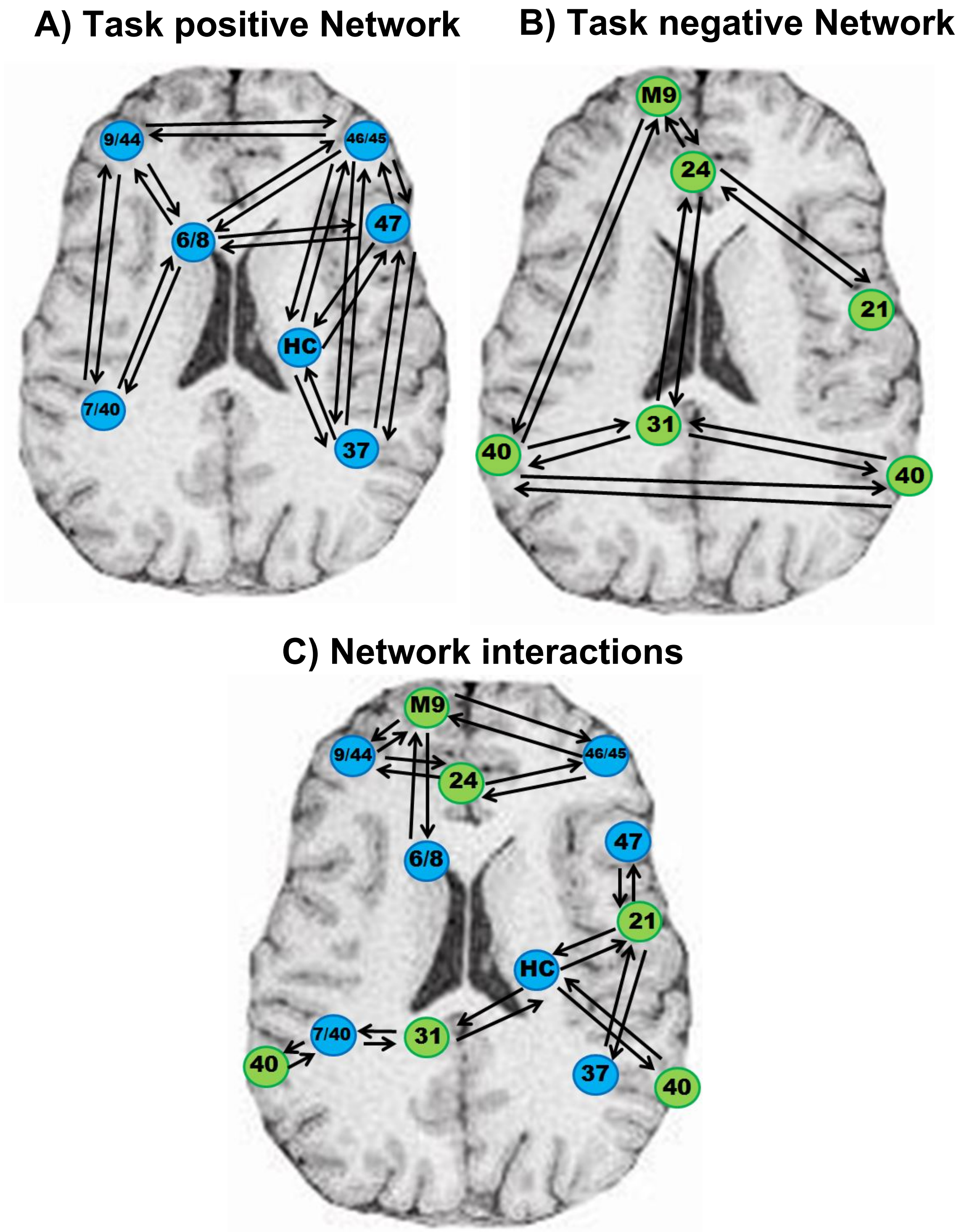
B

Right BA37	1	0.18	0.099	0.29	0.11	-0.0045	0.41	0.036	-0.16	-0.33	0.19	0.018	-0.27
Right BA47	0.18	1	0.42	0.32	0.16	0.16	0.11	0.06	0.09	-0.23	0.28	-0.49	-0.37
Right BA46/45	0.099	0.42	1	0.48	0.51	0.24	-0.06	0.32	0.11	-0.033	-0.053	-0.14	0.24
Left BA9/44	0.29	0.32	0.48	1	0.75	0.64	0.25	0.53	0.31	-0.096	0.11	0.14	0.16
Medial BA6/8	0.11	0.16	0.51	0.75	1	0.48	-0.066	0.51	0.09	-0.067	-0.18	0.19	0.3
Left BA7/40	0.0045	0.16	0.24	0.64	0.48	1	-0.17	0.59	0.45	0.16	-0.12	0.062	0.094
Right HC	0.41	0.11	-0.06	0.25	-0.066	-0.17	1	-0.12	0.15	0.0075	0.56	0.025	-0.013
Left BA31	0.036	0.06	0.32	0.53	0.51	0.59	-0.12	1	0.18	-0.079	0.043	0.2	0.46
Left BA40	-0.16	0.09	0.11	0.31	0.09	0.45	0.15	0.18	1	0.19	0.29	-0.071	0.43
Right BA40	-0.33	-0.23	-0.033	-0.096	-0.067	0.16	0.0075	-0.079	0.19	1	-0.33	-0.077	0.065
Right BA21	0.19	0.28	-0.053	0.11	-0.18	-0.12	0.56	0.043	0.29	-0.33	1	0.12	0.04
Medial BA24	0.018	-0.49	-0.14	0.14	0.19	0.062	0.025	0.2	-0.071	-0.077	0.12	1	0.31
Medial BA9	-0.27	-0.37	0.24	0.16	0.3	0.094	-0.013	0.46	0.43	0.065	0.04	0.31	1

C

Right BA37	1	0.32	-0.2	-0.13	-0.051	0.089	0.49	0.46	-0.22	0.008	-0.028	0.057	0.086
Right BA47	0.32	1	0.15	0.17	0.1	0.11	0.067	0.16	0.31	0.49	0.23	0.26	-0.15
Right BA46/45	-0.2	0.15	1	0.48	0.37	0.19	-0.23	-0.14	-0.13	0.28	-0.17	-0.17	-0.088
Left BA9/44	-0.13	0.17	0.48	1	0.67	0.48	-0.019	0.2	0.38	0.31	0.23	-0.17	0.18
Medial BA6/8	-0.051	0.1	0.37	0.67	1	0.71	-0.21	0.22	0.46	0.33	-0.11	-0.3	0.18
