

# The Cerebellum in Clinical Disorders

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## Overview

- Cerebellum anatomy
- How the cerebellum works
- Description of cerebellar clinical disorders
- Motor signs
- Cognition
- Pilot studies in cognition in cerebellar ataxia

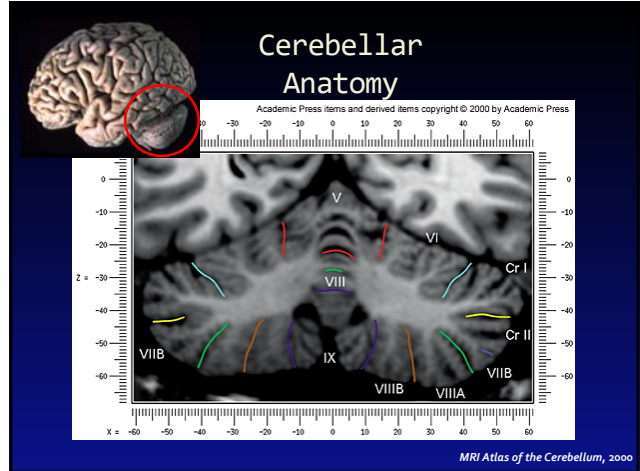
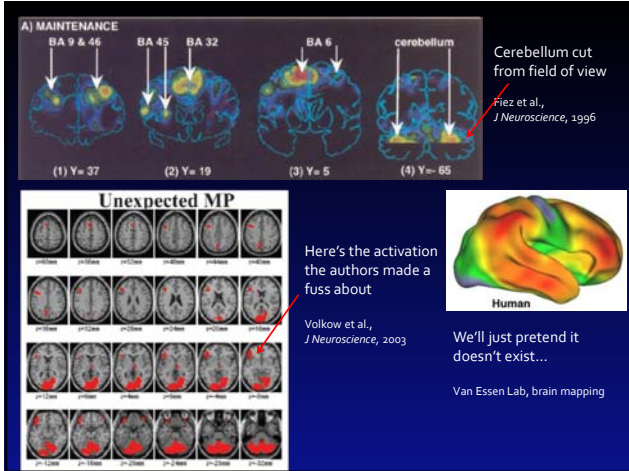
## The Cerebellum



## The Cerebellum

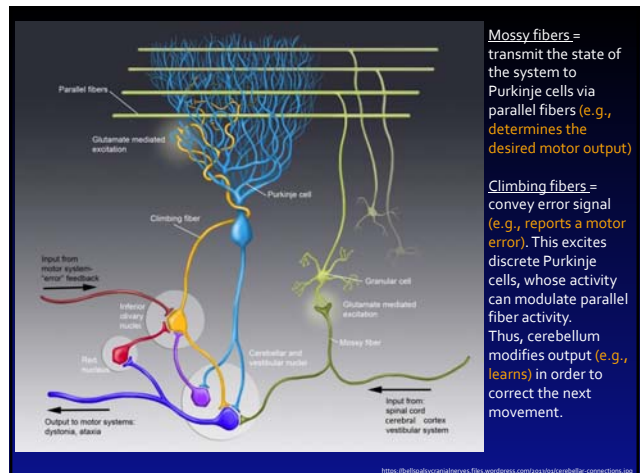


The cerebellum contains more neurons than the rest of the brain put together.  
(3.6x more than the neocortex)



## Cerebellar Anatomy

- The anatomy of the cerebellum is **simple, consistent throughout, and relatively preserved across species.**

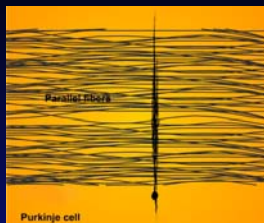


## Purkinje Cells

View from the front – dendrites fan out



View from the side – flat



<http://neuroscience.uth.tmc.edu/lyh/haptencg.html>

## Historical Perspective: Henrietta Leiner

1. Had a background in computers prior to studying neuroanatomy (1940s!)
2. Suggested that the homogeneous, parallel circuitry of the cerebellum allows rapid information processing (like a computer)
  1. Phylogenetically older parts = controlled motor function
  2. Newer parts = controlled cognition



