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Neuroimaging in Dementia and Other Amnesic Disorders

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1. Introduction

Neuroimaging has revolutionized the field of cognitive neuroscience. Early studies of brain-behavior relationships relied on a precise neurological examination as the basis for hypothesizing the site of brain damage that was responsible for a given behavioral syndrome. Episodic amnesia, for example, clearly implicated the hippocampus as the site of recent memory abilities.

Clinicopathological correlations were the earliest means of obtaining precise data on the site of damage causing a specific neurobehavioral syndrome (D'Esposito & Wills, 2000). In 1861, Paul Broca's observations of nonfluent aphasia in the setting of left inferior frontal gyrus damage cemented the belief that this brain region was critical for speech output (Broca, 1861). The advent of structural brain imaging more than 100 years after Broca's observations, first with computed tomography (CT) and later with magnetic resonance imaging (MRI), paved the way for more precise anatomical localization of the cognitive deficits that are manifest after brain injury.

Anatomical analyses of Broca's aphasia using structural neuroimaging (Naeser et al., 1989, Dronkers, 1996, Alexander et al., 1990) have more precisely determined that damage restricted to the inferior frontal gyrus causes only a transient aphasia, with recovery within weeks to months. Instead, damage to deep white matter and insular cortex causes persistent nonfluency. Noninvasive, structural neuroimaging provides the remarkable power to detail anatomical pathology in every stroke patient without re-lying upon the infrequently obtained autopsy.

Neuroimaging is a powerful tool for creative exploration of the epidemiology, diagnostic sensitivity, progression and therapeutic efficacy in many brain diseases featured by memory impairment (Apostolova & Thompson, 2008). Some consider modern functional neuroimaging methods as useful tools to establish similarities and differences between different forms of amnesias with respect to their brain correlates, while others consider them adequate for constituting groups of patients in a research perspective, but still out of reach for the practitioner (Celsis, 2000).

2. Neuroimaging techniques

Functional neuroimaging, broadly defined as techniques that provide measures of brain activity, has further increased our ability to study the neural basis of cognition and behavior. Functional neuroimaging dates back to the use of electrophysiological methods such as electroencephalography (EEG). However, the lack of spatial resolution in these methods (i.e., often limited to hemispheric or anterior-posterior differences) did not allow testing hypotheses regarding the precise anatomical location of a brain region subserving a given cognitive process (D'Esposito & Wills, 2000, Galin & Ornstein, 1972).

The modern era of functional brain imaging, bringing markedly improved spatial resolution, was introduced first in the mid-1970s using the xenon cerebral blood flow technique and later in the mid-1980s using positron emission tomography (Mazziotta & Phelps, 1984, Petersen et al., 1988). In more recent years, functional magnetic resonance imaging (fMRI) has rapidly emerged as an extremely powerful technique with many advantages over positron emission tomography (PET) for studying cognition.

In dementia evaluation, the most commonly used tracers are ^{99m}Tc -HMPAO for SPECT brain perfusion and ^{18}F -FDG for PET glucose's metabolism. For practical purposes, the clinical analysis of brain perfusion and glucose metabolism are equivalent, so that hypoperfusion areas in brain SPECT roughly correspond to glycolytic hypometabolism in PET.

The different syndromes and diseases presenting with dementia have different patterns of brain perfusion abnormalities, so we can distinguish them with good specificity.

3. Normal aging

Brain aging is characterized by numerous physiological, structural, functional, and neurocognitive changes. The interplay of these various processes is complex and characterized by large interindividual differences. The level of cognitive functioning achieved by a group of elderly is largely determined by the health of individuals within this group (Aine et al., 2011). Individuals with a history of hypertension, for example, are likely to have multiple white matter insults which compromise cognitive functioning, independent of aging processes. The health of the elderly group has not been well-documented in most previous studies and elderly participants are rarely excluded, or placed into a separate group, due to health-related problems (Caserta et al., 2009). In addition, recent results show that white matter tracts within the frontal and temporal lobes, regions critical for higher cognitive functions, continue to mature well into the 4th decade of life (Aine et al., 2011). This suggests that a young age group may not be the best control group for understanding aging effects on the brain since development is ongoing within this age range.

Functional neuroimaging studies of cognitively intact older adults have consistently shown volume loss and loss of white matter structural integrity, particularly in prefrontal cortex, which may be associated with cognitive decline (Caserta et al., 2009). For instance, age-related deficits in working memory (WM) and episodic memory abilities are related to changes in prefrontal cortex (PFC) function. Reviews of these neuroimaging studies have generally concluded that with age there is a reduction in the hemispheric specialization of cognitive function in the frontal lobes that may either be due to dedifferentiation of function, deficits in function and/or functional reorganization and compensation. While data are incomplete, another consistent finding has been a decline in other cognitive domains, such as arithmetic/numerical ability and perceptual speed. Alternatively, other cognitive

functions such as verbal ability, word knowledge, and semantic memory remain quite preserved even to old age (Caserta et al., 2009).