Left BA7/40	0.089	0.11	0.19	0.48	0.71	1	-0.15	0.37	0.42	0.43	-0.2	0.016	0.37
Right HC	0.49	0.067	-0.23	-0.019	-0.21	-0.15	1	0.21	-0.42	-0.24	0.42	-0.0089	0.13
Left BA31	0.46	0.16	-0.14	0.2	0.22	0.37	0.21	1	0.19	0.34	-0.021	0.16	0.32
Left BA40	-0.22	0.31	-0.13	0.38	0.46	0.42	-0.42	0.19	1	0.23	0.18	0.13	0.024
Right BA40	0.008	0.49	0.28	0.31	0.33	0.43	-0.24	0.34	0.23	1	-0.24	-0.0044	0.11
Right BA21	-0.028	0.23	-0.17	0.23	-0.11	-0.2	0.42	-0.021	0.18	-0.24	1	0.16	0.078
Medial BA24	0.057	0.26	-0.17	-0.17	-0.3	0.016	-0.008	0.16	0.13	-0.0044	0.16	1	-0.17
Medial BA9	0.086	-0.15	-0.088	0.18	0.18	0.37	0.13	0.32	0.024	0.11	0.078	-0.17	1

Figure 5): Correlations of activity between the regions of interest in the a) recognition, b) spatial context, and c) temporal context task in older adults. Black lines separate the correlation matrix into task positive network regions (top left), task negative network regions (bottom right) and interactions between the two networks (top right). HC = Hippocampus, BA = brodmann area.


A) Task positive Network

B) Task negative Network

C) Network interactions

Figure 6) Anatomical model for the structural equation modeling analysis. Arrows represent anatomical connections between brain regions. Regions are identified by their Brodmaan areas. Task-positive regions are represented in blue, and task-negative regions in green. HC = Hippocampus. The same naming scheme is used in the following figures.

