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Evaluation of Brain Changes in Alzheimer disease Using MRI

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Abstract
Alzheimer's disease (AD) is a multifaceted disease in which cumulative pathological brain insults result in progressive cognitive decline that ultimately leads to dementia. The aim of this article was to evaluate the structural MRI changes in AD, focusing particularly on atrophy in typical late-onset of AD. Also to identify other promising biomarkers that can set structural loss in the broader context of functional changes at different stages of the disease.
The study was conducted in Sudan, 302 subjects were enrolled (200 Male and 102 female).All subjects underwent thorough clinical and cognitive assessments at the time of their MRI scans.MRI studies were performed on 1.5 Tesla Toshiba whole body MR systems using standard imaging head coil. Routine brain MRI was performed in 3 orthogonal planes, including at least T1, T2, and fluid-attenuated inversion recovery (FLAIR) weighted images.
The result of the study revealed that age is the most important risk factor for Alzheimer disease (AD) because it is independently linked to brain atrophy, the common affected age group (70 – 80) years, particularly more than 80 years. The generalized atrophy has been observed in 78.1% of the cases. Furthermore, ventricular enlargement was seen in 65% of the cases.
Structural MRI markers now support earlier and more-precise diagnosis and measurement of progression. The presences of atrophy as well as ventricular changes are a partially validated marker for early diagnosis of the disease.
Keywords: *Alzheimer's disease, MRI, Brain Atrophy, Cerebral Ventricles.*

Introduction

Alzheimer's disease (AD) is a multifaceted disease in which cumulative pathological brain insults result in progressive cognitive decline that ultimately leads to dementia. Amyloid plaques, neurofibrillary tangles (NFTs), neuro degeneration, and inflammation are the well-established pathological hallmarks of AD(Prins and van Swieten, 2010). Neuronal and synaptic losses appear to be key determinants of cognitive impairment in AD (Terry et al., 1991). If neuronal loss leads to cerebral atrophy, then it can be expected that cognitive decline and atrophy will be closely associated(Vemuri and Jack, 2010).

Imaging modalities can be thought of as in vivo indicators of specific pathologies. Amyloid labeling PET ligands, such as ^{11}C Pittsburgh compound B (PIB) primarily measure brain

amyloid plaque load (Klunk et al., 2004). MRI, on the other hand, is an in vivo indicator of neuro degeneration; Serial multi-modality imaging studies which are sensitive to the different aspects of Alzheimer's disease pathology are an ideal way to answer questions about the temporal sequencing of different pathologic features of the disease (Jack et al., 2008).

MRI measures brain morphometry and therefore can capture gray matter atrophy related to the loss of neurons, synapses, and dendritic de-arborization that occurs on a microscopic level in AD; white matter atrophy related to the loss of structural integrity of white matter tracts, presumably resulting from demyelination and dying back of axonal processes; and *ex vacuo* expansion of cerebrospinal fluid (CSF) spaces (Vemuri and Jack, 2010).

In research, imaging is helping address many of the scientific questions outlined in (Selkoe et al., 2012): providing insights into the effects of AD and its temporal and spatial evolution. Furthermore, imaging is an established tool in drug discovery, increasingly required in therapeutic trials as part of inclusion criteria, as a safety marker, and as an outcome measure.

MRI-based measures of atrophy are regarded as valid markers of disease state and progression for several reasons. Atrophy seems to be an inevitable, inexorably progressive concomitant of neuro degeneration. The topography of brain tissue loss correlates well with cognitive deficits, both cross-sectionally and longitudinally (Vemuri et al., 2008). The earliest sites of tau deposition and MRI-based atrophic changes typically lie along the perforant (polysynaptic) hippocampal pathway (entorhinal cortex, hippocampus and posterior cingulate cortex), consistent with early memory deficits (Thompson et al., 2003).

In this article, we aim to evaluate the structural MRI changes in AD, focusing particularly on atrophy in typical late-onset of AD. We also address other promising biomarkers that can set structural loss in the broader context of functional changes at different stages of the disease.

