“Reduced hippocampal metabolism in MCI and AD: Automated FDG-PET image analysis”, Mosconi et al. (2005)

**DESIGN:**

**Aim:** To evaluate voxel-based analysis (VBA) for the hippocampus in order to derive a hippocampus mask computer program (HipMask) to automatically sample for indications of Alzheimer’s disease (AD) and mild cognitive impairment (MCI) before clinical symptoms are present.

**Hypothesis:** Negative VBA findings are due to a failed spatial alignment of memory-related structures such as the hippocampus that are prone to high anatomic variability with aging and neurodegeneration; therefore reductions in glucose metabolism (MRglc) of the hippocampus of healthy individuals are premature symptoms of dementia.

**Null Hypothesis:** Correlations between negative VBA findings and future development of dementia are due to chance.

**METHOD:**

**Research Method:** Longitudinal study

**Sampling Method:** Opportunity sampling was used to first gather subjects from New York University, then purposive sampling was employed when subjects were medically examined and excluded if there were detections of brain-damaging conditions.

**Subjects:** 84 subjects who ranged from ages 50 to 85 and were included in the study. Subjects received an extensive screening and diagnostic battery of medical, neurologic, psychiatric, and neuropsychological tests, and MRI examinations. They were excluded if there was evidence of possible brain-damaging conditions. Two study cohorts were used: a cohort of 48 subjects was used in to develop the HipMask, while another cohort of 36 subjects was used in the program’s implementation.

**Apparatus:**

- MRI – MRI was used in the study to define the hippocampal region and also obtain hippocampal volume data from subjects.
- PET – PET uses radioactively-sensitive glucose, and was applied to demonstrate hippocampal metabolic activity.
- HipMask – HipMask is a novel computer program that was created to obtain approximations of hippocampal metabolic activity in PET.

**Procedure:** Subjects received a MRI scan protocol of the brain. An anatomic MRI elderly brain template was created from the subjects’ data to provide a representative template image of the sample, and the HipMask computer program template was constructed. PET scans were conducted and HipMask was applied. Clinical checkups were given annually. Subjects were observed for 9-24 years for development of dementia in the form of AD or MCI.

**FINDINGS:**

**Results:** There were correspondences between observations via the HipMask and future development of dementia. Subjects who eventually developed forms of dementia demonstrated less hippocampal glucose metabolic rates on PET scans than subjects that remained cognitively stable later on. There was an 80 to 85% accuracy of detections via the program; however differences were not distinguishable between patients that developed AD or MCI.

**Conclusions:** The study supported the initial hypothesis by suggesting that hippocampal metabolic reductions can be used to reliably detect early stages of dementia before symptoms occur such as notable functional deficits. This finding opposes previous knowledge, as hippocampal activity on previous PET scans was previously ignored. The development of dementia is shown as a gradual process that begins years before clinical symptoms are prominent. Individuals develop the diseases slowly through reductions in the functions of memory-related structures, which can be detected via the HipMask. The discovery of this can lead to greater development of drugs to treat the disease and further advances in technology for medical and psychological understandings.

**EVALUATION:**

**Controls:** Subjects were excluded from the study if the MRI detected evidence of conditions affecting the brain or function to gather subjects of similar cognition; same medical examinations were given to subjects; same clinical tools were used throughout study to reduce variability of results because of technology; subjects were extracted from NYU to create low participant variability

**Cultural Influences:** The study was conducted in USA, thus it was an ethnocentric study and results cannot be cross-culturally generalized.

**Influence of Gender:** Clinical data showed no notable differences between sexes, which were not controlled for primarily.

**Method Strength:** In depth investigation of brain’s activity over time; triangulation of observers who made unanimous judgements to confirm observations and increase inter-rater reliability; ecologically valid study; replicable longitudinal study

**Method Limitations:** Low generalization of findings because of small sample size and little participant variability; results may not be representative of condition; difficult to control variables of study in order to identify cause-and-effect relationships; time consuming; replications are required to confirm findings since they challenge past scientific beliefs

**Ethical Concerns:** Written informed consent was obtained from subjects after procedure was explained; confidentiality was guaranteed

**Generalization:** Since the study used a fairly small sample size and there was little participant variability, the results of the study are not generalizable among the entire population. The study can however contribute to theoretical and inferential generalizations regarding the issue, which will lead to future investigations to be conducted to confirm findings of the study.

**Effectiveness of Study:** Mosconi offers a novel method to diagnose AD and MCI before symptoms are present through observations of hippocampal metabolic reductions by the HipMask program. The findings are consistent with the universal observation that when symptoms of the dementia are evident, there are substantial cortical MRglc reductions. Examinations of hippocampal activity are suggested to be useful to characterize the patient’s stage of MCI particularly when memory loss by neocortical damage is minimal. Hippocampal metabolic reductions can be investigated using a new automated sampling technique, the HipMask program and PET, or by the region of interest (ROI) sampling method; however HipMask is time efficient and precise enough for hippocampus sampling on PET scans. With further research and exploration into the HipMask, it will enable the future automated analysis of larger data sets with greater diagnostic accuracy.

**Criticisms:** Findings indicate the presence of hippocampal metabolic reductions in both MCI and AD, which was not reported by most past studies. Mosconi’s HipMask challenges the idea that hippocampal MRglc reductions are not apparent in AD. The ability of medical technology to detect the brain’s functions accurately can also be questioned for the findings’ validity. The study states that further research needs to be conducted using the HipMask on other groups of patients, and even patients with other clinical conditions that may have possible effects on hippocampal size, spatial displacement, and function. Future studies that yield similar results would confirm her findings.

**Similar Studies:** Gomez-Isla et al. (1996) studied cortex neuron atrophy in dementia but ignored hippocampal metabolic activity. Chetelat et al. (2003) was a VBA study that reported a correlation between hippocampal MRglc and memory performance; however it failed to observe hippocampal group differences of cognitive conditions.

**School of Thought:** Use of technology to examine cognition, functionalism

**Learning Outcomes:**
- Discuss how and why particular research methods are used at the cognitive level of analysis (longitudinal study)
- Discuss the use of technology in investigating cognitive processes (PET scans and HipMask to detect AD and MCI)
- Explain how biological factors may affect one’s cognitive process (AD, MCI)

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