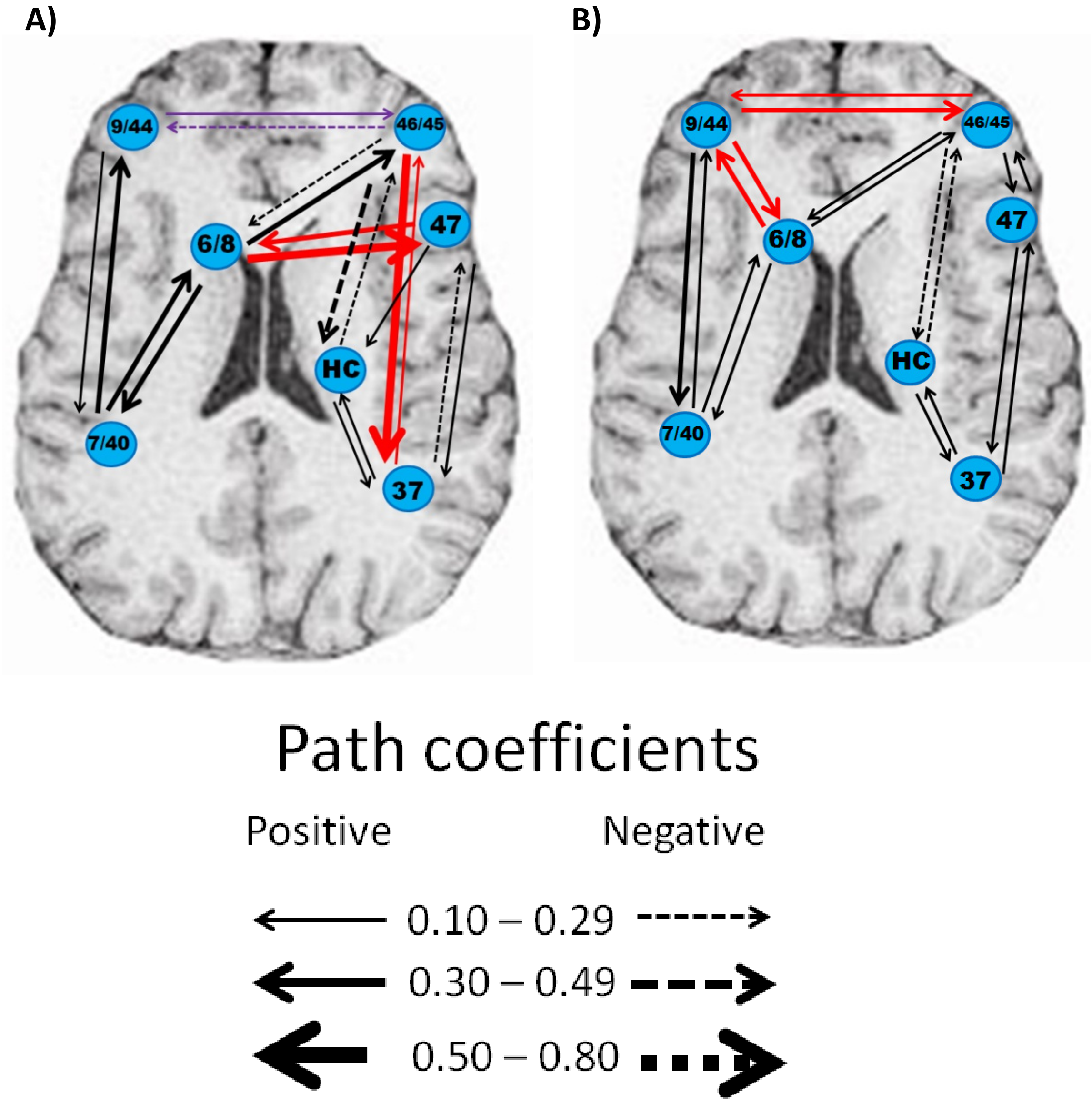
