Evaluating Cerebellar Contributions to Physical Performance and Cognition in Multiple Sclerosis

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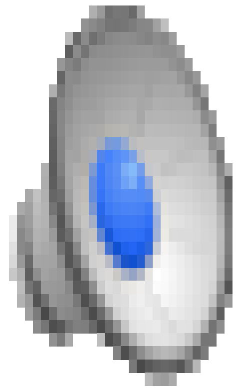
Kennedy Krieger Institute

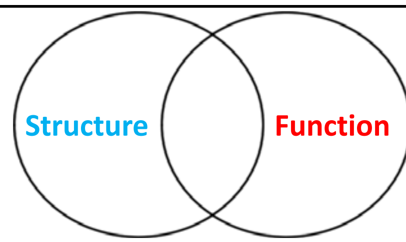
JOHNS HOPKINS

Background

- Individuals with multiple sclerosis (MS):
  - 85% report gait (**motor**) dysfunction that interferes with daily functioning (Kelleher et al. 2010)
  - 40-65% report **cognitive** dysfunction (Amato et al. 2010)
- The cerebellum:
  - Plays an important role in both motor and cognitive processing (Koziol et al. 2014; Stoodley et al. 2012)
  - Is a common site for MS-related disability (Weier et al. 2015)
    - Cerebellar signs and symptoms are the predominant manifestation in 11-33% of individuals with MS (Weier et al. 2015)

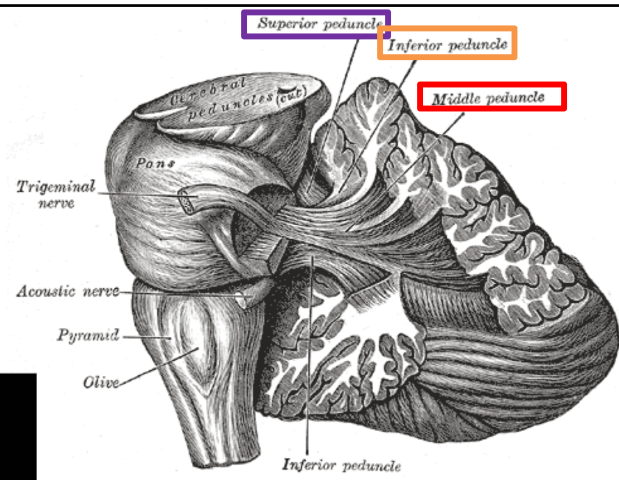


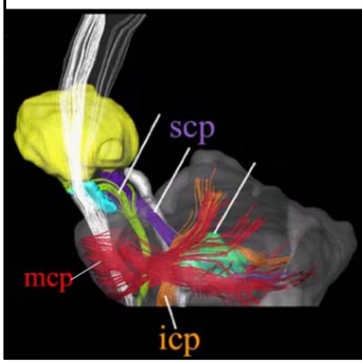
Structure-Function Relationships



- Rehabilitation for individuals with cerebellar dysfunction is limited
  - A better understanding of the relationship of clinical features to structural anatomy would be useful in this heterogeneous patient population.
- Ultimately:
  - Drive clinical practice forward
    - Utilize what we know about these relationships to predict future function
    - Develop more effective rehabilitation protocols that target mechanism of dysfunction/disability

Cerebellar Anatomy



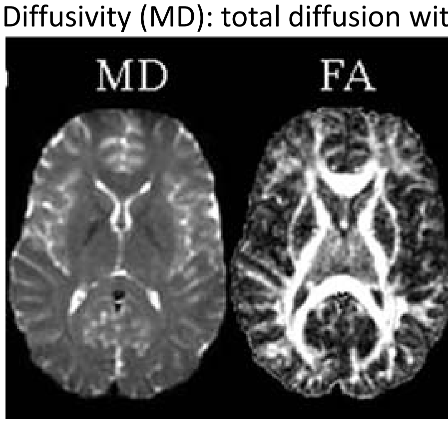


Inferior Cerebellar Peduncle (ICP)
Middle Cerebellar Peduncle (MCP)
Superior Cerebellar Peduncle (SCP)

