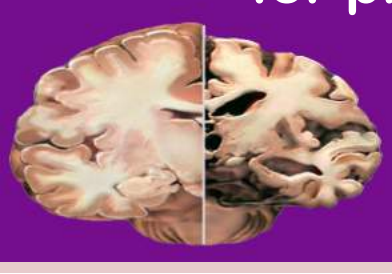
Evaluation of brain functional networks in Mild Cognitive Impairment and Alzheimer's disease individuals Mild Cognitive Impairment as a high risk factor for progression to Alzheimer disease: An fMRI study



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INTRODUCTION

Although progressive functional brain network disorders has been one of the indication of Alzheimer's disease, The major current research on Aging and dementia focus on diagnostics of the cognitive changes of normal aging and Alzheimer Disease (AD), these changes known as Mild Cognitive Impairment (MCI). Functional Magnetic Resonance Imaging (fMRI) is a useful tool to investigate the modifications in functional connectivity, also allow the evaluation of brain changes that occur the progression from healthy aging to MCI and AD. Using fMRI, many studies have extensively investigated functioning and anatomical correlates of the Default mode network (DMN). More importantly, with functional Magnetic Resonance Imaging (fMRI), we investigated resting state network (RSN) activi ties focusing on the Default Mode Network (DMN) resting state (Rs) fMRI data were analyzed by using ICA method.

MCI: A CLININCAL CONCEPT

Mild Cognitive Impairment (MCI) has been actively investigated for the past decade, the term was coined in the late 1980s by the New York University group to identify individuals who were not cognitively normal for age and yet did not have overt dementia. Mild Cognitive Impairment is a medical condition, generally defined as impairment in cognitive abilities (the thinking functions of the brain) greater than expected for age, which does not significantly interfere with daily life and is not severe enough to warrant a diagnosis of dementia. People with MCI have more memory or other thinking problems than would be expected from someone at a similar age, and show some decline in their cognitive skills. While they may experience some increased difficulty in daily activities, people with MCI are mostly able to function independently. The types of Mild Cognitive Impairment MCI vary from person to

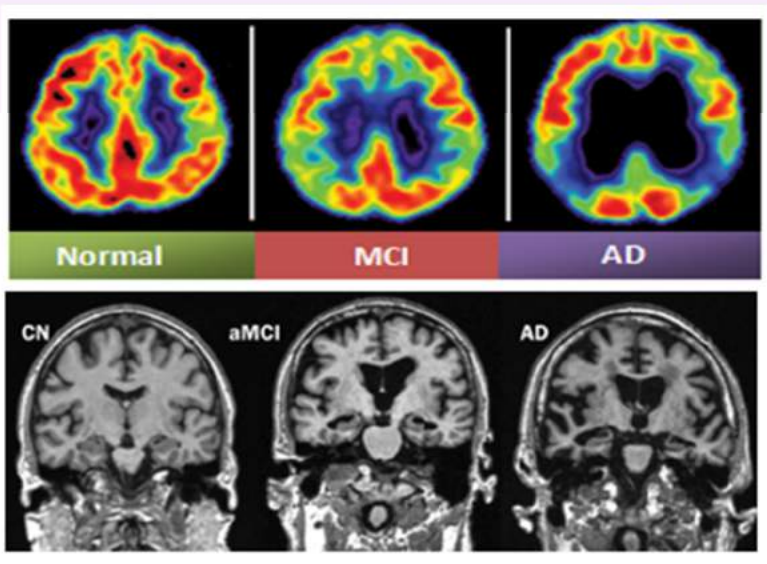

Fig1. Progression of a person developing to Alzheimer's disease
Fig2. Progressive atrophy in an older cognitively normal (CN) subject, an amnestic mild cognitive impairment (aMCI) subject, and an Alzheimer's disease (AD) subject.

Progression and Diagonisis

A person with mild cognitive impairment has an increased risk of developing Alzheimer's disease or another type of dementia. However, only 5 to 10% of people with MCI will progress to dementia each year and in studies to date, typically less than half of people with MCI will progress to dementia and a significant proportion may even improve. Amnestic MCI, where the main problem is memory, has a stronger association with Alzheimer's disease than nonamnestic MCI. In some cases, the brain changes seen in people with amnestic MCI are similar to the changes seen in Alzheimer's disease, although they tend to be less severe. Some people with nonamnestic MCI may develop Front temporal dementia or a case of dementia, and either type of MCI may lead to vascular dementia. So it is not yet possible to predict with certainty whether a specific reason will go on to develop Alzheimer's or another type of dementia, remain stable or improve over time.