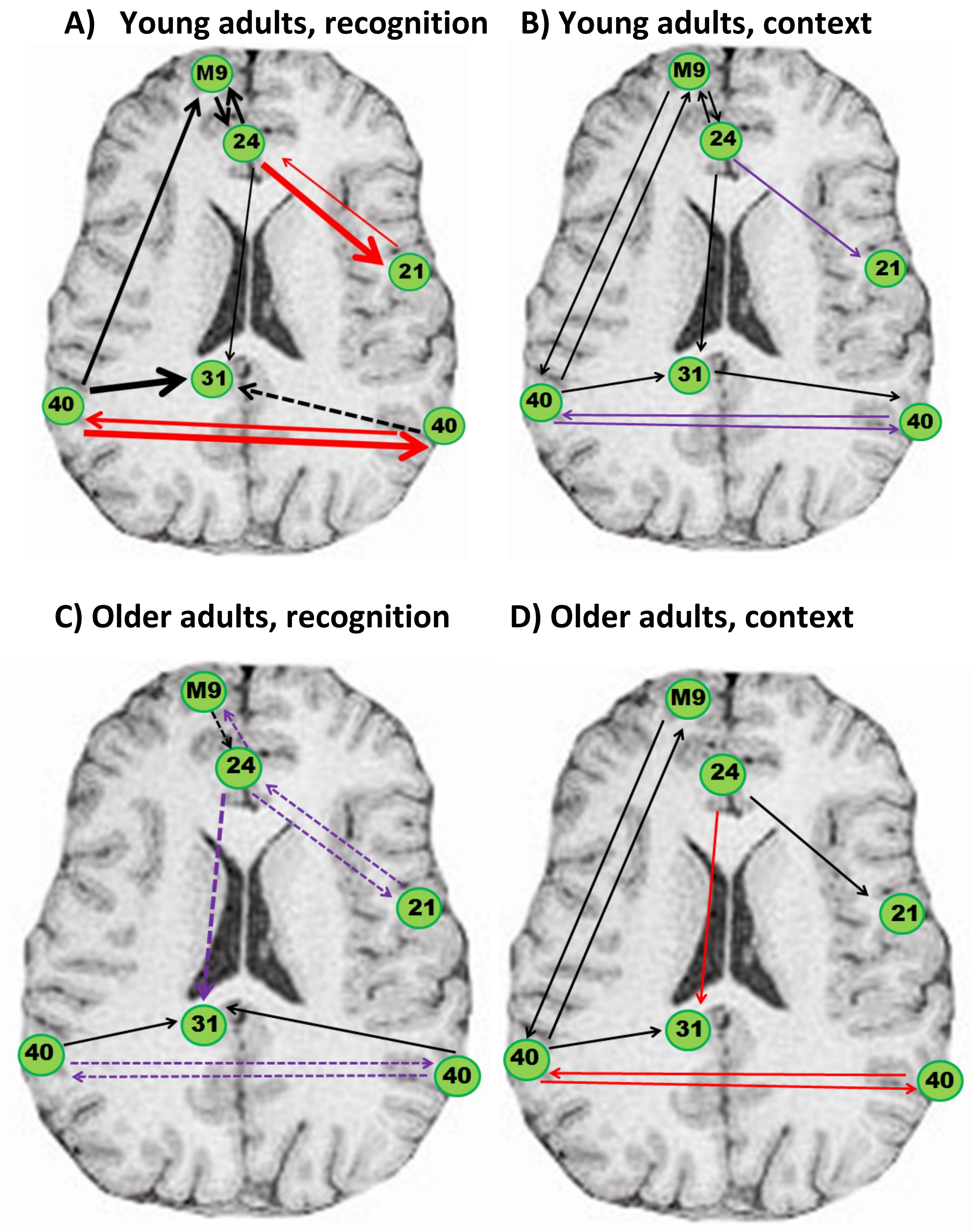