Methods:

This study conducted in Sudan, 302 subjects were enrolled in the study (200 Male and 102 female). All subjects underwent thorough clinical and cognitive assessments at the time of their MRI scans. Each subject's cognitive evaluation included: (i) the Mini-Mental State Examination (MMSE) to provide a global measure of mental status; (ii) the Alzheimer's disease Assessment Scale-Cognitive Subscale (ADAS-Cog). They have been classified as predementia, early stage of AD, moderate AD and late stage of AD. Consent was obtained and the Ethical Committees of the Hospital in which the work was performed approved the study.

MRI studies were performed on 1.5 Tesla Toshiba whole body MR systems using standard imaging head coil. Routine brain MRI was performed in 3 orthogonal planes, including at least T1, T2, and fluid-attenuated inversion recovery (FLAIR) weighted images. T1-weighted images after intravenous gadolinium-based contrast material administration were obtained in at least 2 planes.

Coronal-oblique T1-weighted images are used for the assessment of medial temporal lobe and hippocampal atrophy. They are obtained in a plane orthogonal to the long axis of the hippocampus; this plane is orientated parallel to the brainstem. These should be thin-section images and are ideally obtained by reformatting a sagittal 3D T1 sequence through the entire brain. Additional sagittal reconstructions will enable the assessment of midline structures as well as parietal atrophy, which may be involved in certain neurodegenerative disorders. FLAIR images are used to assess global cortical atrophy (GCA), vascular white matter hyper intensities and infarctions.

Result:

Table 1: Gender distribution

	Frequency	Percent
Male	202	66.9
Female	100	33.1
Total	302	100.0

Table 2: Age distribution

	Frequency	Percent
50 - 59	11	3.6
60 - 69	4	1.3
70 - 79	75	24.8
> 80	212	70.2
Total	302	100.0

Table 3: Subject classification

	Frequency	Percent
Pre-dementia	107	35.4
Early stage of AD	33	10.9
Moderate stage of AD	96	31.8
Late stage of AD	66	21.9
Total	302	100.0

