



**Karolinska
Institutet**

Institutionen för Neurobiologi, Vårdvetenskap och Samhälle

When I show the Beatles then you say: “Ramones!”: imaging semantic memory in Alzheimer’s Disease and Semantic Dementia

AKADEMISK AVHANDLING

som för avläggande av medicine doktorexamen vid Karolinska
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av

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ABSTRACT

Elderly people contacting the health care system because of suspected dementia very often report word forgetfulness, a clinical condition referred as anomia, often one of the first signs of cognitive decline. Considering the complexity of human language it is no wonder that dementia disorders can affect language processing, which in its turn relies heavily on the intactness of the semantic memory system. In an attempt to study language impairment in dementia, this thesis aimed to investigate semantic memory, from its normal degradation in healthy ageing, to its disruption in dementia, and from controlled to unconscious semantic processing. Moreover we chased the anatomical locus of semantic memory with the combination of several neurophysiological and neuroimaging techniques.

In **Study I** we investigated controlled semantic retrieval together with pattern of blood perfusion through the performance of verb fluency (VF) and animal fluency (AF), combined with Single-Photon Emission Computed Tomography (SPECT) in patients suffering from Alzheimer's disease (AD), Mild Cognitive Impairment (MCI), and Subjective Cognitive Impairment (SCI).

In **Study II** we enquired automatic semantic retrieval in healthy young and healthy elderly, combining a novel semantic priming paradigm to Event Related Potential (ERP) Electroencephalography (EEG).

In **Study III** we used the same semantic paradigm and ERP EEG measurement as in Study II to investigate automatic semantic retrieval in AD, Semantic Dementia (SD), and an healthy elderly population. The result was then correlated to measure of blood perfusion by means of Pulsed Continuous Arterial Spin Labelling (PCALS) Magnetic Resonance Imaging (MRI).

In **Study IV** we chased the anatomical locus of semantic memory through the study of grey (GM) and white matter (WM) pathology in AD, SD, and healthy ageing, combining Voxel-Based Morphometry (VBM) MRI and Diffusion Tensor Imaging (DTI) MRI.

We could show that controlled semantic retrieval, and in particular VF is impaired in dementia and that this correlates to hypoperfusion in particular anatomical regions. Moreover, we could prove the automatic semantic retrieval remains stable under the span of healthy adulthood while controlled retrieval is not, and that this processes activates neurophysiologically comparable neural networks for healthy young as well as for healthy elderly. In addition we could show that automatic spread of activation is spared in mild dementia despite the deviant result in measures of controlled semantic processes and we found a possible early marker differentiating SD from AD and healthy ageing. We could even associate patterns of hypoperfusion to impairment in controlled semantic memory processing, this indicating that the altered electrophysiology of dementia patients is closely related to their structural and baseline blood degeneration. Finally we could detect different patterns of GM and WM loss in the AD compared to the SD group. In particular we could detect a specific area of WM disruption significantly separating AD from SD.