Fig3. A Model for Alzheimer's disease (AD) progression by using Biomarkers [Alfa,Beta, Brain structure, Memory

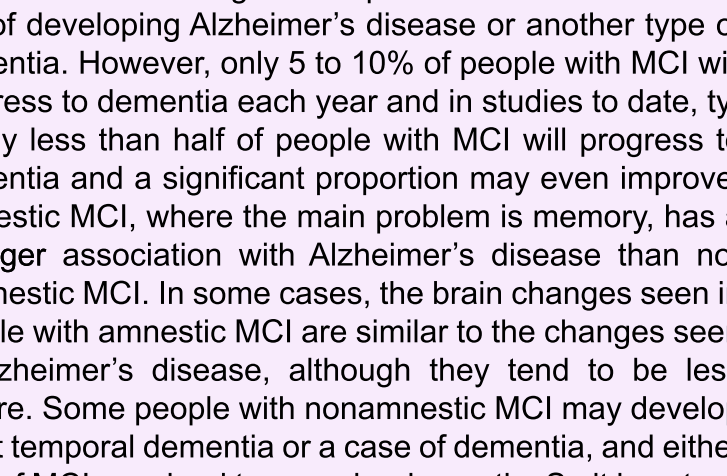

Fig4. Figure 1: Progression of a person developing to AD) from surely MCI to a probable AD.

MATERIALS AND METHODS

The objective of this study is to identify the modifications of the brain functional connectivity in MCI subjects. The subjects were compared with healthy normal cognitively (NC) subjects, particularly, the experimental study focus on the Default Mode Network (DMN), we investigated resting state network (RSN) activities. Resting state (Rs) fMRI data were analyzed by means of (ICA). The data used in experimental study were downloaded from the Alzheimer's disease Neuroimaging Initiative (ADNI) (http://adni.loni.usc.edu/). USC, University of Southern California, USA, We enrolled 51 subjects (age between 60-90 years old) with mixed sex (Female/Male). 22 subjects were affected by Mild Cognitive Impairment (MCI) and 29 were cognitively normal (CN), More importantly, with functional Magnetic Resonance Imaging (fMRI), we investigated resting state network (RSN) in the

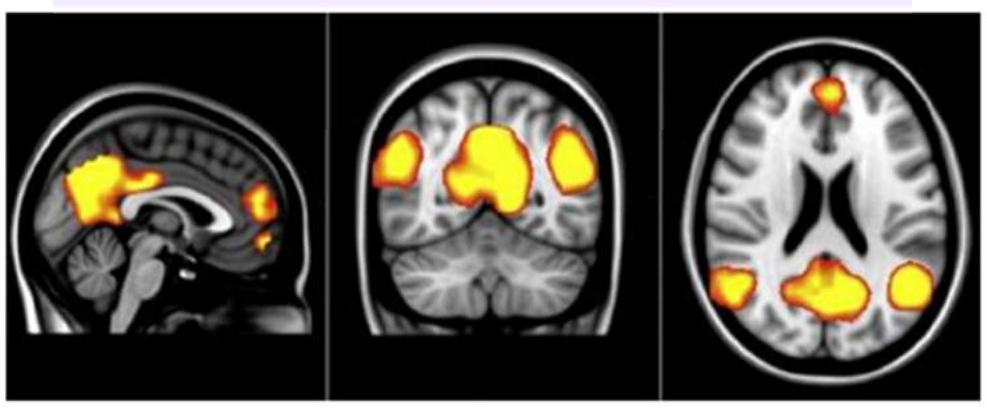

Fig5: The default mode network. Specific brain structures that are particularly active in the resting brain and deactivate during a variety of t asks. Including the medial Prefrontal Cortex (mPFC), Posterior cingulate cortex (PCC) and Anterior cingulate cortex ACC, and the parietal cortex.

