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BIOMARKERS

POSTER PRESENTATION

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Altered structural connectivity detected with dilated convolutional neural network analysis in the DIAN study and the Wisconsin Registry for Alzheimer's Prevention

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Abstract

Background: Dominantly inherited Alzheimer's disease (DIAD) and late onset Alzheimer's disease (LOAD) are characterized by the accumulation of amyloid pathology, and neurodegeneration which heralds the onset of dementia. Loss of structural connectivity prior to development of dementia may be measured using techniques that are sensitive to subtle neurodegeneration such as diffusion MRI (dMRI). We have previously shown the utility of deep learning (using a dilated convolutional neural network (DCNN) model) for analysis of sequential manifold-valued data. Here, we apply this approach to dMRI data to test for loss of structural connectivity among mutation carriers who will develop DIAD, as well as among individuals who are at risk for LOAD due to amyloid pathology.

Method: Dataset 1 comprised 170 cognitively unimpaired participants from the Wisconsin Registry for Alzheimer's Prevention study who underwent [11C]PiB-PET to determine amyloid status, and dataset 2 comprised 440 participants in the Dominantly Inherited Alzheimer Network (DIAN) study. Demographics are shown in Table 2. Participants underwent diffusion weighted imaging which was processed using MRTrix3 and FSL toolkits. TractSeg was performed on both datasets to generate 50 white matter tracts, and tractometry was performed to generate mean representations of the tracts. Similar to previous work, we trained the dilated CNN model (Figure 1) using DTI values along the tracts for each group. The distance between the parameters of two models is treated as the difference between two groups. We performed permutation testing of 5000 runs on the distance to determine significant group differences within each dataset.

Result: The p-values for each tract are shown in Table 1. Within the 50 fibers, we identified 14 tracts that differed by amyloid status, and 16 tracts that differed by mutation status. Across the two data sets, 9 tracts, e.g. Arcuate fascicle, and Cingulum, were found to be in common.

Conclusion: We demonstrate the ability to use the dilated CNN model to capture alterations along tract fibers among cognitively unimpaired individuals with preclinical amyloid as well as among mutation carriers who will develop DIAD. Longitudinal studies are needed to determine the temporal relationship between the accumulation of amyloid and neurodegeneration in the development of dementia.

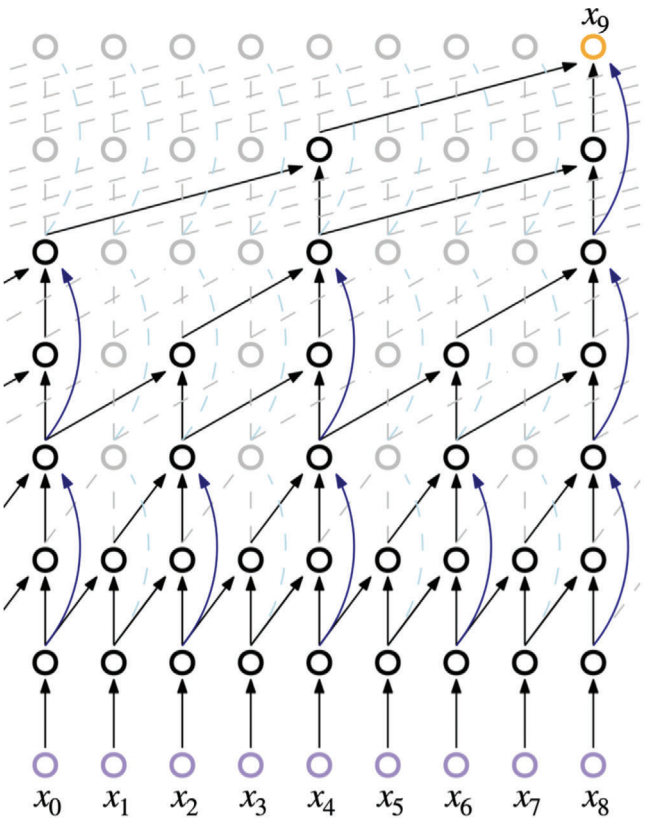

Figure 1: The DCNN neural network which is used to represent the fibers. The input is a sequence of DTI voxels along the fiber, while the output is the next voxel in this fiber. When fully trained, the parameters of network can be viewed as the representation of the fiber for one group.

FIGURE 1

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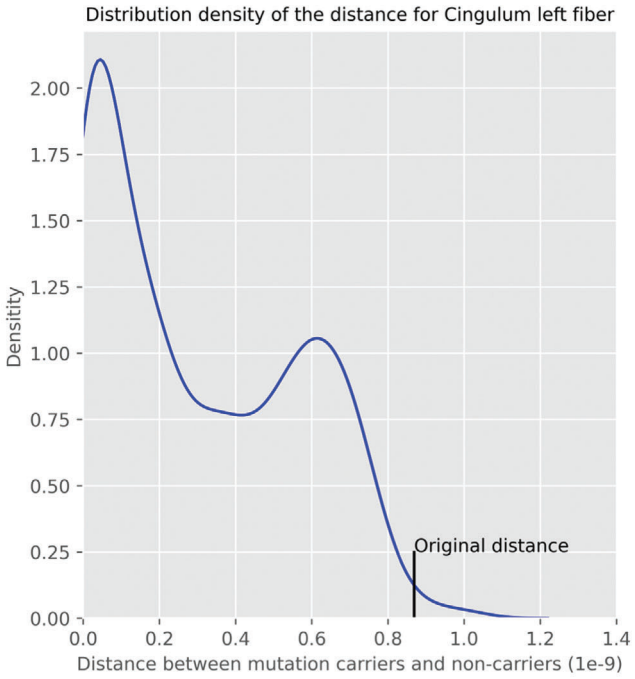