Some functional neuroimaging studies on normal aging showed the involvement of different patterns of activation in comparison with control populations, such as increased frontal activity. These differences have been interpreted as reflecting the implementation of compensatory processes (Kalpouzos et al., 2008). Some authors (Rajah & D'Esposito, 2005) argue that in normal ageing distinct PFC regions exhibit different patterns of functional change, suggesting that age-related changes in PFC function are not homogeneous in nature. Specifically, these authors hypothesize that normal ageing is related to the differentiation of cortical function in a bilateral ventral PFC and deficits in function in right dorsal and anterior PFC (Rajah & D'Esposito, 2005). As a result of these changes, functional compensation in left dorsal and anterior PFC may occur.

Factors identified for healthy cognitive (brain) aging are multifactorial, and likely incorporate biological systems as well as cognitive reserve (i.e. the capability of an individual to cope with a task in order to optimize his/her performance by the recruitment of different neural networks and/or by using alternative cognitive strategies).

4. Mild cognitive impairment (MCI)

Mild cognitive impairment (MCI), a transitional state between normal aging and dementia, carries a four- to sixfold increased risk of future diagnosis of dementia (Caixeta, 2006). As complete drug-induced reversal of AD symptoms seems unlikely, researchers are now focusing on the earliest stages of AD where a therapeutic intervention is likely to realize the greatest impact. Recently neuroimaging has received significant scientific consideration as a promising *in vivo* disease-tracking modality that can also provide potential surrogate biomarkers for therapeutic trials (Apostolova & Thompson, 2008).

Evidence to date indicates that functional brain decline precedes structural decline in prodromal dementia, including adults with MCI (Jak et al., 2009). Therefore, functional neuroimaging techniques may offer the unique ability to detect early functional brain changes in at-risk adults and identify the neurophysiological markers that best predict dementia conversion.

While several volumetric techniques laid the foundation of the neuroimaging research in AD and MCI, more precise computational anatomy techniques have recently become available. This new technology detects and visualizes discrete changes in cortical and hippocampal integrity and tracks the spread of AD pathology throughout the living brain. Related methods can visualize regionally specific correlations between brain atrophy and important proxy measures of disease such as neuropsychological tests, age of onset or factors that may influence disease progression (Apostolova & Thompson, 2008).

Given that AD neuropathology preferentially targets the medial temporal lobe (MTL) early in the course of the disease, thereby resulting in the hallmark episodic memory decline, and amnesic MCI is thought to represent prodromal AD, the majority of fMRI studies of MCI involve memory processing (particularly encoding) in amnesic samples (Jak et al., 2009). No known fMRI studies have been published focusing on other clinical subtypes of MCI. While several studies demonstrate increased blood oxygen level dependent (BOLD) response in the MTL (Dickerson et al., 2004, Hamalainen et al., 2007; Kircher et al., 2007; Sperling, 2007), others report decreased MTL activity in MCI (Johnson et al., 2006; Mandzia et al., 2009). These discrepant findings have been interpreted as reflecting bimodal functional activity

whereby less impaired MCI subjects show increased BOLD response in the hippocampus corresponding to a slight or moderate neuronal dysfunction, and more impaired MCI subjects demonstrate decreased BOLD response—similar to the levels observed in mild AD patients—as the cortical neuronal networks become more severely impaired with greater disease progression (Dickerson et al., 2004, Hamalainen et al., 2007; Johnson et al., 2006). However, this interpretation is primarily derived from cross-sectional studies and can only adequately be tested with longitudinal designs.

Few longitudinal fMRI studies of MCI have been reported. Although these studies are often limited by small sample sizes, they demonstrate promise for the use of fMRI to detect early AD. Those MCI patients who converted to AD showed a stronger relationship between brain activity in the left superior parietal lobe and the left precuneus during an angle discrimination task in the context of comparable performance (Vannini et al., 2007). Similarly, despite equivalent memory performance, Dickerson et al. (2004) reported that MCI patients who subsequently declined during a 2.5-year follow-up period demonstrated increased right parahippocampal gyrus activity during picture encoding. In a more recent study, the same research group reported increased hippocampal activation predicted greater degree and rate of cognitive decline during a 6-year follow-up period, even after controlling for baseline level of impairment (Miller et al., 2008).

