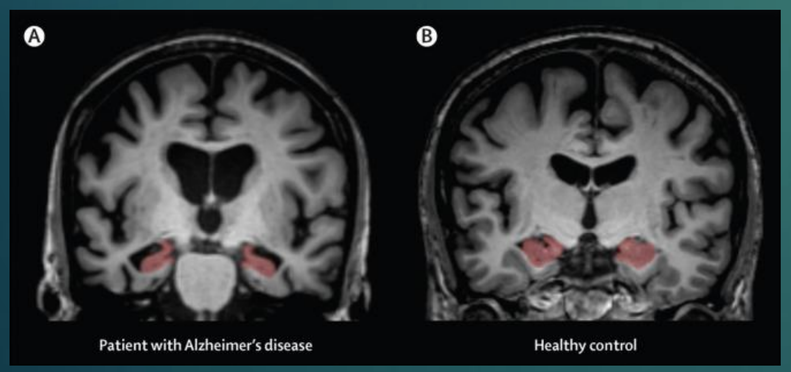
Studying Alzheimer's Disease with MRI and Positron Emission Tomography Scanning

22

Introduction: Alzheimer's Disease (AD) is a progressive neurodegenerative disease that causes a gradual increase of dementia and brain atrophy (Ramachandran, 2016). The dementia is caused by the death of neurons in the brain and this results in the inability to remember or think clearly. Brain atrophy can be seen on the overall gray matter (cortex) and most commonly seen in the medial temporal lobe. With neuroimaging modalities it possible to detect changes in the brain earlier and more precisely track the disease. Structural MRI, Functional MRI and Positron emission tomography each offer unique capabilities to research and study AD.

Structural MRI

- Allows for 3-D examination and measurement of brain volume loss (Johnson et al., 2012)
- Can provide a clear distinction between gray matter, white matter, and cerebrospinal fluid (Adlard, 2014).
- Can reveal structural changes of the medial temporal and memory structures year before full blown AD(Kivisto, Pihlajamamaki & Soininen, 2014).
- Atrophy in the medial temporal lobe is considered an early determining factor for AD(Kivisto, Pihlajamamaki &Soininen, 2014).
- Medial temporal lobe atrophy is then followed by atrophy in the hippocampus, amygdala, and Para hippocampus (Johnson, et al., 2012).
- Ventricular enlargement(Ferreira & Busatto, 2011).
- Relatively easy and non-invasive way to evaluate early AD(Ferreira, Busatto, 2011).
- Can also be used to monitor treatment effects over time(Khachaturian & Weiner, 2005).



Teipel, Stefan et al. (2015)

Functional MRI (fMRI)

- fMRI is used to visualize the functional changes within the brain of AD patients (William, 2016).
- Can reveal alterations of the brain in the preclinical stage of the disease (the stage before symptoms are apparent) (William, 2016).
- fMRI does this by measuring blood flow in the brain (William, 2016).
- This is helpful in determining which parts of the brain are active(William, 2016).
- Blood will flow to where neurons are active (William, 2016).
- Goal of fMRI is to develop a way to recognize functional changes earlier in the disease, before irreversible structural damage occurs (Kivisto, Pihlajamamaki & Soininen, 2014).
- During the exam the patient may be asked to memorize, recite a task or rest to see which areas of the brain are activated(Johnson, et al., 2012).
- Patients with mild AD have decreased fMRI activation in the medial temporal lobe and hippocampus-during the formation of new memories (Johnson, et al., 2012).
- Can be used to track the disease in the early stages and test new medications that could stop further damage(Johnson, et al., 2012).
- fMRI also demonstrates hyperactivity in the prefrontal cortex (Johnson, et al., 2012).
- Temporary increase of activity in the prefrontal cortical region-which is believed to be an attempted compensatory mechanism during AD during the early stages.(Johnson, et al., 2012)
- Hyperactivity in the prefrontal cortex can be a predictor of cognitive decline (Johnson, et al., 2012).

Positron emission tomography (PET)

- Molecular imaging method that demonstrates the location and severity of neuronal and synaptic loss (Foster, 2005).