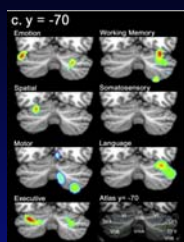
S. G. Leiner, J. Leiner and R. Leiner (1988)  
*Neuropsychology Review*,  
2010

## How does the Cerebellum Work?

- Uniform circuitry = whatever the cerebellum is doing, it does it the same way for every computation
- Difference in outcome-- depends upon the connections: where is information coming from and where is it going to?
- Outcome may also depend upon when the disruption occurred (pre-natal, developmental, sudden injury– as a child or as an adult)

## The Cerebellum's Role in Cognition

- Shows activation during:
  - Executive functions
  - Spatial skills
  - Working memory
  - Language
  - Emotions
- Cognitive deficits can occur in each of these domains as a function of cerebellar injury.
  - Effects may be subtle, in the low-normal range, but significantly lower than well-matched controls.

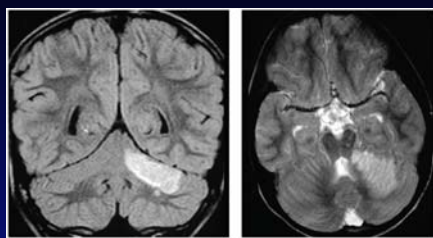


(Stoodley, 2009)

*With cerebellar degeneration, patients may become unable to manage the finely tuned process of thought coordination (e.g., for planning, language, sequencing). This can lead to an array of cognitive and psychiatric dysfunctions.*

## Cerebellum: Neurological Damage

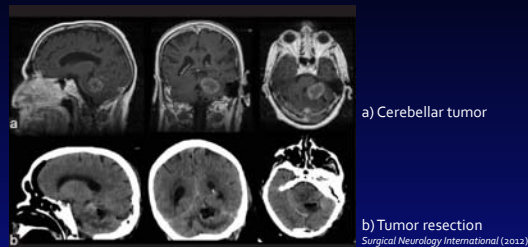
- Stroke



Left superior cerebellum  
*Stroke Research and Treatment, 2011*

## Cerebellum: Neurological Damage

- Tumor or tumor resection

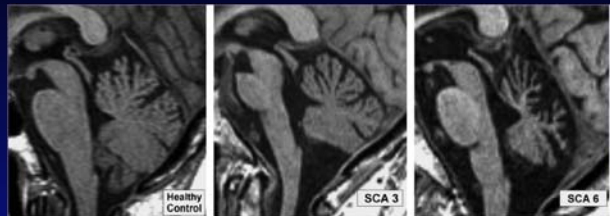


a) Cerebellar tumor

b) Tumor resection  
*Surgical Neurology International (2012)*

## Cerebellum: Neurological Damage

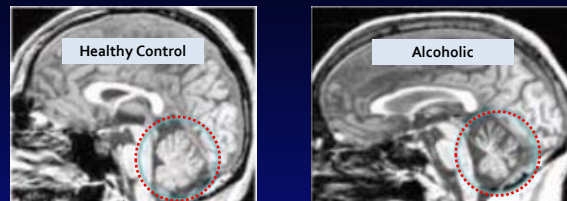
- Degeneration due to endogenous factors (e.g., inherited disease of spinocerebellar ataxia, SCA)



Marked cerebellar atrophy in the SCA patients  
*American Journal of Neuroradiology (2011)*

## Cerebellum: Neurological Damage

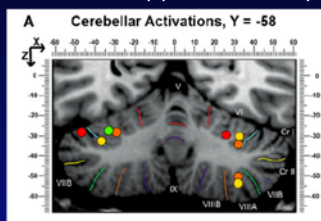
- Degeneration due to exogenous factors (e.g., alcoholism)