Mandzia et al. (2009) reported that MTL activation during recognition was positively correlated with behavioral performance. However, unlike their healthy peers, MCI adults did not show a strong relationship between MTL activity during picture encoding and subsequent retrieval success, highlighting the complexity of the relationship between BOLD signal and effectiveness of encoding strategies. In contrast, Johnson et al. (2006) found reduced BOLD signal change in the right hippocampus during picture encoding and in the posterior cingulate during recognition of learned items in an amnesic MCI group despite comparable performance to their healthy peers. However, when activation corresponding only to successfully learned words was examined, an increase in hippocampal activity was seen, suggesting that an increase in MTL activity may support successful memory encoding (Kircher et al., 2007). Similarly, a positive correlation between extent of parahippocampal and hippocampal activation and memory performance was found in MCI but, in a paradoxical fashion, greater clinical impairment, was also associated with recruitment of a larger region of the right parahippocampal gyrus during encoding (Dickerson et al., 2004). Data from Johnson et al. (2004) provided further evidence for hippocampal dysfunction in MCI, suggesting that adults with MCI do not habituate to increasingly familiar items in the same manner as healthy older adults who show expected reductions in BOLD response to repeated items over time.

Despite the prevalence of studies examining medial temporal cortex function supporting memory, other cortical areas have also been implicated in MCI. For example, a reduction in functional activity in the posterior cingulate cortex (PCC) during recognition and episodic retrieval of previously learned line drawings (Johnson et al., 2006) and object working memory, but not during self-appraisal, has implicated this region in the memory retrieval difficulty seen in amnesic MCI. The degradation of PCC functioning in MCI is not surprising given that PET metabolic alterations in the temporoparietal cortices and in the posterior cingulate have been reported in MCI and AD as well as in nondemented young and middle-aged adults at genetic risk for AD (Jak et al., 2009). Similarly, dedifferentiation in the retrosplenial cortex during the retrieval of recent versus remote autobiographical memories and during episodic versus semantic memory retrieval has been reported in

amnesic MCI, further implicating the medial posterior cortex in MCI (Jak et al., 2009). Additionally, the neural substrates of visual working memory, self-appraisal, and emotional working memory in MCI have also been examined, and generally implicate a greater number of cortical regions (Jak et al., 2009). However, results are varied and highlight the need for greater attention to other cognitive processes in MCI in order to more fully understand changes in cortical functioning that may signal impending cognitive decline.

5. Dementias

5.1 Alzheimer's disease

AD is the commonest form of dementia worldwide. It manifests with relentlessly progressive cognitive decline presenting initially as memory loss and then spreads to affect all other cognitive faculties and the patients' ability to conduct an independent lifestyle (Caixeta, 2006). Post-mortem examination reveals abundant cortical and hippocampal neuritic plaques (NP) and neurofibrillary tangles (NFT) as well as pancerebellar atrophy upon gross inspection of the brain. The neuronal degeneration pattern in Alzheimer's disease (AD) spreads from the temporal mesial areas to the posterior regions of the cingulate cortex and then to the parietal lobes and the rest of the temporal lobes, asymmetrically or not. Pre-mortem, AD-associated brain changes can be clinically evaluated with the help of neuroimaging. They consist of global dysfunction with an early predilection for the hippocampal region and the temporo-parietal cortical areas (Caixeta, 2006). In advanced cases, the hypoperfusion pattern may reach the frontal lobes, but even in these cases the perfusion remains normal in thalamus, basal ganglia, motor cortex and occipital lobes.

Among patients presenting with bilateral parietotemporal hypoperfusion, 82% have AD, while the rest are due to Parkinson dementia or cerebrovascular disease. On the other hand, in patients with diagnosed AD, 100% have hypoconcentration of 18F-FDG and 90% have parietal and temporal hypoperfusion with 99mTc-HMPAO. These typical findings are also found among those with early AD, while hippocampal hypoperfusion as only finding has low specificity for AD diagnosis. In individuals with mild cognitive impairment, the posterior cingulate hypometabolism can predict who is going to develop AD. However, not all patients with AD have Bilateral parietotemporal hypoperfusion. In a study conducted by our group in 104 patients fulfilling NINCDS-ADRDA criteria for probable AD, bilateral parietotemporal hypoperfusion was more frequent in patients with severe AD, in those with early onset of the symptoms, and in men (Nitrini et al., 2000).

5.2 Lewy body dementia

The metabolic defects described in this disease are very close to those found in AD, but there is also hypoperfusion in the occipital lobes. One must have in mind that a patient with AD and cerebrovascular disease can mimic the LBD pattern, and it's not uncommon to find these pathologies at the same patient (Caixeta, 2006).

5.3 Vascular dementia

Arteriosclerotic brain disease presents as multiple focal areas of hypoperfusion randomly distributed in the cortex, also compromising subcortical structures. This particular pattern is never been observed in A.D., but the dual pathology is described as being present in 4 to 10% of patients. The differential diagnosis is AIDS dementia complex. When

cerebrovascular disease is predominantly microangiopathic there is significantly more diffuse cortical hypoperfusion and ventricle enlargement (Caixeta, 2006).