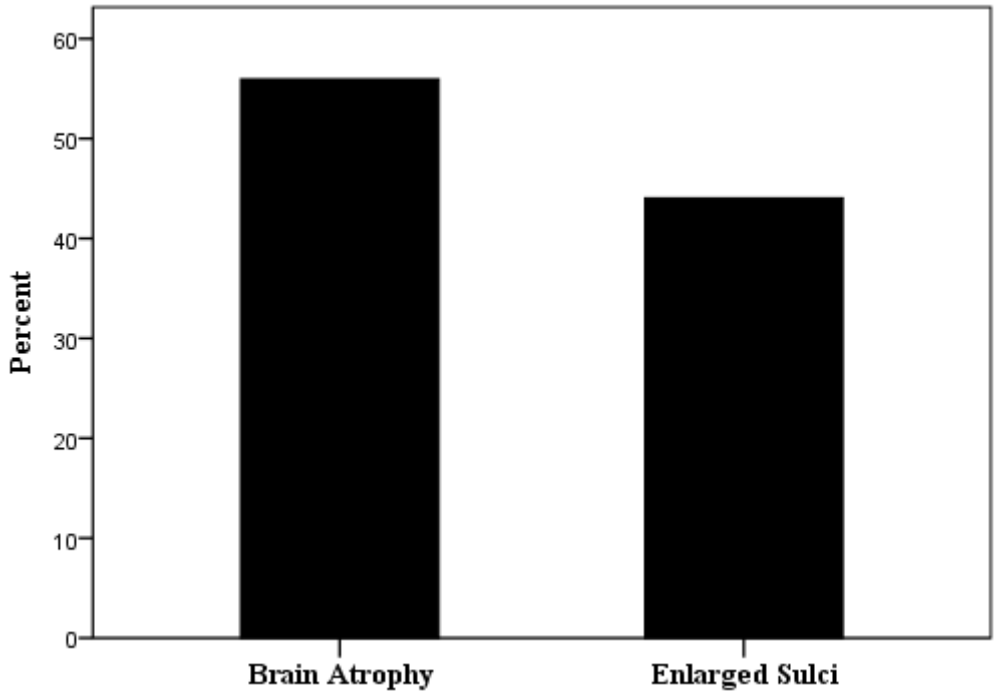

Figure 1: MRI findings

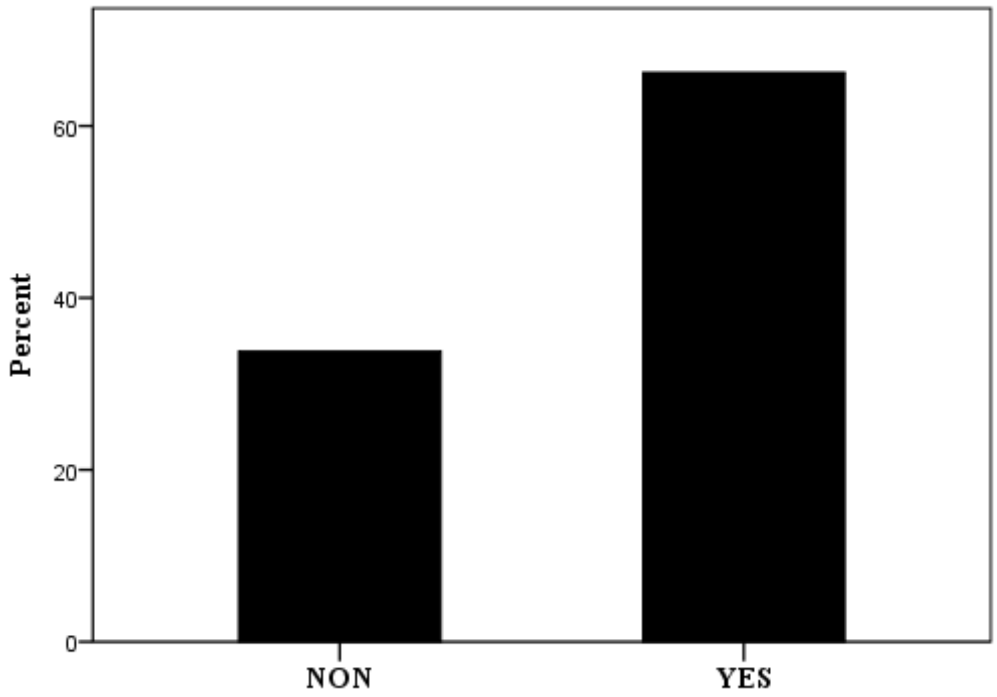

Figure 2: Ventricular size enlargement

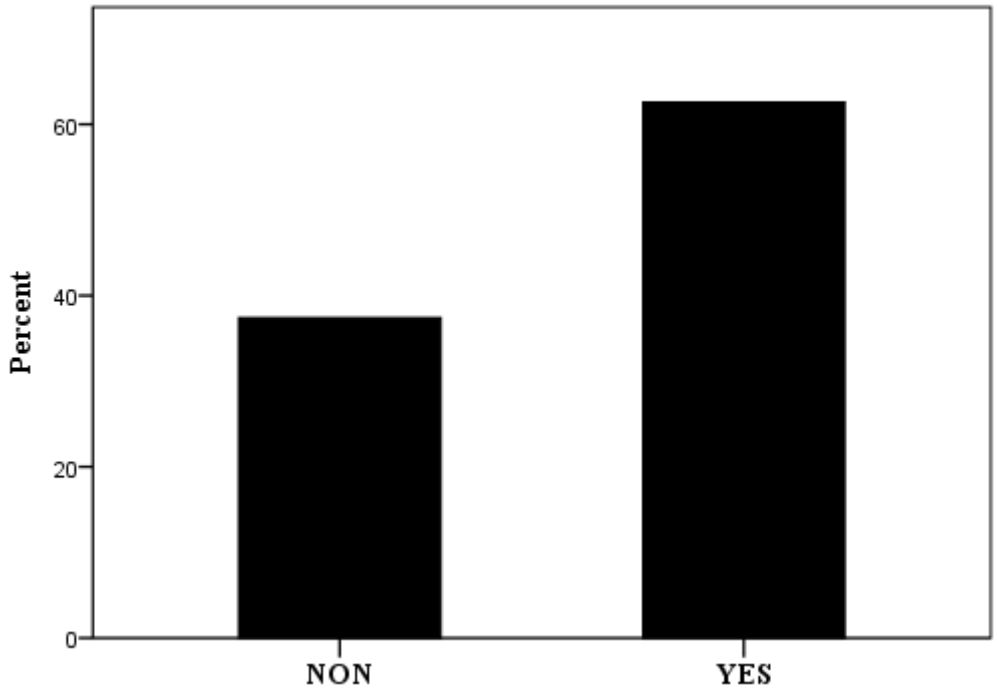

Figure 3: White Matter Lesions (Fazekas Scales)

Table 4: Site of Brain Atrophy

	Frequency	Percent
Hippocampus	46	15.2
Temporal	20	6.6
Genelized Brain Atrophy	236	78.1
Total	302	100.0

Table 5: Correlation between Stage of AD and MRI Finding

		MRI Findings		
		Brain Atrophy	Enlarged Sulci	Total
Types	Pre-dementia	49	58	107
	Early stage of AD	11	22	33
	Moderate stage of AD	70	26	96
	Late stage of AD	39	27	66
Total		169	133	302

Discussion

The aim of this article was to evaluate the structural MRI changes in AD, focusing particularly on atrophy in typical late-onset of AD. We also address other changes that can set structural loss in the broader context of functional changes at different stages of the disease.

Age is the most important risk factor for Alzheimer disease (AD), with the prevalence rising

substantially between ages 65 and 85. AD develops in the context of normal aging, and the brains of elderly adults without dementia have lower brain weight, reduced tissue volume, and expansion of both the cerebral ventricles and sulci. The result of this study showed that the common affected age group (70 – 80) years, particularly more than 80 years. This result was in line with the previous studies (Raji et al., 2009), this is might be due to the fact that the in older age, there is loss of neuronal cells in neocortical, hippocampal, and cerebellar areas, shrinkage of neurons, and suboptimal DNA repair, leading to compromised neuronal integrity and reduction in synaptic density. As a consequence, age is believed to increase risk for AD because it is independently linked to brain atrophy.

Monitoring structural changes in the brain over time is important in observing the progression of the AD. Tracking the disease progression is especially important since atrophy rates can predict subsequent clinical progression of AD. In this study the generalized atrophy has been observed in 78.1% of the cases, because most of the subjects were in different