IMAGING ACQUISITION AND PREPROCESSING

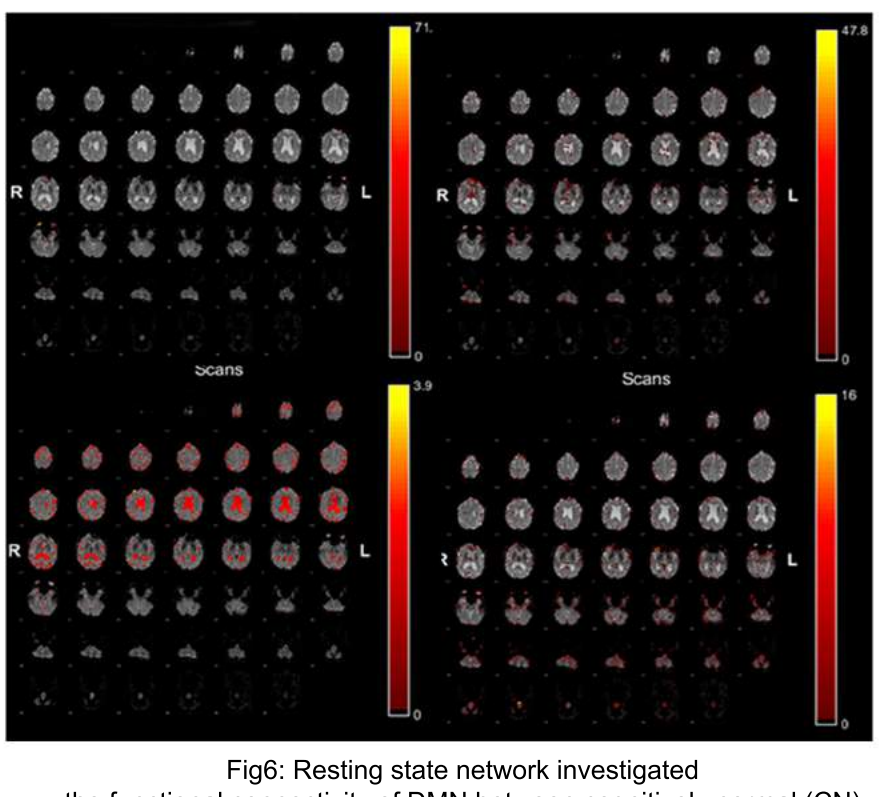

Fig6: Resting state network investigated the functional connectivity of DMN between cognitively normal (CN) and Mild Cognitive Impairment (MCI) patients,

RESULTS

Patients showed decreased functional connectivity within the DMN. The decreased connectivity was observed in the PCC, mPFC, ACC, and hippocampus, MCI converters showed severe decreased functional connectivity compared to non-converters. These results suggest that resting-state fMRI could be helpful in the classification of subjects with MCI, AD and cognitively normal subjects.

- **Resting state**

- DMN functional connectivity showed that the connectivity was decreased.
- Analysis data using Independent Component Analysis (ICA)

1. Decreased DMN functional connectivity.
2. Decreased Resting state in PCC and Hippocampus (These two regions are disconnected)

- Task induced deactivation showed decreased in DMN regions.
- **Alzheimer's and DMN**

1. Decreased functional connectivity in DMN and disease severity.
2. fMRI showed decreased DMN deactivation (mPFC, PCC, ACC)
3. Decreased in (Functional connectivity and BOLD deactivation).

DISCUSSION AND CONCLUSION

Mild cognitive impairment is a term in evolution, and while it still seeks precise ontological definition, the term reflects an important clinical entity. Mild cognitive impairment has been defined by phenomenological, epidemiological, clinical, neuropsychological, and biological variables with its core characteristics drawn from concepts of dementia. Other terms describe related clinical and pathological states, but amnestic mild cognitive impairment relates to a pathological state which differs from normal ageing, there is objective evidence of memory impairment, and patients are more likely to develop Alzheimer's disease than the normal population. At present research in mild cognitive impairment is suffocated by too many heterogeneous definitions. Mild Cognitive Impairment is becoming a very important subject for researchers and deserves more recognition and further study, in order to increase the ability to recognize earlier symptoms of Alzheimer's disease.

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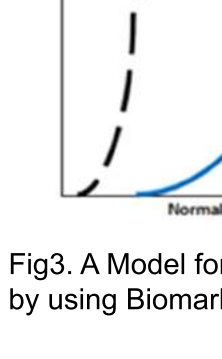

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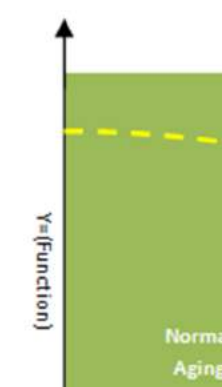

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