5.4 Frontotemporal lobar degeneration

Patients with the different diseases in this group present severe bilateral hypoperfusion in the frontal lobes, predominantly in the mesial structures (Caixeta & Nitrini, 2001). There is also perfusion deficit in the anterior regions of the temporal lobes and each subtype has other characteristic findings, like asymmetrical parietal hypoperfusion in primary progressive aphasia.

Also depressive disorders and transient global amnesia can show prefrontal symmetric hypoperfusion, but there is unilateral basal ganglia hypoperfusion in the later, more commonly in the right. Also Huntington's disease can show bilateral frontotemporal hypoperfusion, but it presents later in the progression of the disease, while the first sign is severe bilateral basal ganglia hypoperfusion.

5.5 Dementia associated with parkinsonism

As described in Lewy body dementia, idiopathic Parkinson disease with dementia can show hypoperfusion patterns similar to those observed in AD, but basal ganglia hypoperfusion is far more frequent, as is frontal precentral hypoperfusion (Caixeta & Vieira, 2008).

Corticobasal degeneration presents as bilateral asymmetrical frontal, parietal and basal ganglia hypoperfusion. Supranuclear palsy also presents frontal hypoperfusion, predominantly in the mesial regions, but what specifically distinguishes this disease is symmetric severe basal ganglia hypoperfusion.

Multiple system atrophy has a very specific finding, which is cerebellar hypoperfusion, besides symmetric basal ganglia hypoperfusion.

Hippocampal hypoperfusion with bilateral frontal and parietal hypoperfusion is found in normal pressure hydrocephalus.

6. Other amnesic syndromes

6.1 Transient global amnesia

Almost 60 years after its initial description, transient global amnesia (TGA) remains one of the most enigmatic syndromes in clinical neurology.

Recent diffusion-weighted imaging (DWI) data suggest that a transient perturbation of hippocampal function is the functional correlate of TGA because focal diffusion lesions can be selectively detected in the CA1 field of the hippocampal cornu ammonis. The vulnerability of CA1 neurons to metabolic stress plays, therefore, a pivotal part in the pathophysiological cascade, leading to an impairment of hippocampal function during TGA (Bartsch et al., 2006, Bartsch & Deuschl, 2010). The maximum level of detection of these lesions is 24–72 h after onset of symptoms. Although the diagnosis of TGA is primarily a clinical one, neuroimaging in TGA can positively support the diagnosis.

Although various factors, such as migraine, focal ischemia, venous flow abnormalities, and epileptic phenomena, have been suggested to be involved in the pathophysiology of TGA, the factors triggering the emergence of these lesions are still elusive. (Bartsch & Deuschl, 2010).

To date, data from MRI has not found evidence for structural sequelae of these hippocampal lesions, and recent neuropsychological findings have also not found evidence for clinically relevant chronic neuropsychological deficits.

Quantitative imaging of changes of regional cerebral glucose, oxygen metabolism, or cerebrovascular blood flow in TGA have been studied by use of PET and single photon emission computed tomography (SPECT). In some studies, mesiotemporal flow changes have been described (Guillery et al., 2002, Eustache et al., 2000, Warren et al., 2000). However, most studies have also noted concomitant decreased or increased changes in cerebral blood flow in other anatomical structures, such as unilateral or bilateral thalamic, prefrontal, frontal, amygdalian, striatal, cerebellar, occipital, precentral, and postcentral areas (Nardone et al., 2004, Eustache et al., 2000). In some studies, either no mesiotemporal changes, no cerebral changes, or a global hypoperfusion were detected (Chung et al., 2009, Fujii et al., 1989). In summary, the imaging data derived from PET and SPECT studies are difficult to compare and interpret. Most changes normalised on follow-up examination. The variabilities in PET and SPECT are probably associated with differences in the study designs, such as the imaging protocol and resolution, and the latency of scanning, frequently done days or weeks after the acute TGA and thus not covering the initial pathophysiological event. A correlation between SPECT and MRI in the time window of 24–73 h after onset has been found in a study including only six patients. In five patients, a predominant hypoperfusion in the cerebellar vermis was observed in combination with punctuate DWI lesions in the hippocampus, whereas in another patient a bilateral hypoperfusion in the temporal lobes was detected by use of SPECT (Bartsch & Deuschl, 2010). Functional MRI was used in two patients during an acute TGA to assess memory function and cerebral activation patterns. In both patients, there was reduced or no activation in temporal lobe structures during encoding of visual scenes or recognition of old scenes, thus reflecting the functional impairment of temporal lobe structures (Bartsch & Deuschl, 2010).

Use of structural imaging with MRI has detected abnormalities in memory-relevant structures of the mesiotemporal region. Early results have been inconsistent and controversial about the type and location of signal abnormalities described in some patients (Matsui et al., 2002, Huber et al., 2002). Recent data from studies that used high-resolution MRI have shown that focal hyperintense lesions correlating to restricted diffusion in the lateral hippocampus can now be reliably detected (Bartsch et al., 2006, 2007). The detection rate of these lesions can be improved by up to 85% with optimised MRI parameters and by acknowledging the time course of the lesion.

