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Biomedical Image Quantification

Connectivity analysis to distinguish normal, mild cognitive impaired and Alzheimer subjects based on MRI data

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Abstract

This work investigates a novel way of looking at the different regions in the brain and their relationship to each other as possible markers to classify normal control (NC), mild cognitive impaired (MCI) and Alzheimer (AD) subjects. MRI scans from a subset of 101 subjects from the ADNI study from baseline and again from month 12 were used for this study. 40 regions of the brain including hippocampus, amygdala, thalamus, white and gray matter were segmented using FreeSurfer and manually inspected and possible corrected. From this data we calculate the distance of center of mass positions between all centers, the number of voxels and the percentage volume and surface connection shared between the regions in a non-symmetrical way. The data were used in a linear discriminant analysis in a leave-one-out manner. We found that the percentage of surface and volume connection in-between regions give an significant classification of NC and AD and also of AD and MCI, when corrected for whole brain volume. The result is significant better than only including whole brain volume, but the hippocampus volume change alone give more significant results.

Introduction

•Alzheimer's Disease (AD) is caused by the degeneration and eventually death of neurons in several areas of the brain
•AD accounts for 50-56 % of the cases of dementia.
•In the U.S. 5.4 million have Alzheimer's disease in 2011.
•The brain changes with AD is thought to begin 10 years or more before symptoms as memory loss appear, so early markers of Alzheimer's would give be significant aid in helping therapies to slow down cognitive decline in AD.
• We look at 40 regions in the brain and their physical interaction as a way of characterizing the anatomy of the brain in NC, MCI and AD subjects.

Study Population

•The study population is based on 101 baseline (bl) subjects obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) and the corresponding 12-month follow-up 1.5 T T1-weighted MRI scans.
•The population included 24 NC, 28 MCI and 49 AD subjects.
•The segmentation was performed by FreeSurfer

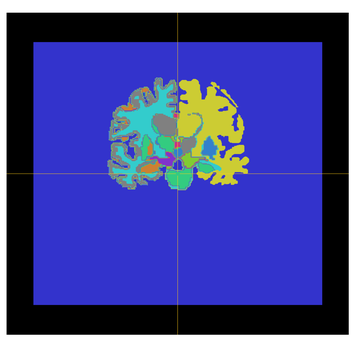

Figure1 shows a slides of the segmented brain, where each color represents a segmented region.

Connectivity markers

• We use 40 different regions based on the segmentation, including, hippocampus, amygdala, thalamus, white and gray matter.
•We calculate a distance marker based on the center of mass position of each region and the Euclidean distances in between the regions.
• We calculate a volume connectivity marker based on the percentage of total volume of each region that is connected to another region.
•We calculate a surface connectivity marker based on the percentage of total surface of each region that is connected to another region.

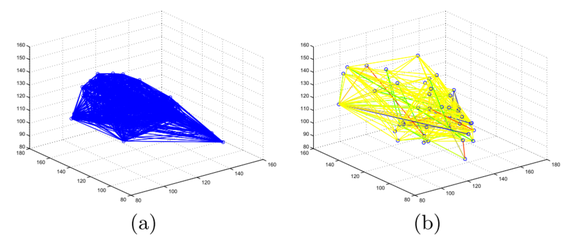

Figure 2 a shows the distance markers and figure 2b shows the volume connectivity marker, where the colors correspond to the ncreasing percentage connectivity.

Classification

•We use a Partial least square regression (PLS) to reduce the number of parameters
•We use a linear discriminate analysis for classification (LDA).
•Our classification is done in a leave-one-out manner.

Results

Group	Time point	Hippocampus volume (mm^3)	Whole brain volume (mm^3)
NC (n=24)	bl	4981.833 (± 624.932)	971143.250 (± 97901.683)
	month12	5001.167 (± 662.997)	968911.917 (± 98579.104)
	delta	-19.333 (±351.357)	2231.333 (±17964.822)
MCI (n=28)	bl	4436.214 (±566.754)	976490.536 (± 115784.396)
	month12	4461.893 (± 547.068)	970396.679 (± 109146.990)
	delta	-25.679 (±320.269)	6093.857 (± 31452.988)
AD (n=49)	bl	3885.551 (± 894.682)	915673.429 (± 107516.552)
	month12	3748.020 (±982.085)	897252.592 (± 112548.229)
	delta	137.531 (±290.595)	18420.837 (± 20295.285)

Table 1 shows the volume scores for whole brain and hippocampus for baseline and month 12 and the corresponding delta values for the three subject groups NC, MCI and AD,

Marker	NC-AD	NC-MCI	MCI-AD
Distance	0.421	0.748	0.535
Volume connectivity	0.001	0.258	0.072
Surface connectivity	0.001	0.166	0.099
Nb of voxel	0.000	0.317	0.161
Nb of voxel normalised	0.024	0.317	0.322

Table 3 shows the p values from a ranksum tests comparing the three groups NC, MCI and AD adjusted for whole brain volume for our markers. This indicate that our connectivity markers are better than using a distance marker.

	NC-AD AUC	NC-AD acc	NC-MCI AUC	NC-MCI acc	MCI-AD AUC	MCI-AD acc
Volume	0.642	60.274	0.152	26.923	0.618	57.143
Distance	0.558	56.164	0.469	48.077	0.502	54.545
Volume connectivity	0.746	69.863	0.469	53.846	0.623	57.143
Surface connectivity	0.744	71.233	0.457	55.769	0.603	57.143
nb of voxel	0.796	72.603	0.673	61.538	0.564	55.844
nb of voxel normalised	0.684	65.753	0.673	57.692	0.590	55.844

Table 2 shows our classification results for baseline splitted into three groups Normal control (NC) and Alzheimer's (AD), NC and Mild cognitive impaired (MCI) and MCI and AD. The results show the Area under the curve (AUC) and the accuracy (acc) in percentage. Notice that we get better results for the connectivity scores than for only using volume.

Discussion and conclusion

• Classification based in whole brain volume between NC and AD has previously been reported as 81 % using a kNN classification [1].
•Our whole brain volume is not nearly as high as in [1] but still our other connectivity markers shows promise.
•One of the problems with using the whole brain is that it is non-specific and has limited application in the differential diagnosis of dementia.
•Our results can be used to gain new insights in how the different regions and their connectivity is affected during Alzheimer's

•The future work could be in combining these markers with shape markers of the different regions to get a more sophisticated image of Alzheimer's disease.

[1] S. Klein, M. Loog, F. van der Lijn, T. den Heijer, A. Hammers, M. de Bruijne, A. van der Lugt, R.P.W. Duin, M. M. B. Breteler, and W. J. Nissen. Early diagnosis of dementia based on intersubject whole-brain dissimilarities. In *Proceedings of the 2012 IEEE international conference on Biomedial imaging: from nano to Macro, ISBI'10* pages 249-252, IEEE Press