The cerebellum and its role in motor networks and performance:A volumetric approach

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Introduction:

The cerebellum acts as a motor modulator by performing fine adjustment of motion. While structural alterations can result in dysfunction [1], lifestyle behaviours (e.g. physical activity) cause adaptions in cerebellar volume (CV) and activation patterns [2], pointing to neuronal plasticity. While motion is planned in motor association cortices, the integration of various motor information originating from cerebellar (CL) or basal ganglia loop (BGL) occurs subcortically [1]. This study investigated whether a higher CV relates to a better motor performance (MP) and whether this is driven by a direct or more indirect path between the cerebellum and cortical motor areas [1, 3].

Methods:

Our sample included 656 participants (307 females, age 57±14 years) from the population-based 1000BRAINS cohort [4]. MP was measured by gait test (GT; number of steps and time needed for walking 25 meters at internal pace) and balance test (BT; ability to maintain balance while standing on an oscillating platform). Regions of interest (ROIs) were the cerebellar cortex, the deep cerebellar nuclei (DCN; fastigial, interposed, dorsal and ventral dentate nuclei), the supplementary (SMA), pre-SMA, primary, and dorsal pre-motor areas, the pallidum, caudate, putamen, substantia nigra and hippocampus (HC). Apart from HC, all areas are crucial in MP. HC was selected as it has been mentioned as a compensatory structure in MP [3]. Based on T1-weighted MR images, grey matter volume was extracted using the default pre-processing of FreeSurfer for subcortical ROIs and the voxel-based pipeline of CAT [5] for cortical and cerebellar ROIs defined via the Julich-Brain Atlas [6]. Age, body mass index, Beck's Depression Inventory, height and total cerebral volume or hemispheric CV were defined as covariates. By default, the cerebral volume was calculated as a whole [5], while hemispheric CVs were considered separately to avoid an overcorrection of the comparably small DCN. We implemented a moderated mediator analysis [Fig. 1, 2] to analyse which brain areas modulate and mediate (in-)directly the path between the cerebellar ROIs, motor cortex and MP [1].

Results:

Significant correlations between GT and the right dentate (time: $r=0.11$, $p=0.005$), the right (steps as well as time: $r=0.1$, $p=0.001$) and left dorsal dentate (steps: $r=0.083$ $p=0.003$) were found. The BT showed no significant results. First, we implemented anatomically motivated moderated mediator analyses which examined the relation between the CV and MP while considering the influences of the CL and BGL [Fig. 1]. None of these models were significant. Then, we computed mediator models adding the HC as a possible compensatory area (Fig. 2, [3]). These models showed a significant correlation between DCN and MP directly and for an indirect pathway via (i) the BGL and (ii) the HC.