6.2 Psychogenic amnesias

Commonly, memory disturbances are related to organic brain damage. Nevertheless, especially the old psychiatric literature provides numerous examples of patients with selective amnesia due to what at that time was preferentially named hysteria (Markowitsch, 2003) and which implied that both environmental circumstances and personality traits influence bodily and brain states to a considerable degree. Awareness of the existence of relations between cognition, soma, and psyche has increased especially in recent times and has created the research branch named cognitive neuropsychiatry. Within this branch, psychopathologic processes, deviating from normal information processing, are studied with a combination of methods derived from neurology, psychiatry, psychology, neurobiology, and neuroinformatics in order to provide a deeper understanding of psychic disease processes (Halligan & David, 2001).

Modern imaging methods have helped to establish similarities between organic and functional (psychogenic) amnesias with respect to their brain correlates. In fact, it was found that also environmental-related amnesias—caused by stress and trauma situations with which individuals cannot cope appropriately—may alter the brain's metabolism in a predictable way and that even therapy-induced reestablishments of memory may be related to gains in brain metabolism. These results support the view, according to Markowitsch (1996), that organic and functional amnesias are two sides of the same coin Markowitsch, 1996. H.J. Markowitsch, Organic and psychogenic retrograde amnesia: two sides of the same coin?. *Neurocase* (1996), pp. 357–371. Full Text via CrossRef | View Record in Scopus | Cited By in Scopus (69). According this author, both kinds of phenomena may derive from a common brain mechanism leading to blockade, disruption, or disconnection mechanisms affecting the processes of memory and disintegrating widespread memory networks in the brain. This disintegration may be a consequence of “mechanical alterations” in the brain of organic amnesics and may be a consequence of biochemical alterations in the brain of psychogenic amnesics. For these, such processes may be induced during autobiographical information processing by desynchronization memory patterns, resulting in the reduction of discomfort for the subject.

Functional amnesias and psychogenic amnesias are discussed and their symptomatology is compared to that of organic amnesias. The term "mnestic block syndrome" (Markowitsch, 2003) is introduced and defined as a syndrome of its own. Experimental data, obtained especially with functional imaging methods, are presented to elucidate changes in neural activation during functional amnesic states.

Functional amnesic states, confined to a patient's biography, can be triggered by environmentally induced stress and trauma, leading to lasting inability to retrieve autobiographical events. Such an impairment may be identified at the brain level using functional imaging techniques (Markowitsch, 2003).

6.3 Illusory memories

A key point of agreement between cognitive and biological theories is that memories do not preserve a literal representation of the world; memories are constructed from fragments of information that are distributed across different brain regions, and depend on influences operating in the present as well as the past. Memory illusions and distortions have long been of interest to psychology researchers studying memory, but neuropsychologists and neuroscientists have paid relatively little attention to them (Schacter, 1996).

Memory distortions and illusions have long been of interest to psychopathology, dating to the classic 1932 study by Bartlett on the reconstructive nature of memory. Three decades later, Neisser (1967) put forward similar ideas. His monograph stimulated intensive interest on the part of cognitive psychologists in questions concerning memory distortions, resulting in many striking demonstrations of erroneous remembering in laboratory studies. Cognitive studies concerning memory distortion continued through the 1980s and have grown dramatically during the 1990s, inspired in part by controversies over the accuracy of memories retrieved in psychotherapy and effects of suggestive questioning on the reliability of childrens' recollections (Peres et al., 2008, Schacter, 1996).

Neuroimaging studies have highlighted important issues related to structural and functional brain changes found in sufferers of psychological trauma that may influence their ability to synthesize, categorize, and integrate traumatic memories (Peres et al., 2008).

A number of neuropsychologists have noted that damage to the ventromedial aspects of the frontal lobes and basal forebrain are often associated with the memory distortion known as

confabulation, where patients describe detailed recollections of events that never happened (Johnson, 1991, Moscovitch, 1997). Moscovitch (1997) has contended that confabulation arises as a result of impairment to strategic retrieval and monitoring processes that depend on frontal regions.

Illusory memory conjunctions appear to be attributable to inadequate binding of features at the time of encoding, a process that likely depends on the hippocampal formation.