Mori S, Zhang J. *2006*

Background

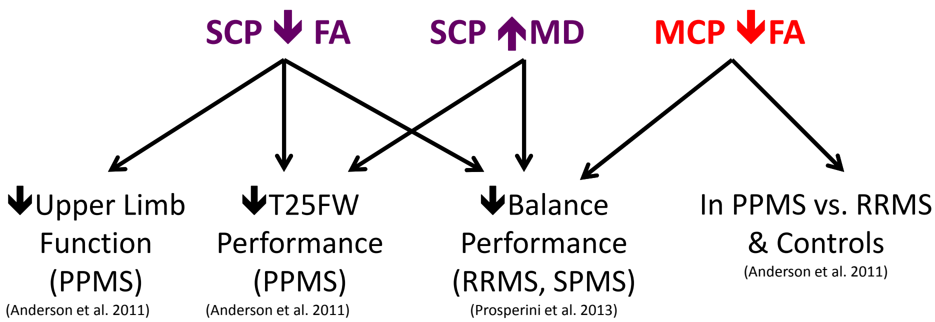
- <u>Diffusion:</u>
  - Primary outcome measures:
    - Fractional Anisotropy (FA): degree of anisotropy in a given voxel
    - Mean Diffusivity (MD): total diffusion within a voxel



Alexander et al. 2007

Background

- <u>Diffusion</u>
  - SCP ↑ FA Linked with rate of learning a visuomotor task in healthy adults (Della-Maggiore et al. 2009)



Background

- <u>Volumes</u>
  - Reduction in total cerebellar volume in MS compared to controls; more prominent in PPMS (Anderson et al. 2009; Calabrese et al. 2010)
  - Established Relationships Between:
    - Cerebellar lesion volume and cognition (Damasceno et al. 2014)
    - Cerebellar grey matter volume and fine motor skill (Anderson et al. 2009)

Objective

To examine the relationship of

motor and cognitive performance

to

cerebellar volumes and diffusivity measures

in individuals with MS.

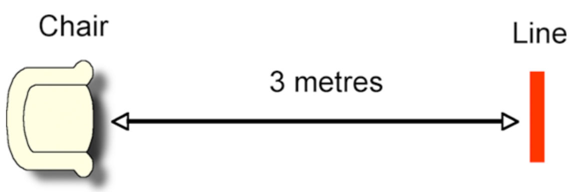
Physical Function Measures

- Strength
- Sensation

Vibratron Physiotemp, Huron NJ
Hand Held Dynamometer; Hoggan Health Industries, W Jordan UT

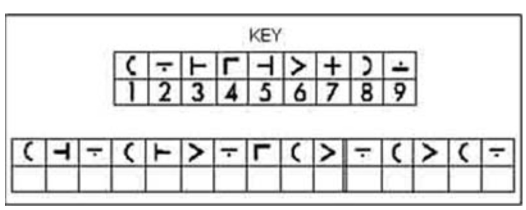
Physical Function Measures

- Walking
  - Timed Up and Go (TUG)
  - Timed 25 Foot Walk (T25FW)
  - Two Minute Walk Test (2MWT)
  - Fast Walking Velocity
- Fall History



Cognitive Measures

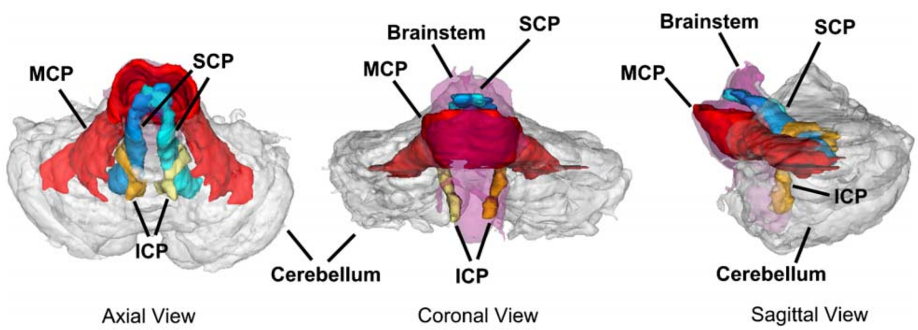
- Symbol Digit Modality Test (SDMT)



(Parmenter et al. 2007; Deloire et al. 2006; Genova et al. 2009; Strauss et al. 2006; Drake et al. 2010; Rao 2004.)