Figure 2: The distribution of the distance by permutation testing of the fiber – Cingulum left. Original distance between mutation carriers vs. non-carriers, shown in black, lies in the extreme end which has < 0.05 probability to happen by chance.

FIGURE 2

TABLE 1

Fiber Name	Datasets		Fiber Name	Datasets	
	PiB+ vs. PiB-	Carriers vs. Non-carriers		PiB+ vs. PiB-	Carriers vs. Non-carriers
AF_left	**0.034**	0.181	POPT_left	**0.037**	0.578
AF_right	**0.029**	**0.006**	POPT_right	**0.039**	**0.000**
ATR_left	0.895	**0.007**	SCP_left	0.200	0.605
ATR_right	0.200	0.103	SCP_right	0.087	0.699
CC_1	0.391	0.591	SLF_I_left	**0.005**	**0.001**
CC_2	0.585	**0.018**	SLF_I_right	**0.007**	**0.000**
CC_3	0.471	0.231	SLF_II_left	0.246	**0.008**
CC_4	**0.038**	**0.019**	SLF_II_right	**0.026**	**0.000**
CC_5	**0.032**	0.295	SLF_III_left	0.417	0.681
CC_6	**0.003**	0.270	SLF_III_right	0.569	0.217
CC_7	0.310	0.473	ST_FO_left	0.588	**0.021**
CG_left	**0.000**	**0.009**	ST_FO_right	0.060	0.096
CG_right	**0.014**	**0.005**	ST_PREM_left	0.857	0.740
CST_left	0.846	0.712	ST_PREM_right	0.308	**0.004**
CST_right	0.846	0.495	STR_left	0.241	0.084
FPT_left	0.118	0.373	STR_right	0.344	0.158
FPT_right	0.833	0.336	T_OCC_left	0.394	0.702
ICP_left	0.296	0.894	T_OCC_right	0.462	0.461
ICP_right	0.138	0.581	T_PAR_left	0.692	0.675
IFO_left	**0.043**	0.115	T_PAR_right	0.533	0.749
IFO_right	**0.006**	**0.018**	T_PREM_left	0.918	**0.027**
ILF_left	0.190	0.155	T_PREM_right	0.507	0.378
ILF_right	0.129	**0.012**	UF_left	0.400	0.404
MCP	0.871	0.611	UF_right	0.116	0.773
OR_left	0.130	0.280			
OR_right	0.188	0.189			

* Full name of the tracks:
AF: Arcuate fascicle; ATR: Anterior Thalamic Radiation; CC: Corpus Callosum; CG: Cingulum; CST: Corticospinal tract; FPT: Fronto-pontine tract; ICP: Inferior cerebellar peduncle; IFO: Inferior occipito-frontal fascicle; ILF: Inferior longitudinal fascicle; MCP: Middle cerebellar peduncle; OR: Optic radiation; POPT: Parieto-occipital pontine; SCP: Superior cerebellar peduncle; SLF: Superior longitudinal fascicle; ST-FO: Striato-fronto-orbital; ST-PREM: Striato-premotor; STR: Superior Thalamic Radiation; T-OOC: Thalamo-occipital; T-PAR: Thalamo-parietal; T-PREM: Thalamo-prefrontal; UF: Uncinate fascicle.

Table 1: The p-value (uncorrected) for all fibers from TractSeg for two groups: PiB+ vs. PiB-, and Mutation carriers vs. Non-carriers. The significant level is set as $\alpha = 0.05$ and the values are highlighted in blue. The green color highlights the fibers that are shared between two groups, while pink color highlights the fibers that are found significant in one dataset.

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TABLE 2

Group 1	PiB+	PiB-
Sample size	$n = 46$	$n = 124$
Sex	Female ($n = 31$) Male ($n = 15$)	Female ($n = 82$) Male ($n = 42$)
Age [y]	70.46 ± 5.35	70.41 ± 5.30
Group 2	Cognitively unimpaired (CU) & mutation non-carrier (NC)	Cognitively unimpaired (CU) & mutation carrier (MC)
Sample size	$n = 219$	$n = 221$
Sex	Female ($n = 125$) Male ($n = 94$)	Female ($n = 136$) Male ($n = 85$)
Age [y]	36.47 ± 10.03	40.51 ± 11.13

Table 2: The demographics used in the study. Original PiB- group contains $n = 280$ samples with age 61.77 ± 6.27. Since the age difference is too significant, we iteratively choose a subset so that the mean of ages matches the PiB+ group. The final subset is shown in this table with Age- Sex- matched.