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Analysis of Imaging Database and Identifying Novel MRI Diffusion Abnormalities in Alzheimer's Disease

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ABSTRACT

Alzheimer's disease (AD) is presumably caused by two neuropathological protein markers: amyloid beta (Aβ) and neuro fibrillary tangles. Alzheimer's Disease Neuroimaging Initiative (ADNI) collects high quality patient data from standardized clinical trials using Magnetic Resonance Imaging (MRI), Positron Emission Tomography (PET), and Cerebral Spinal Fluid (CSF) biomarkers to diagnose and evaluate the effectiveness of treatment for AD. MRI and PET screening for Alzheimer's Disease aim to find structural, functional, and neurochemical abnormalities causing or caused by AD brain diffusion tensor imaging (DTI) and Resting State functional MRI (RSfMRI) are emerging AD MRI tools. Tau PET is a promising method for predicting cognitive abnormalities, more accurate than amyloid PET and MRI. To our knowledge, metal exchange among key bio metals like Fe, Cu, Mn, and Ca (transmetallation) has not yet been explored in neurobiology of AD. However, our research in carbohydrate and animal protein matrix (fruits and chicken eggs) has demonstrated transmetallation and chelation in such biological media. Exogenous chemical stress from radiology contact agents or environmental metallo-toxins could also alter homeostasis of brain bio metals. Iron transporter proteins in deep brain areas have been researched with little success in Alzheimer's and Parkinson's and their role in protein aggregation and oxidative stress, leading to neuronal loss is not clear. We not that when iron is shielded from bioreactions it is non-magnetic while if it takes part in metal exchange it could be in charged states that are paramagnetic. We hypothesize that changes in brain iron levels or brain iron electron charge states are reflected in magnetic susceptibility changes in white and gray matter leading to diffusion tract abnormalities in MRI of the AD brain. It is not possible to perform invasive biopsy and thus pathologically correlate iron or any other metal in AD brain with cognitive dysfunction in AD patients during their lifetime or even post-mortem since the disease is not in the presence or absence of the metals but presumably in the functional form of the propose biometals (Fe, Cu) in the neuro-biochemical pathway. Both diffusion MRI and magnetic susceptibility measurements to localize abnormal iron provide complementary information and are affected in AD. We have analyzed ADNI database for DTI abnormalities and have identified two parameters (Fractional Anisotropy and Mean Diffusivity) that show significant fluctuations only in the Fornix region with AD progression that we are modeling as presumably due to abnormal CSF dynamics.

INTRODUCTION

- MRI measurements of whole brain and hippocampus volume changes are mostly focused on imaging techniques for AD progression.[1]
- Brain capacity In the elderly declines while cerebrospinal fluid volume grows.[1]
- The entorhinal cortex and hippocampus play a significant role in the early stages.[2]
- AD is a complex illness resulting from inherited and environmental factors[3]
- Metal ions are essential for cell structure, gene expression, antioxidant defense, and neurotransmission.[3]

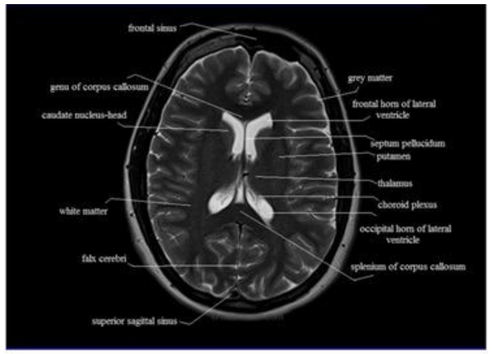

Figure 1: The glymphatic system clears amyloid-β (Aß), which is the main component of Alzheimer's disease brain plaques. Blocking glymphatic transport causes Aß to accumulate, And deleting the aquaphorin-4 gene impairs clearance of soluble Aß. [5][6]

METHOD

- We were able to utilize research-based projects from meta-analysis acquisitions.
- We compared V11 and V31 using cleaned Mean and Fractional Diffusion date from twelve columns including ALIC, ACR GGC, GCH FX, and GCC (left and right) for the first and second year.[5]
- Mean, Standard Deviation, and Cov% were calculated.[5]

DISCUSSION

- The Fornix areas bilaterally suffer most for AD patients due to FA loss.[5]
- Covariance significantly increases in the third year, suggesting heterogeneity of FA values among survivors.[5]
- MD increases in brain regions during AD, particularly in the bilateral Fornix, needing more study and modeling.[5]
- COV% decreases in most regions, except Cingulum of Hippocampus, showing varied aging effects among patients in this region.[5]
- Survivors with high COV% show uneven FA decreases, while MD increases (with decreasing COV%) independent of progression severity, mainly in the Fornix area.[5]
- COV trend is crucial in our research, identifying AD markers as patients age.[5]
- We believe it is the Fornix area that characterizes and defines AD progression, with its FA and MD patterns.[5]