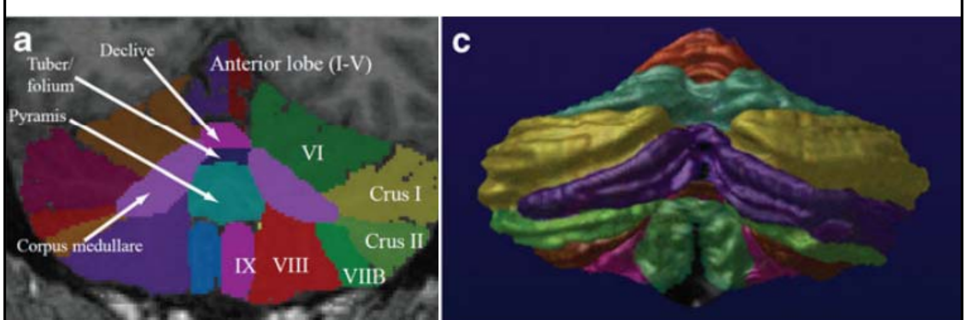
Structural Measures

- Philips 3T Scanner
- DWI for FA & MD measurement
- Automatic segmentation method (Ye et al., 2015)



Structural Measures

- MPRAGE for volume measurement
- Automatic Segmentation with lobule parcellation (Yang et al. 2013; Bogovic et al. 2013)
- Lobules I-V, VIII: related to motor function
- Lobules VI-VII: related to cognitive function (Stoodley & Schmahmann, 2010)



(Schmahmann, 2000; Jung et al., 2012)

Inclusion Criteria & Demographics

- Diagnosis of Relapsing Remitting MS
- No active exacerbations
- No corticosteroid use in past 30 days
- No other orthopedic or neurologic disorders that would influence walking
- Able to follow study-related commands

	Age Mean (SD)	Gender	Symptom Duration Mean (SD)	EDSS Median (range)
MS n=29	50.0 ± 11.3 Years	18F; 11M	12.8 ± 9.9 years	4.0 [1-6.5]
Control n=23	51.9 ± 11.0 Years	15F; 8M	--	--

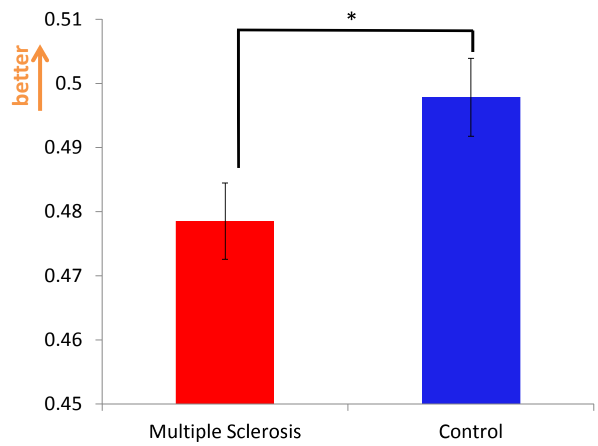
All values listed mean±SD with the exception of EDSS, which is listed median[range]

Comparisons between Individuals with MS and Controls

	MS Mean (SD)	Control Mean (SD)	P-value
Falls (>1 past month)	0.52 (0.51)	0 (0)	**0.0001**
Summed Strength (lbs)	235.4 (89.6)	305.1 (64.4)	**0.0029**
Vibration Sensation (vu)	6.7 (3.5)	3.1 (2.3)	**0.0001**
Walk Velocity (m/s)	1.6 (0.49)	2.0 (0.35)	**0.0077**
TUG (s)	7.7 (2.3)	5.9 (1.1)	**0.0021**
T25FW (s)	5.6 (2.3)	4.2 (0.73)	**0.0139**
2MWT (m)	163.8 (45.4)	197.0 (32.4)	**0.0057**
SDMT	47.7 (12.4)	59.9 (6.2)	**0.0001**

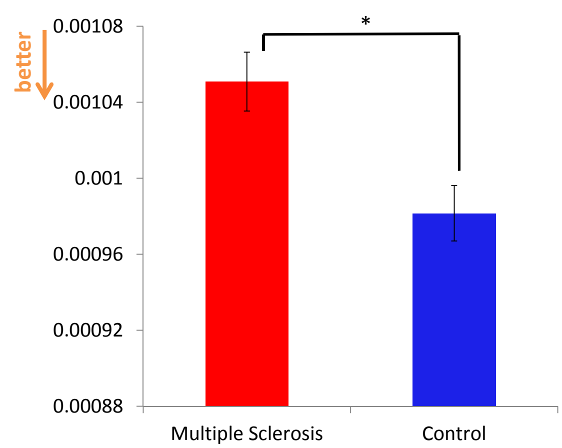
Diffusion Results

- Diffusivity of the **SCP**, was significantly worse in individuals with RRMS compared to controls.
  - FA: p=0.029