Figure 7) Between group differences in path coefficients between a) young and b) older adults in the TPN, across all tasks. The strength of each path coefficient is proportional to the width of the arrow. Black arrows indicate paths with no age differences, red arrows indicate paths that were stronger (more positive) in one age group, and purple arrows indicate paths which were weaker (less positive). The same legend for path coefficient is used in the following figures.

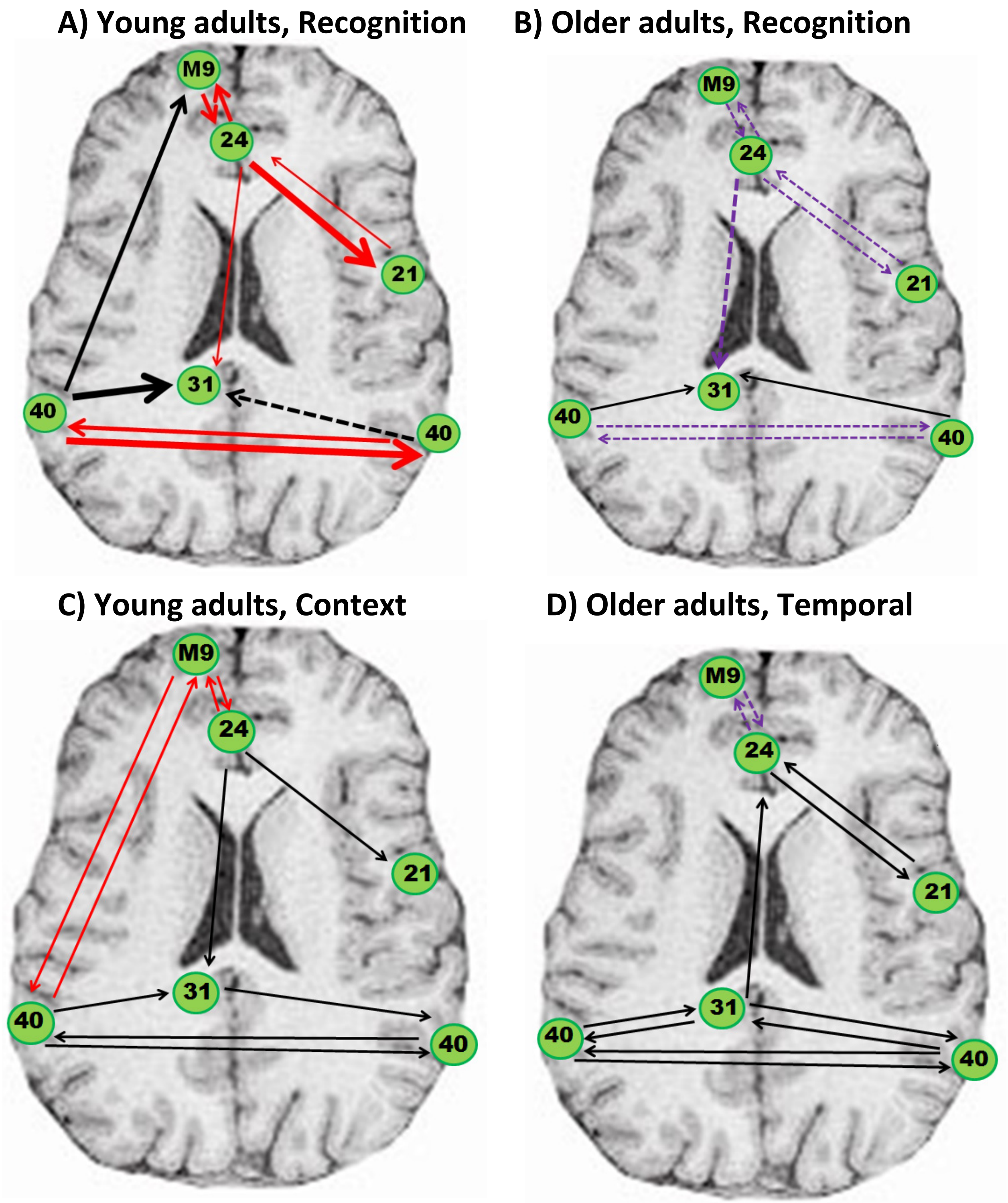

A) Young adults, recognition

B) Young adults, context

C) Older adults, recognition

D) Older adults, context

Figure 8) Within-group differences in path coefficients in the TNN in young (A and B) and older adults (C and D). Black arrows indicate paths with no within-group task differences, red arrows indicate paths that were stronger (more positive) in one task, and purple arrows indicate paths which were weaker (less positive).