- PET scanner is an imaging device used along with a radiotracer that is injected into the patient (Foster, 2005).
- Once injected, the tracer interacts with elections on the body and this interaction produces an energy that the scanner can detect (Khachaturian & Weiner, 2005).
- The scanner then creates a 3-D image of the area of study (Khachaturian & Weiner, 2005).
- Studies are performed with patient at rest (Khachaturian & Weiner, 2005).
- Can also be used to visualize and measure cerebral glucose metabolism within the brain (Khachaturian & Weiner, 2005).
- Characteristic pattern found with AD patients- glucose hypometabolism in the temporoparietal cortex(Busatto & Ferreira, 2011).
- Caused by neuronal cell loss and decreased synaptic activity (Ramachandran, 2016).
- Hypometabolism measurements are progressive and correlate with dementia severity(Khachaturian & Weiner, 2005).
- Patients with severe AD have reductions in cerebral metabolic glucose rate throughout the whole brain(Khachaturian &Weiner, 2005).

Amyloid Plaques

- Investigation of the accumulation of B-amyloid peptide in the brain (Busatto & Ferreira, 2005).
- Hallmark of AD(Busatto & Ferreira, 2005).
- A negative result would mean AD is unlikely(Busatto & Ferreira, 2005).
- Tracer molecules are injected intravenously, travel to the brain and attach to amyloid plaques (Busatto & Ferreira, 2005).
- Help locate areas in brain that may be affected (Busatto & Ferreira, 2005).
- Images provided by this modality visualize how the amyloid plaques affect synaptic activity and neurodegeneration (Nordberg, 2011).
- Plaques begin years before clinical symptoms of the disease are apparent (Busatto & Ferreira, 2011).

Tau Tangles

- Tau is a microtubule protein that is responsible for maintaining the structure of the neurons (William, 2013)
- When they get twisted and tangles together, it impairs their ability to support synaptic connections (William, 2013).
- Through PET scans it has been confirmed that with advancing age, there can be an accumulation of tau proteins in the medial temporal lobe (William, 2013).
- PET scans have confirmed that higher tau tangle levels in the medial temporal lobes equals greater decline in memory (William, 2013).
- Tracer molecule will attached to tau proteins (William, 2013).

Conclusion

- Neuroimaging modalities such as MRI and PET scanning provide important insight into the pathological process of AD and monitoring of drug therapy.

- Further research is needed to visualize the pathological and functional process and decline of AD

- Medial temporal lobe atrophy and parietal hypometabolism is a common finding in patients with AD

- The research and study of AD with these modalities can hopefully one day provide a prevention and/or cure for this mentally crippling disease.

References

Adlard, P., Tran, B., Finkelstein, D., Desmond, P., Johnston, L., Bush, A., Egan, G. (2014, October) A review of b-amyloid neuroimaging in Alzheimer's disease. *Frontiers in neuroscience*. 8, 1-23. doi:10.3389/fnins.2014.00327

Ferreira, L. & Busatto, G. (2011) Neuroimaging in Alzheimer's disease current role in clinical practice and potential future applications. *Clinics, (S1)* 19-24. Retrieved from http://www.scielo.br/pdf/clin/v66s1/03.pdf

Johnson, K. A., Fox, N. C., Sperling, R. A., & Klunk, W. E. (2012). Brain Imaging in Alzheimer Disease. *Cold Spring Harbor Perspectives in Medicine*, *2*(4), a006213. http://doi.org/10.1101/cshperspect.a006213

Khachaturian, Z., Weiner, M. (2005) The use of MRI and PET for clinical diagnosis of dementia and investigation of cognitive impairment: a consensus report. *Alzheimer's Association, Chicago, IL*.

Kivisto, J., Soininen, H., Pihlajamaki, M. (2014) *Functional MRI in Alzheimer's Disease*. http://dx.doi.org/10.5772/47912

Nordberg, A. (2011). Molecular imaging in Alzheimer's disease: new perspectives on biomarkers for early diagnosis and drug development. *Alzheimer's Research & Therapy*, *3*(6), 34. http://doi.org/10.1186/alzrt96

Ramachandran, T. (2016). *Alzheimer's disease imaging: Overview*. Retrieved from http://emedicine.medscape.com/article/336281-overview

William, S. (2013). Mapping the brain's decline. *Nature, 502*, S84-S85.