Diffusion Results

- Diffusivity of the **SCP**, was significantly worse in individuals with RRMS compared to controls.
  - MD: p=0.002

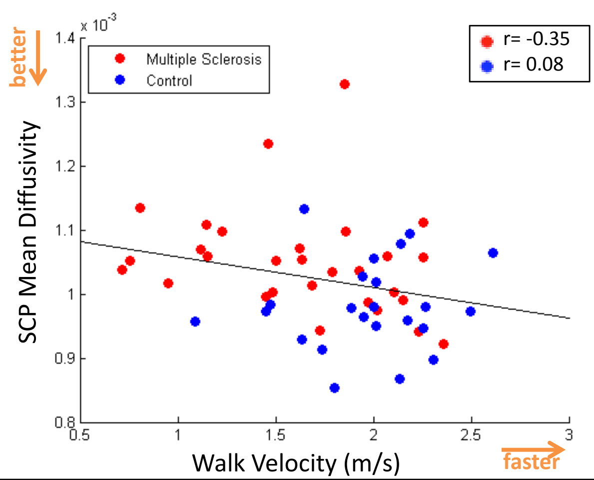


Diffusion Results

- Decreased MD in the SCP was significantly associated with:
  - Reduced falls in the past month
    - r=-0.37; p=0.007
  - Better SDMT performance
    - r=-0.45; p=0.0009

Diffusion Results

- Decreased MD in the SCP was significantly associated with:
  - Better performance on walking tests
    - T25FW: r=0.29; p=0.044
    - TUG: r=0.33; p=0.025
    - 2MWT: r=-0.39; p=0.009
    - **Walking speed: r=-0.28; p=0.041**

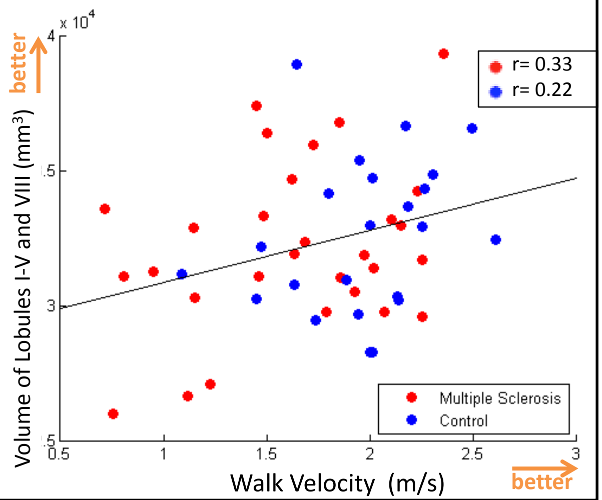


Volume Results

- Higher volume of the motor lobules (I-V, VIII) was significantly associated with:
  - Higher strength
    - r=-0.37; p=0.007
  - Better performance on the T25FW
    - r=-0.30; p=0.035

Volume Results

- Higher volume of the motor lobules (I-V, VIII) was significantly associated with:
  - **Faster walking speed**
    - **r=0.30; p=0.032**

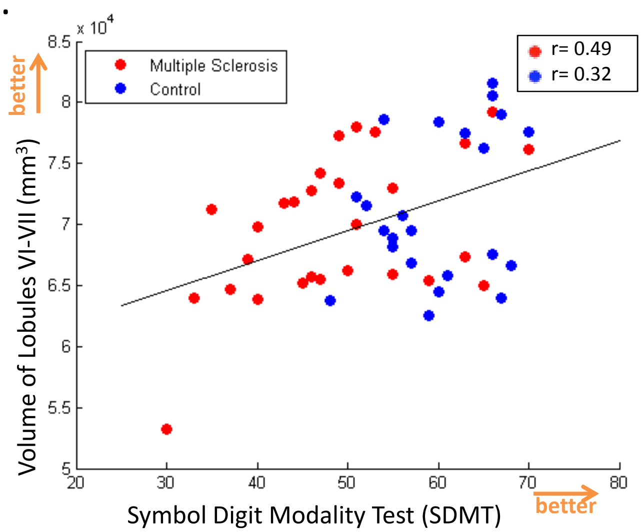


Volume Results

- Motor lobule volume was **not** related to sensory performance (r=0.23; p=0.108).

