Multivariate Association Between Cognitive Function and Brain Tissue in Healthy Older Adults

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Introduction

Cognitive function alterations are a feature of the cognitive aging process. Additionally, aging is marked by macro- and micro-structural changes in the brain, such as gray matter (GM) atrophy, iron accumulation, and demyelination. Thanks to the novel neuroimaging techniques, we are able to obtain relative information for these brain tissue properties in-vivo.

Recent studies show that cerebellum, known to be involved in motor control, also plays role in cognition.

Objective #1: Explore the association between cognitive function and co-occurrence of brain micro- and macro-structural changes in healthy older adults.

Objective #2: To show the relevance of property alterations within cerebellum in cognitive aging.

Methods

Cognitive Assessment: All participants underwent a complex battery of cognitive tests, assessing different aspects of memory, attention and executive function. The preclinical Alzheimer's cognitive composite **(PACC5)** was calculated for all participants from the normalized cognitive scores.

Image data: MRI data was acquired on a 3T whole-body MRI-scanner (MAGNETOM Prisma, Siemens Medical Solution, Erlangen, Germany) using a standard 64-channel head receiving coil. The whole-brain MRI acquisitions included a multiparameter mapping protocol (MPM). All MRI data is processed using the hMRI toolbox.

Statistical analyses: We used four composite cognitive scores (**episodic memory, executive function, attention, and PACC5**) for statistical analysis on gray matter. All data were Z-transformed. Separate linear regression models within the SPM12 GLM framework were applied to five parameter maps (MTsat, R1, R2*, PD, GM volume), with age, gender, and education as covariates, and each composite score as the regressor of interest. A **multivariate GLM model** processed all standardized maps to examine the relationship between brain tissue properties and cognition, using the MSPM toolbox in SPM12. **Canonical vector analysis** was performed to assess the level of contribution of each brain tissue property with respect to each cognitive composite score.

	Mean	s.d.	Min	Max
	#Participants = 101			
Age	59.44	5.29	50	69
Bmi	24.62	2.89	18	30
Education (years)	15.22	3.01	9	25
Attention	0	0.99	-2.37	2.06
Executive	0	0.99	-2.14	2.76
Memory	0	0.99	-3.88	1.66
PACC5	0	2.91	-7.94	8.35

Results

Voxel-wise multivariate GLM analyses revealed significant associations after family-wise error rate correction between executive functions and the combination of macro- and micro-structural changes within the cerebellum including right crus I and II, VII-b (see Figure 1). With gray matter volume playing the most important role with 63%, followed by the water content with 20% contribution to the multivariate model.

We also detected a correlation between memory and combined microstructural alterations in the in the left Cerebellum VIII-b, as well as bilaterally within the cingulate gyrus and insula as reported below.

peak [x y z] Coordinates	Tissue	Cluster P-value (voxel-level)	Cluster Size #voxels	Brain Region
		Executive function		
[41 -53 -45]	GM	0.026(0.089)	1370	Right Curs II
[36 -54 -46]				Right VII-b
[49 -54 -42]				Right Crus I
		Memory		
[3 34 -12]	GM	0.015(0.057)	1557	Right ACG
[-7 36 -3]				Left ACG
[4 39 0]				Right ACG
[47 10 4]	GM	0.005(0.435)	1974	Right Insula
[40 10 4]				Right Insula
[36 3 -11]				Right Insula
[-13 -44 -55]	GM	0.001(0.005)	1060	Left VIII-b
		PACC5		
[-2 36 -9]	GM	0.026(0.254)	1379	Right ACG
[9 39 -13]				Right ACG
[-6 48 -5]				Left ACG

Key: GM: gray matter; ACG: anterior cingulate gyrus.

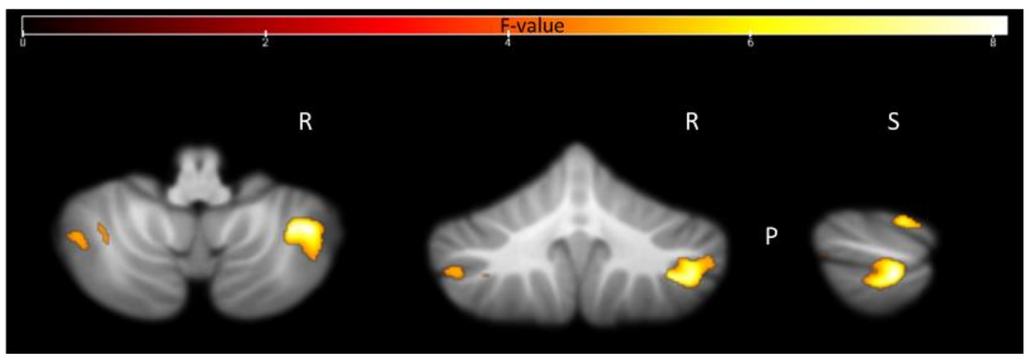

Figure 1. Statistical parametric map for the multivariate regression analysis within gray matter, showing the correlation between executive function and alterations in brain tissue properties within the cerebellum.

Discussion

These findings highlight the role of the cerebellum in cognition besides the complex relationship between cognition and brain micro- and macro structural properties in aging. As such, the involvement of the cerebellum in motor coordination and procedural memory may potentially influence executive functions

Toolboxes & acknowledgments

Toolboxes: hMRI, https://hmri.info/, and MSPM https://github.com/LREN-CHUV/MLM & https://tinyurl.com/ypem8ue2

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