Table V11 - Fractional Anisotropy

Potential Biomarkers	FA_Anterior limb of internal (ALIC)_Left	FA_Anterior limb of internal (ALIC)_Right	FA_Anterior corona radiata (ACR) Left	FA_Anterior corona radiata (ACR) Right	FA_Cingulum (CGC) Left	FA_Cingulum (CGC) _Right	FA_Cingulum (hippocampus) _GCH_Left	FA_Cingulum (hippocampus) _CGH_Right	FA_Fornix (FX)_Left	FA_Fornix (FX)_Right	FA_Genu of corpus callosum (GCC)_Left	FA_Genu of corpus callosum (GCC)_Right
1st Yr. Mean	0.355	0.373	0.275	0.284	0.269	0.258	0.223	0.256	**0.264322**	**0.354942**	**0.373**	**0.275**
1st Yr. Std Dev. (SD)	0.036	0.038	0.035	0.038	0.028	0.03	0.03	0.033	**0.0435**	**0.0402**	**0.064**	**0.064**
1st Yr. Cov%= SD/Mean *100	**10.1**	**10.1**	**12.8**	**13.3**	**10.4**	**11.2**	**13**	**12.7**	**16.5**	**15.3**	**15.2**	**15**

Table V31 - Fractional Anisotropy

Potential Biomarkers	FA_Anterior limb of internal (ALIC)_Left	FA_Anterior limb of internal (ALIC)_Right	FA_Anterior corona radiata (ACR) Left	FA_Anterior corona radiata (ACR) Right	FA_Cingulum (CGC) Left	FA_FA_ Cingulum (CGC) _Right	FA_Cingulum (hippocampus) _GCH_Left	FA_Cingulum (hippocampus) _CGH_Right	FA_Fornix (FX)_Left	FA_Fornix (FX)_Right	FA_Genu of corpus callosum (GCC)_Left	FA_Genu of corpus callosum (GCC)_Right
3rd Yr. Mean	0.352	0.368	0.269	0.274	0.261	0.255	0.219	0.251	**0.164242**	**0.211685**	0.413	0.414
3rd Yr. Std Dev (SD)	0.037	0.038	0.032	0.035	0.025	0.03	0.03	0.032	**0.0515**	**0.044**	0.049	0.053
3rd Yr. Cov%= SD/Mean *100	**10.6**	**10.3**	**12**	**12.9**	**9.6**	**11.4**	**13.4**	**12.7**	**31.4**	**20.7**	**11.9**	**12.7**

Table V11 - Mean Diffusion

Potential Biomarkers	MD_Anterior limb of internal (ALIC)_Left	MD_Anterior limb of internal (ALIC)_Right	MD_Anterior corona radiata (ACR) Left	MD_Anterior corona radiata (ACR) Right	MD_Cingulum (CGC) Left	MD_Cingulum (CGC) _Right	MD_Cingulum (hippocampus) _GCH_Left	MD_Cingulum (hippocampus) _CGH_Right	MD_Fornix (FX)_Left	MD_Fornix (FX)_Right	MD_Genu of corpus callosum (GCC)_Left	MD_Genu of corpus callosum (GCC)_Right
1st Yr. Mean	0.001	0.001	0.001	0.001	0.001	0.001	**0.000968**	**0.000946**	**0.00135**	**0.001303**	0.001	0.001
1st Yr. Std Dev. (SD)	0.001	0.000	0.000	0.000	0.000	0.000	**0.0001**	**0.0001**	**0.000297**	**0.000273**	0.000	0.000
1st Yr. Cov%= SD/Mean *100	**11.9**	**9.8**	**10.9**	**11.7**	**11.6**	**10.4**	**13.2**	**11.3**	**22**	**20.9**	**13.7**	**13.7**

Table V31 - Mean Diffusion

Potential Biomarkers	MD_Anterior limb of internal (ALIC)_Left	MD_Anterior limb of internal (ALIC)_Right	MD_Anterior corona radiata (ACR) Left	MD_Anterior corona radiata (ACR) Right	MD_Cingulum (CGC) Left	MD_Cingulum (CGC) _Right	MD_Cingulum (hippocampus) _GCH_Left	MD_Cingulum (hippocampus) _CGH_Right	MD_Fornix (FX)_Left	MD_Fornix (FX)_Right	MD_Genu of corpus callosum (GCC)_Left	MD_Genu of corpus callosum (GCC)_Right
3rd Yr. Mean	0.001	0.001	0.001	0.001	0.001	0.001	**0.001006**	**0.000979**	**0.002563**	**0.002253**	0.001	0.001
3rd Yr. Std Dev (SD)	0.000	0.000	0.000	0.000	0.000	0.000	**0.000160**	**0.000130**	**0.00043**	**0.00031**	0.000	0.000
3rd Yr. Cov%= SD/Mean *100	**10.7**	**11.3**	**8**	**9.2**	**7.5**	**6**	**15.9**	**13.3**	**16.8**	**13.3**	**10.6**	**11.4**

RESULTS

- Metals are vital in the body such as enzyme cofactors and for neuronal communication.[3]
- The body regulates metal transit and reactivity with a protein network.[3]
- Chronic metal exposure from anthropogenic activity is increasing.[3]

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