stages of AD rather than Pre-dementia stage. This result was in line the previous studies which revealed that Rates of whole-brain and hippocampal atrophy are sensitive and powerful markers of progression of neuro degeneration and, as a result, are increasingly used, along with clinical metrics, as outcomes in clinical trials of potential disease-modifying therapies (Ridha et al., 2006).

Ventricular enlargement is a highly reproducible measure of disease progression, owing to the high contrast between the CSF and the surrounding brain tissue on T1-weighted images. In this study ventricular enlargement was seen in 65% of the cases, the result was in line with the study of (Nestor et al., 2008) where the ventricular enlargement has been noticed in 60% of subject with AD. This is might be due to the fact that the cortical regions associated with dynamic changes in ventricular volume are among those that are regarded as most susceptible to AD-related pathologies, including accumulation of amyloid plaques and tau neurofibrillary tangles, metabolic disruption, functional and connectivity alterations (Apostolova et al., 2012). Ventricular enlarge-ment also demonstrated sensitivity to disease progression by way of discriminating between subjects with stable MCI and those that progressed to AD. Furthermore, ventricular enlargement measures would significantly reduce the number of subjects required to demonstrate a change from the natural history of Alzheimer's disease progression.

Structural imaging based on MRI is an integral component of the clinical assessment of patients with suspected AD. Structural MRI markers now support earlier and more-precise diagnosis and measurement of progression. The presences of atrophy as well as ventricular changes are apartially validated marker for early diagnosis of the disease at the MCI stage. Rates of whole-brain and hippocampal atrophy are sensitive and

powerful markers of progression of neuro degeneration and, as a result, are increasingly used, along with clinical metrics, as outcomes in clinical trials of potential disease-modifying therapies.

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