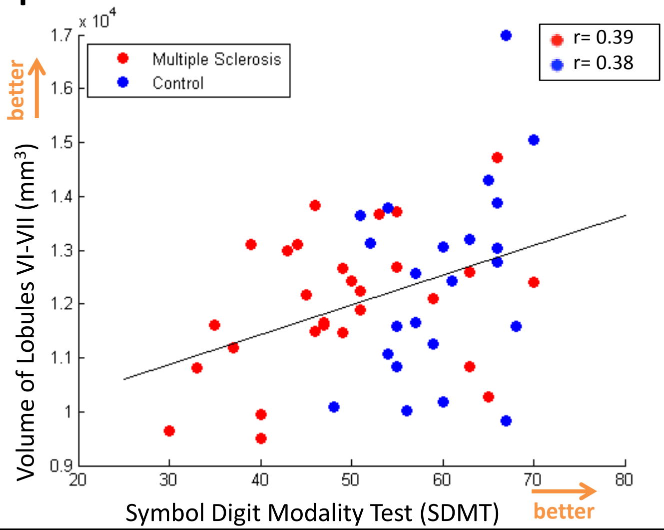
Volume Results

- Higher volume of the cognitive lobules (VI-VII) was associated with:
  - **Better performance on the SDMT**
    - **r=0.43; p=0.002**



Volume Results

- Larger MCP Volume is related to:
  - **Better SDMT performance**
    - **r=0.3703; p=0.0075**

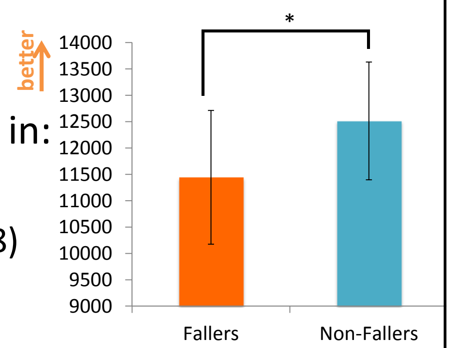


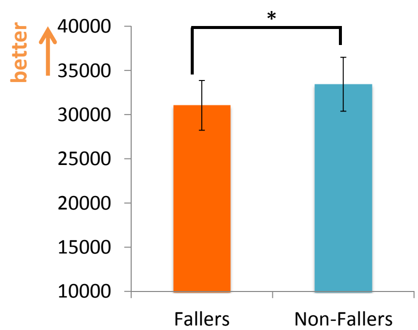
Volume Results

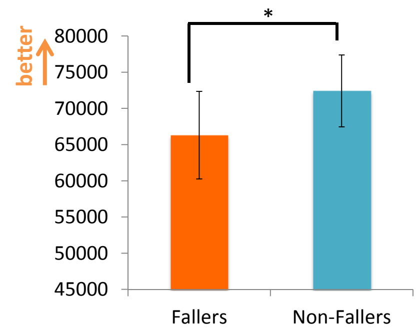
- Fallers (n=15) vs. non-fallers (n=14)
- Fallers perform significantly worse on:
  - Walk velocity (p=0.026)
  - SDMT (p=0.010)

Volume Results

- Fallers have lower volumes in:
  - MCP (p=0.033)
  - Lobules I-V and VIII (p=0.038)
  - Lobules VI-VII (p=0.008)





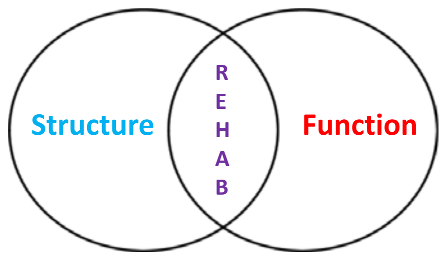


Summary

- Cerebellar volumes and diffusivity are selectively associated with:
  - **Physical performance**
  - **Cognition**
- Unique Findings in RRMS:
  - Differences in diffusivity among RRMS & controls.
  - Differences among fallers and non-fallers.
  - Relationships among clinical impairment and diffusivity measures.

Conclusion

- **Cerebellar MRI:**
  - Improves our understanding of:
    - **Structure-function relationships** in individuals with MS
    - **Individualized differences** in this heterogeneous group
  - May provide an avenue for:
    - Understanding motor skill learning in MS
    - Targeted, ***individualized rehabilitation***



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