Schacter et al. (1996) conducted a PET study using a specific paradigm: before scanning, subjects listened to a long list of words that were grouped into semantic categories that each included 20 associates of a non-presented critical lure; then was administered yes/no recognition tests in separate 60-sec scans for old words that had appeared on the study list ("true targets"), critical lures that had not appeared but were related to previously presented words ("false targets"), and new words that had not appeared and were not systematically related to previously presented words ("true target controls" and "false target controls," respectively); in a separate passive fixation scan, subjects simply looked at a crosshair for 60 sec. Compared to the passive fixation condition, both accurate recognition of true targets and illusory recognition of false targets were accompanied by significant blood flow increases in many of the same brain regions, including bilateral anterior/dorsolateral frontal cortex, precuneus, bilateral cerebellum, and the left medial temporal lobe, in the vicinity of the parahippocampal gyrus. This latter observation is intriguing in light of previously mentioned findings that amnesic patients with medial temporal damage exhibited little false recognition of critical lures and that medial temporal blood flow increases are associated with successful recollection (23, 51, 52). However, the evidence linking parahippocampal gyrus activation with episodic recognition (as opposed to visual or lexical processing) was equivocal, so this finding must be viewed cautiously pending further research.

Direct comparison between veridical and illusory recognition in this paper yielded virtually no significant findings, suggesting that brain activity during the two forms of recognition is quite similar. Nonetheless, the authors did observe some suggestive differences. Veridical recognition was accompanied by significantly greater blood flow than illusory recognition in the vicinity of the left supramarginal gyrus and superior temporal gyrus. Previous PET studies have implicated these regions in the processing and storage of phonological information (cf., refs. 81, 82, 83). Moreover, studies of brain-damaged patients have linked the supramarginal gyrus with disruptions of phonological analysis and retrieval (84). In light of these observations, authors hypothesized that temporoparietal increases associated with veridical recognition may reflect subjects' recognition of having heard or rehearsed the target words at the time of study; no such auditory/phonological information was available for critical lures. Although alternative interpretations are possible, this idea fits with the previously mentioned finding reported by Norman and Schacter (74) that people report more extensive memories of having heard or thought about presented words than critical lures.

One further suggestive finding from this PET study relates to the previously mentioned observations of a link between frontal lobe impairments and heightened susceptibility to false recognition. The authors found that false recognition was associated with trends for greater blood flow increases in inferior frontal regions (orbitofrontal cortex) bilaterally and right anterior prefrontal cortex than was veridical recognition. One possible interpretation of this finding is that subjects were trying to oppose or inhibit the sense of familiarity or recollection associated with the critical lures. That is, when subjects were deciding whether a critical lure had appeared previously, they likely experienced a strong feeling that it did. At

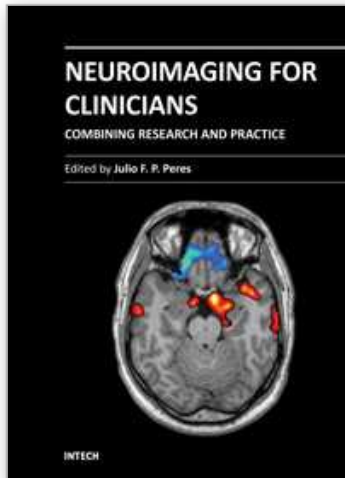
the same time, knowing that many associatively related items were on the list, they may have engaged in effortful retrieval processes as they tried to remember specific information about the test item's appearance in the study list.

7. References

- Aine CJ, Sanfratello L, Adair JC, Knoefel JE, Caprihan A, Stephen JM. Development and Decline of Memory Functions in Normal, Pathological and Healthy Successful Aging. *Brain Topogr.* 2011; 24: 135-142.
- Alexander MP, Naeser MA, Palumbo C. Broca's area aphasias: aphasia after lesions including the frontal operculum. *Neurology* 1990;40:353-362.
- Apostolova LG, Thompson PM. Mapping progressive brain structural changes in early Alzheimer's disease and mild cognitive impairment. *Neuropsychologia.* 2008;46(6):1597-612.
- Bartlett F C. *Remembering.* Cambridge, U.K.: Cambridge Univ. Press; 1932.
- Bartsch T, Alfke K, Stingle R, et al. Selective affection of hippocampal CA-1 neurons in patients with transient global amnesia without long-term sequelae, *Brain* 129 (2006), pp. 2874-2884.
- Bartsch T, Alfke K, Deuschl G, Jansen O. Evolution of hippocampal CA-1 diffusion lesions in transient global amnesia, *Ann Neurol* 62 (2007), pp. 475-480.
- Bartsch T, Deuschl G. Transient global amnesia: functional anatomy and clinical implications. *Lancet Neurol.* 2010; 9(2):205-14.
- Broca P. Remarques sur le siège de la faculté du langage articulé suivies d'une observation d'amphémie (perte de la parole). *Bull Mem Soc Anat Paris* 1861;36-45.
- Caixeta L, Nitrini R. Subtipos clínicos da demência frontotemporal. *Arq Neuropsiquiatr.* 2001 Sep;59(3-A):577-81.
- Caixeta L. *Demência - Abordagem Multidisciplinar.* São Paulo, Atheneu, 2006. ISBN 85-7379-864-5.
- Caixeta L, Vieira RT. Demência na doença de Parkinson. *Rev Bras Psiquiatr.* 2008 Dec;30(4):375-83.
- Caserta MT, Bannon Y, Fernandez F, Giunta B, Schoenberg MR, Tan J. Normal brain aging clinical, immunological, neuropsychological, and neuroimaging features. *Int Rev Neurobiol.* 2009;84:1-19.
- Celsis P. Age-related cognitive decline, mild cognitive impairment or preclinical Alzheimer's disease? *Ann Med.* 2000 Feb;32(1):6-14.
- Chung YA, Jeong J, Yang DW, et al.. A Tc-99m SPECT study of regional cerebral blood flow in patients with transient global amnesia, *Neuroimage* 47 (2009), pp. 50-55.
- D'Esposito M, Wills H. Functional Imaging of Neurocognition. *Semin Neurol* 20(4):487-498, 2000.
- Dickerson BC, Salat DH, Bates JF, Atiya M, Killiany RJ, Greve DN, Dale AM, Stern CE, Blacker D, Albert MS, Sperling RA. Medial temporal lobe function and structure in mild cognitive impairment. *Ann Neurol.* 2004;56:27-35.
- Dronkers NF. A new brain region for coordinating speech articulation. *Nature* 1996;384:159-161.
- Eustache F, Desgranges B, Aupee AM, Guillery B, Baron JC. Functional neuroanatomy of amnesia: positron emission tomography studies, *Microsc Res Tech* 51 (2000), pp. 94-100.

