QUANTIFIED MULTIMODALITY MR IMAGING BIOMARKERS FOR DIAGNOSIS OF COGNITIVE IMPAIRMENT IN ELDERLY PATIENTS

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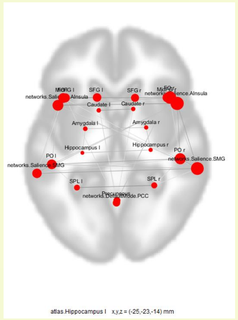
BACKGROUND

- The early diagnosis of mild cognitive impairment (MCI) and prediction of risk of progression to Alzheimer's disease (AD) based on structural and functional MRI.
- The challenge is to diagnose MCI from Normal Control (NC) and AD with higher sensitivity to avoid false-negative results.
- We combined two biomarkers indicating structural atrophy and quantifying resting-state functional connectivity.

METHODOLOGY

- Three groups of 23NC, 34MCI, and 29 AD (n=86) in our study who were age (60-79), gender, and educational background (10-20 years) controlled were selected. (Figure1)
- Binary connectivity matrices were created using conventional graph algorithm with 22 ROIs; Betweeness Centrality, Cluster coefficient, and Degree measures were computed in each subgroup using the connectivity matrices.
- Grey matter volume calculated using structural MRI
- For cognitive analysis; MMSE, ACE-total, RAVLT-total, RAVLT- 20 min delayed.



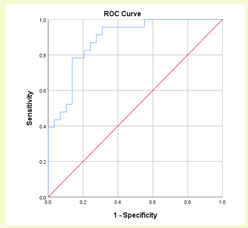
RESULTS

Characteristic	HC(n=23)	MCI(n=34)	AD(n=29)	Corrected *p*-value (ANOVA)		
				MCI versus HC	AD versus HC	AD versus MCI
Sex (M/F)	12/11	23/11	18/11	.247	.483	.65
Age (mean ± SD in years)	68.04 ± 6.66	68.06 ± 4.13	69.24 ± 4.6	.991	.446	.285
Years of formal education(mean ± SD)	14.4 ± 5.0	13.4 ± 3.5	13.2 ± 3.4	0.487	.456	.877
MMSE	29.04 ± 1.94	27.67 ± 2.17	22.7 ± 4.2	.018	<.001	<.001
ACE(TOTAL	91.87± 7.4	84 ± 9.6	68.6 ± 13.9	<.001	<.001	<.001
RAVLT(TOTAL)	46 ± 11.32	35.24 ± 10.3	23.59 ± 7.24	<.001	<.001	<.001
RAVLT 20 min Delayed	9.6 ± 3.4	5.65 ± 4.1	1.28 ± 1.6	<.001	<.001	<.001
Absolute Grey matter volume	556.43 ± 37.85	553.9 ± 42.68	511.79 ± 42.0	.82	<.001	<.001

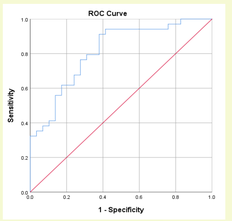
Figure: 1 Demographic Classification

- Hippo_L showed significant positive correlation (r = 0.424, p = 0.013) of graph measures with cognitive score among MCI.
- Also, reduction in gVol showed significant positive correlation with cognitive scores in Hippo_L (r = 0.483, p = 0.008) & SMG_R (r = 0.407, p = 0.028) while significant negative correlation with graph measures in Hippo_L (r = 0.526, p = 0.003) among AD subgroups. (Figure 2)
- Accuracy to classify AD from NC is 88.6% using the model of Hippo_L and SMG_R gVol with **91.3% - 78.3% sensitivity and 72.4% - 86.2% specificity (Figure 3)**
- The centroids in the graph (Figure 4) depicts - along the x axis (D1), AD is far away from MCI and NC; along the y axis, AD is in between NC and MCI and are separate enough to achieve statistical significance.

AD with NC = 88.6%



AD with MCI = 81.2%



AD with NC + MCI = 72.5 %

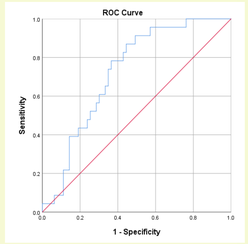


Figure: 3

MCI with NC = 69.6 %

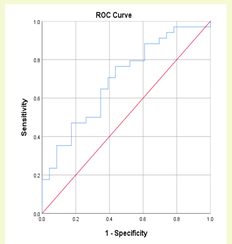


Figure: 4

Scan for Figure 2

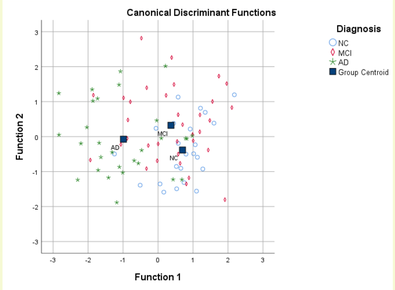


Figure: 4

DISCUSSION

- The multimodality and graph theory approach allows for the characterization of functional connectivity changes in each diagnostic group
- Functional connectivity seems to have a bearing on brain volumes in AD and neuropsychological test performances in MCI
- larger sample size and a longitudinal study will be required to validate our findings with regard to multimodality integration of imaging biomarkers for screening or classification of elderly patients into diagnostic subgroups.

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