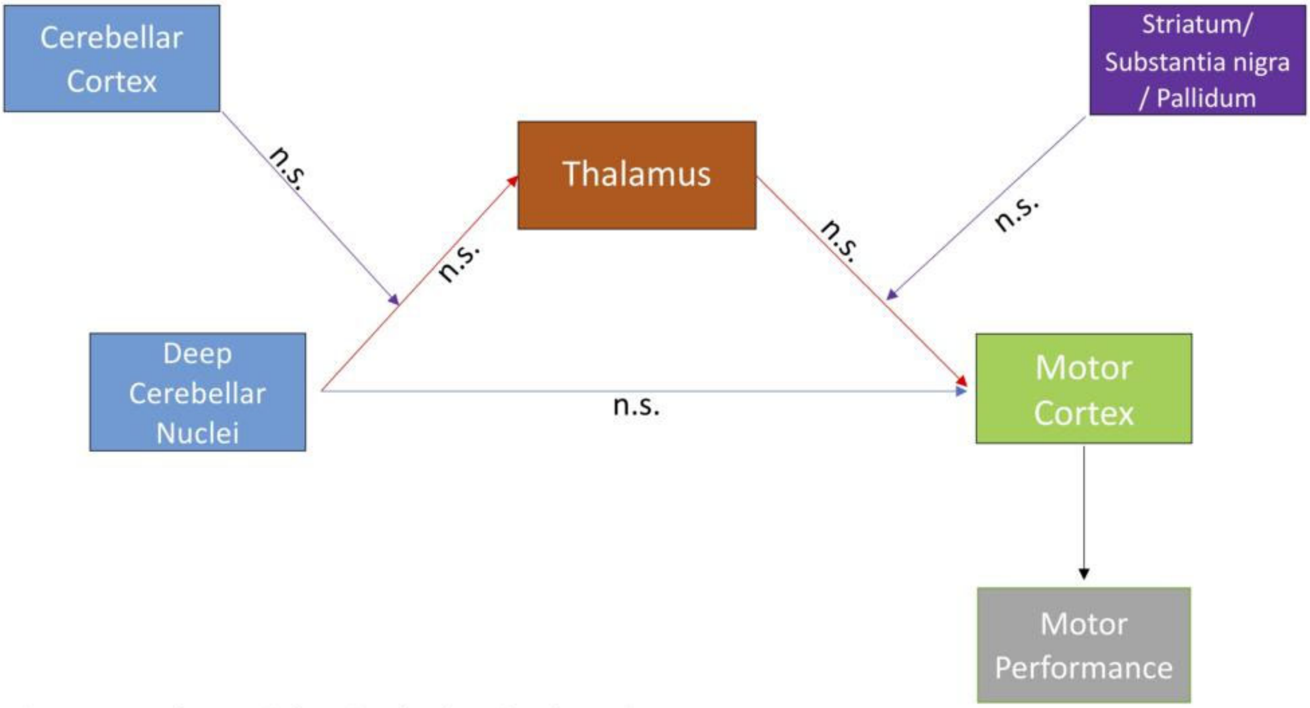

Fig. 1 represents the anatomically motivated moderated mediator analyses

This model examines the relation between the volume of regions belonging to the cerebellar and BGL towards motor performance as the outcome of interest. Blue colour represents analysed regions belonging to the CL, i.e. the cerebellar cortices, purple colour represents the BGL (i.e. striatum, substantia nigra, pallidum), orange colour encodes the thalamus, green represents cerebral cortical areas belonging to the motor system, grey represents motor performance. n.s. = not significant

The blue arrow describes the direct correlations between DCN and motor cortex, while the "indirect" correlations via thalamus is shown in red. The purple arrows represent the modulating effect on the indirect pathway. The correlation coefficients for each statistically connection (i.e. each arrow) were calculated for all selected regions. Except the HC as it is not seen as a classic contributor of the motor system. The model is based on model 21 of PROCESS [10].

(https://files.aievolution.com/prd/hbm2101/abstracts/abs_1754/Figure1.jpg)

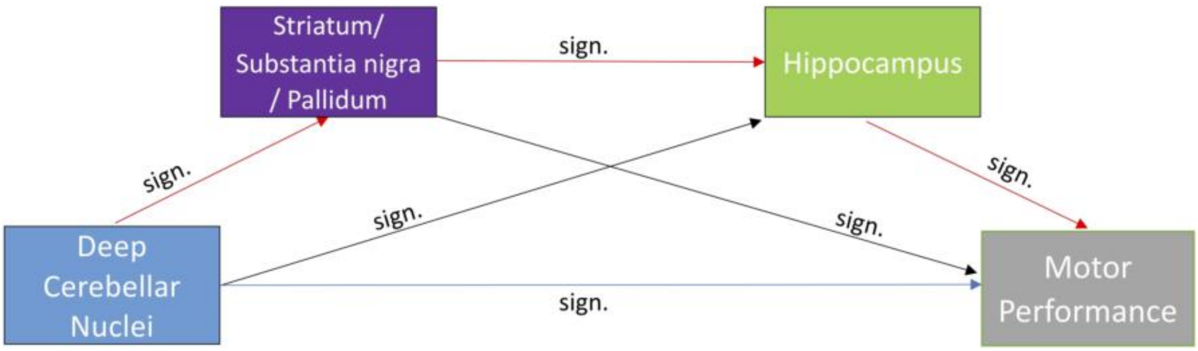

Fig. 2 describes the mediator analyses including the HC.

This model examines the HC as a possible compensatory structure which influences the relation of the cerebellar structures and BG towards motor performance. Colours and the arrows indicate the same neuronal motor systems as described in Figure 1. sign = significant.

The correlation coefficients for each statistically connection (i.e. each arrow) were calculated for all selected regions. The model is based on Model 6 of PROCESS [10].

(https://files.aievolution.com/prd/hbm2101/abstracts/abs_1754/Figure2.jpg)

Conclusions:

The current results suggest that volume of the DCN can predict performance in the GT: However, it seems counter-intuitive, that with higher volume of the dorsal dentate more steps and time were required. Potentially, age-related atrophy of the cerebellar cortex [7] may cause disinhibition and consecutive hypertrophy of the DCN [similar to 8] with less functional connectivity, resulting in worse MP. Interestingly, we observed HC-volume as a significant mediator between the dorsal dentate and MP, suggesting a supportive effect on the relation between the cerebellum and MP: Whereas the direct correlation path between the DCN and the MP suggest worse MP with higher DCN volume, the indirect path via BGL/HC was associated with a better MP [Fig 2]. This observation suggests that (i) MP, can only be inferred from brain circuits but not from single structures alone (e.g. dorsal dentate), (ii) the HC volume seems to be an integral part of circuits explaining the relations between cerebellar structures and MP and (iii) a compensatory function of the HC for MP [3], e.g. by providing visuo-spatial integration [9], is further supported.

Motor Behavior:

Motor Planning and Execution [1]

Neuroanatomy, Physiology, Metabolism and Neurotransmission:

Subcortical Structures [2]

Keywords:

Cerebellum
Motor
MRI
STRUCTURAL MRI
Sub-Cortical

[1|2]Indicates the priority used for review

My abstract is being submitted as a Software Demonstration.

No

Please indicate below if your study was a "resting state" or "task-activation" study.

Other

Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

Healthy subjects

Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.

Yes

Was any animal research approved by the relevant IACUC or other animal research panel? NOTE: Any animal studies without IACUC approval will be automatically rejected.

Not applicable

Please indicate which methods were used in your research:

Structural MRI

For human MRI, what field strength scanner do you use?

3.0T

Which processing packages did you use for your study?

Free Surfer
Other, Please list - CAT

Provide references using author date format

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