- Fujii K, Sadoshima S, Ishitsuka T, et al. Regional cerebral blood flow and metabolism in patients with transient global amnesia: a positron emission tomography study, *J Neurol Neurosurg Psychiatry* 52 (1989), pp. 622–630.
- Galin D, Ornstein R. Lateral specialization of cognitive mode: an EEG study. *Psychophysiology* 1972;9:412-418
- Guillery B, Desgranges B, de la Sayette V, Landeau B, Eustache F, Baron JC. Transient global amnesia: concomitant episodic memory and positron emission tomography assessment in two additional patients, *Neurosci Lett* 325 (2002), pp. 62–66.
- Halligan PW, David AS. Cognitive neuropsychiatry: towards a scientific psychopathology. *Nat. Rev. Neurosci.* 2 (2001), pp. 209–215.
- Hamalainen A, Pihlajamaki M, Tanila H, Hanninen T, Niskanen E, Tervo S, Karjalainen PA, Vanninen RL, Soininen H. Increased fMRI responses during encoding in mild cognitive impairment. *Neurobiol Aging.* 2007;28:1889–1903.
- Huber R, Aschoff AJ, Ludolph AC, Riepe MW. Transient global amnesia. Evidence against vascular ischemic etiology from diffusion weighted imaging, *J Neurol* 249 (2002), pp. 1520–1524.
- Ingvar DH, Schwartz MS. Blood flow patterns induced in the dominant hemisphere by speech and reading. *Brain* 1974;97: 273-278
- Jak AJ, Bangen KJ, Wierenga CE, Delano-Wood L, Corey-Bloom J, Bondi MW. Contributions of neuropsychology and neuroimaging to understanding clinical subtypes of mild cognitive impairment. *Int Rev Neurobiol.* 2009;84:81-103.
- Johnson M K. In: Awareness of Deficit After Brain Injury: Clinical and Theoretical Issues. Prigatano G P, Schacter D L, editors. New York: Oxford Univ. Press; 1991. pp. 176–197. ISBN 0195059417.
- Johnson SC, Baxter LC, Susskind-Wilder L, Connor DJ, Sabbagh MN, Caselli RJ. Hippocampal adaptation to face repetition in healthy elderly and mild cognitive impairment. *Neuropsychologia.* 2004;42:980–989.
- Johnson SC, Schmitz TW, Moritz CH, Meyerand ME, Rowley HA, Alexander AL, Hansen KW, Gleason CE, Carlsson CM, Ries ML, Asthana S, Chen K, et al. Activation of brain regions vulnerable to Alzheimer's disease: The effect of mild cognitive impairment. *Neurobiol Aging.* 2006;27:1604–1612.
- Kalpouzos G, Eustache F, Desgranges B. Cognitive reserve and neural networks in normal aging and Alzheimer's disease. *Psychol Neuropsychiatr Vieil.* 2008 Jun;6(2):97-105.
- Kircher TT, Weis S, Freymann K, Erb M, Jessen F, Grodd W, Heun R, Leube DT. Hippocampal activation in patients with mild cognitive impairment is necessary for successful memory encoding. *J Neurol Neurosurg Psychiatry.* 2007;78:812–818.
- Mandzia JL, McAndrews MP, Grady CL, Graham SJ, Black SE. Neural correlates of incidental memory in mild cognitive impairment: An fMRI study. *Neurobiol Aging.* 2009;30:717–730.
- Markowitsch HJ. Organic and psychogenic retrograde amnesia: two sides of the same coin? *Neurocase* 2 (1996), pp. 357–371.
- Markowitsch HJ. Functional neuroimaging correlates of functional amnesia. *Memory* 7 (1999), pp. 561–583.
- Markowitsch HJ. Psychogenic amnesia. *Neuroimage.* 2003;20 Suppl 1:S132-8.