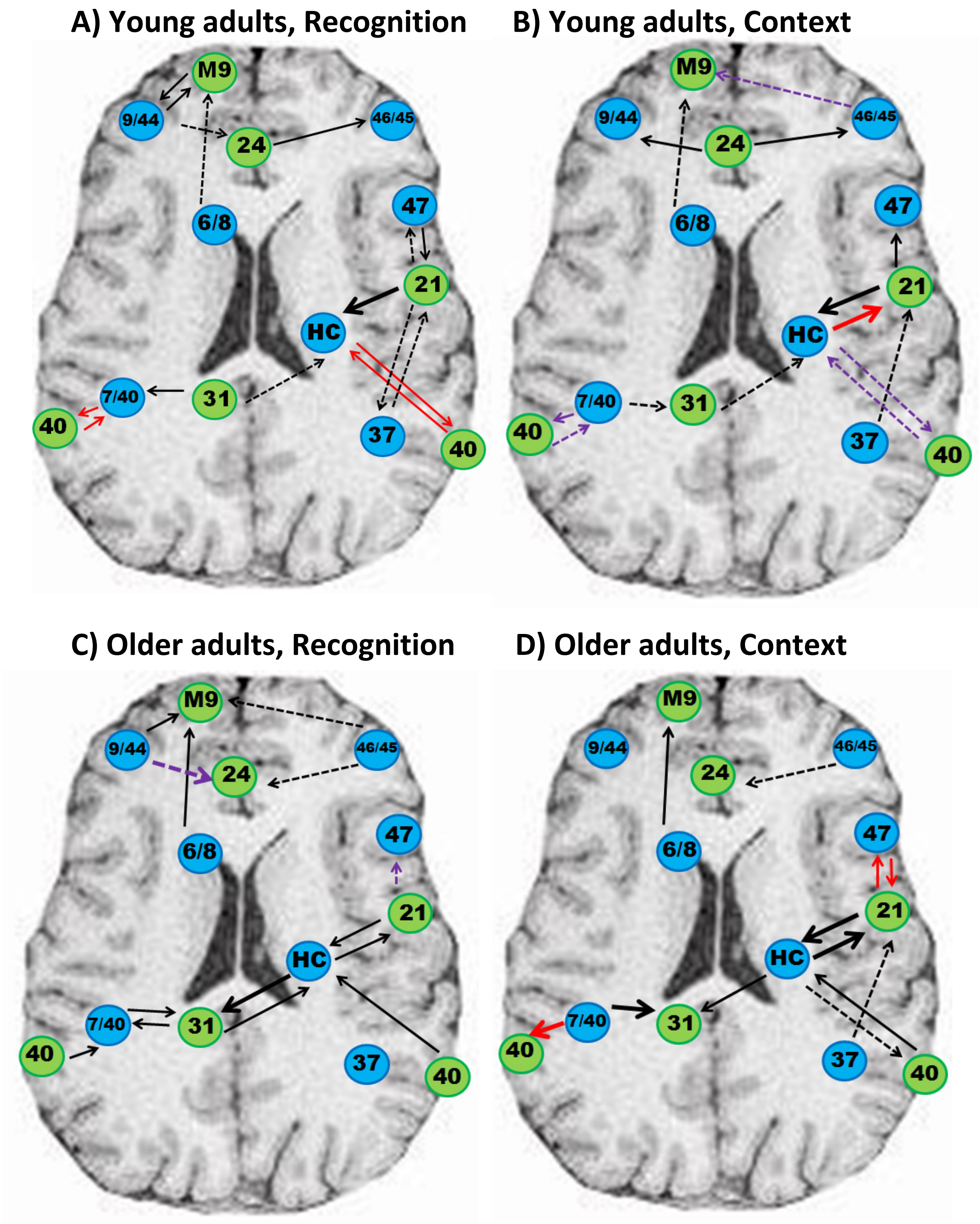

A) Young adults, Recognition

B) Older adults, Recognition

C) Young adults, Context

D) Older adults, Temporal

Figure 9) Between-group differences in the TNN. A) and B): Between group differences in the item recognition task. C) and D): Between group differences in the context tasks (spatial and temporal) in young and the temporal context task in older adults (see text for rationale of this comparison). Black arrows indicate paths with no between-group differences, red arrows indicate paths that were stronger (more positive) in one age group, and purple arrows indicate paths which were weaker (less positive).