- Matsui M, Imamura T, Sakamoto S, Ishii K, Kazui H, Mori E. Transient global amnesia: increased signal intensity in the right hippocampus on diffusion-weighted magnetic resonance imaging. *Neuroradiology* 44 (2002), pp. 235–238.
- Mazziotta JC, Phelps ME.. Human sensory stimulation and deprivation: positron emission tomographic results and strategies. *Ann Neurol* 1984;15:S50-S60
- Moscovitch M. In: *Memory Distortion: How minds, Brains, and Societies Reconstruct the Past*. Schacter D L, editor. Cambridge, MA: Harvard Univ. Press; 1997. pp. 226–254. ISBN 0674566769.
- Miller SL, Fenstermacher E, Bates J, Blacker D, Sperling RA, Dickerson BC. Hippocampal activation in adults with mild cognitive impairment predicts subsequent cognitive decline. *J Neurol Neurosurg Psychiatry*. 2008;79:630–635.
- Naeser M, Palumbo C, Helm-Estabrooks N. Severe nonfluency in aphasia: role of the medial subcallosal fasciculus plus other white matter pathways in recovery of spontaneous speech. *Brain* 1989;112:1-38.
- Nardone R, Buffone EC, Matullo MF, Tezzon F. Motor cortex excitability in transient global amnesia. *J Neurol* 251 (2004), pp. 42–46.
- Neisser U. *Cognitive Psychology*. New York: Appleton-Century-Crofts; 1967, ISBN 0521485002.
- Nitrini R, Buchpiguel CA, Caramelli P, Bahia VS, Mathias SC, Nascimento CM, Degenszajn J, Caixeta L. SPECT in Alzheimer's disease: features associated with bilateral parietotemporal hypoperfusion. *Acta Neurol Scand*. 2000 Mar;101(3):172-6.
- Peres JF, McFarlane A, Nasello AG, Moores KA. Traumatic memories: bridging the gap between functional neuroimaging and psychotherapy. *Aust N Z J Psychiatry*. 2008;42(6):478-88.
- Petersen SE, Fox PT, Posner MI, Mintun M, Raichle ME. Positron emission tomographic studies of the cortical anatomy of single word processing. *Nature* 1988;331:585-589.
- Rajah MN, D'Esposito M. Region-specific changes in prefrontal function with age: a review of PET and fMRI studies on working and episodic memory. *Brain*. 2005 Sep;128 (Pt 9):1964-83.
- Schacter DL, Reiman E, Curran T, Yun LS, Bandy D, McDermott KB, Roediger HL. Neuroanatomical correlates of veridical and illusory recognition memory: evidence from positron emission tomography. *Neuron*. 1996;17:267–274.
- Schacter DL. Illusory memories: a cognitive neuroscience analysis. *Proc Natl Acad Sci U S A*. 1996;93(24):13527-33.
- Sperling R. Functional MRI studies of associative encoding in normal aging, mild cognitive impairment, and Alzheimer's disease. *Ann NY Acad Sci*. 2007;1097:146–155.
- Vannini P, Almkvist O, Dierks T, Lehmann C, Wahlund LO. Reduced neuronal efficacy in progressive mild cognitive impairment: A prospective fMRI study on visuospatial processing. *Psychiatry Res*. 2007;156:43–57.
- Warren JD, Chatterton B, Thompson PD. A SPECT study of the anatomy of transient global amnesia. *J Clin Neurosci* 7 (2000), pp. 57–59.



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Neuroimaging for clinicians sourced 19 chapters from some of the world's top brain-imaging researchers and clinicians to provide a timely review of the state of the art in neuroimaging, covering radiology, neurology, psychiatry, psychology, and geriatrics. Contributors from China, Brazil, France, Germany, Italy, Japan, Macedonia, Poland, Spain, South Africa, and the United States of America have collaborated enthusiastically and efficiently to create this reader-friendly but comprehensive work covering the diagnosis, pathophysiology, and effective treatment of several common health conditions, with many explanatory figures, tables and boxes to enhance legibility and make the book clinically useful. Countless hours have gone into writing these chapters, and our profound appreciation is in order for their consistent advice on the use of neuroimaging in diagnostic work-ups for conditions such as acute stroke, cell biology, ciliopathies, cognitive integration, dementia and other amnesic disorders, Post-Traumatic Stress Disorder, and many more

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