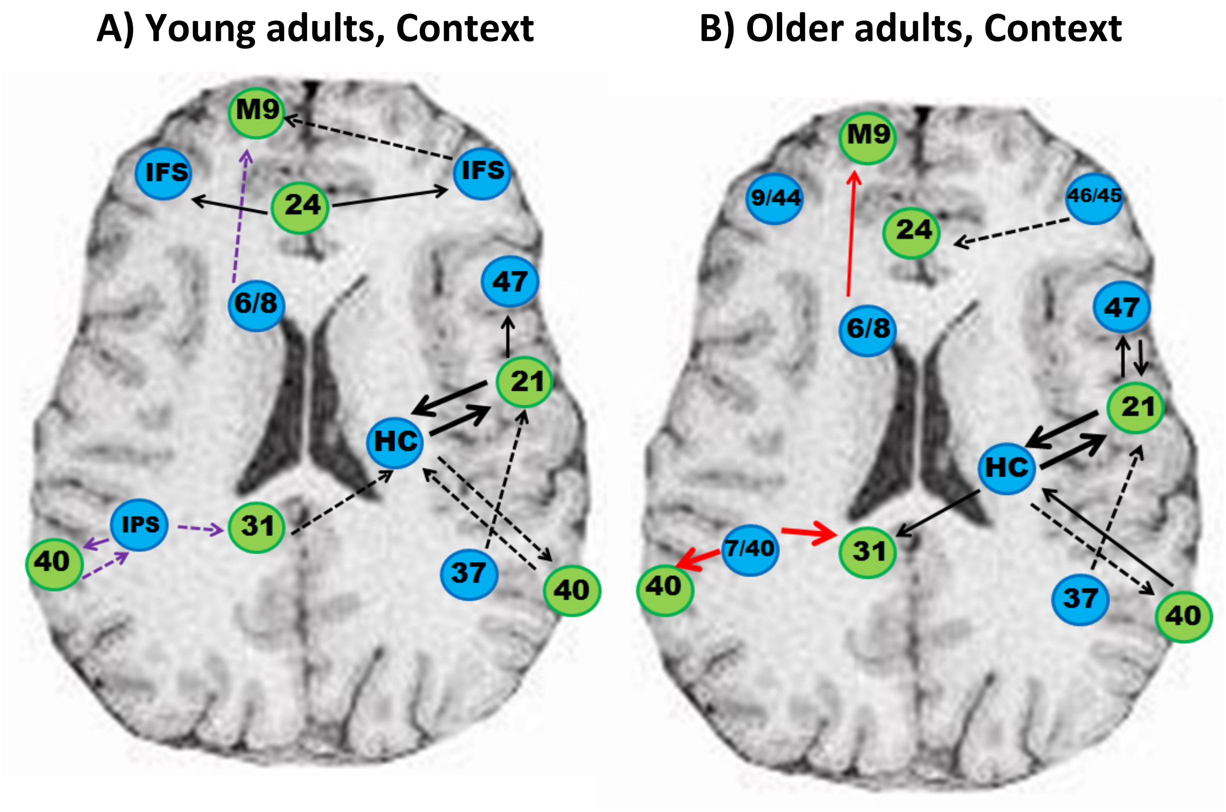
A) Young adults, Recognition

B) Young adults, Context

C) Older adults, Recognition

D) Older adults, Context

Figure 10) Within-group differences in path coefficients between regions of the TPN and TNN in young (A and B) and older adults (C and D). Black arrows indicate paths with no within-group task differences, red arrows indicate paths that were stronger (more positive) in one task, and purple arrows indicate paths which were weaker (less positive).



A) Young adults, Context

B) Older adults, Context

Figure 11) Between-group differences in the path coefficients between regions of TPN and TNN in the context tasks. Black arrows indicate paths with no age group differences, red arrows indicate paths that were stronger (more positive) in one age group, and purple arrows indicate paths which were weaker (less positive).