Marked cerebellar atrophy in the alcoholic patient  
*Alcohol Research and Health, Sullivan et al., 2010*

## Cerebellum: Environmental Contributors

- Alcohol and drug addiction: increased activity during fMRI for working memory vs. controls
- Chemotherapy: same fMRI pattern as in addiction



Red = alcohol  
Green = cocaine  
Orange = heroin  
Yellow = controls

*Neuroimage, 2003; Cerebellum, 2012; Breast Cancer Res Treat, 2007*

## Motor Signs

- Unsteady gait, poor balance, incoordination
- Dysarthric speech: reduced fluency, slurring
- Oculomotor problems: nystagmus, abnormal saccades (over or undershoot to target), jerky saccadic pursuit
- Associated with damage to anterior lobe (I – V) but not usually seen when damage is confined to inferior lobes (VII – X)

*Neuroscience (2009), Neuroimage (2006)*

## Cerebellar Ataxia



## Cerebellar Ataxia



## Cerebellum: Developmental Disorders

- Autism
  - Purkinje cell loss, mainly in the posterior cortex
- Schizophrenia
  - Smaller total cerebellar volumes
  - Cerebellar signs (e.g., unsteady tandem gait, intention tremor)
  - Poor premorbid social outcome
- Dyslexia
  - Anterior cerebellum may be involved but anatomical data are mixed
- Children born very pre-term (< 33 weeks)
  - Smaller lateral lobes

Cerebellum, 2012; Biol Psych, 2004; Cortex 2011; Brain, 2001

## Working Hypothesis

- The cerebellum refines the timing and sequencing of movements
- Results in:
  - Coordinating finely timed movements
  - Initiating a procedural approach to problem solving
  - Enabling a successful sequence of thoughts

# Implicit Sequence Learning

*Brain* (1997), 120, 1753-1762

**Cerebellum and procedural learning: evidence from focal cerebellar lesions**

Maria Molinari,<sup>1,2\*</sup> Maria G. Leggio,<sup>1,2</sup> Alessandro Solida,<sup>2</sup> Roberto Ciarami,<sup>2</sup> Sandro Miscuglio,<sup>2</sup> Maria C. Silveri<sup>1</sup> and Laura Petrosini<sup>3</sup>

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*Eur Brain Res* (1998) 120:25-38

**RESEARCH ARTICLE**

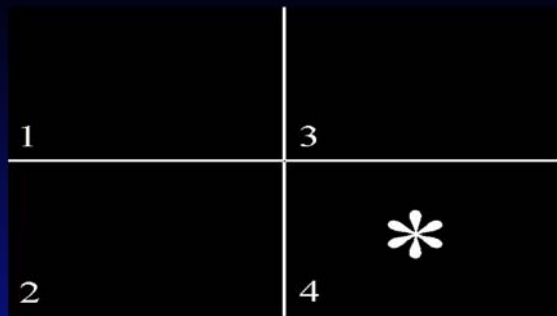
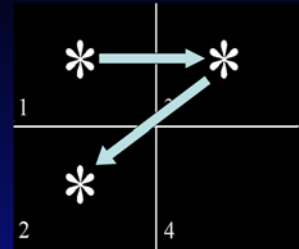
M. Gilman-Belardinelli · J.C. Garbin-Mancini · B. Babiloni · An. Pascual-Leone

**Effect of focal cerebellar lesions on procedural learning in the serial reaction time task**

- Cerebellar patients show less pattern learning
- Hand and lesion on same side: no pattern learning
- Hand and lesion on opposite side: pattern learning

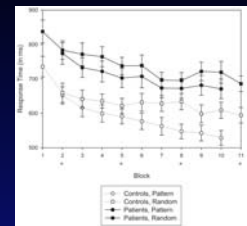
# Rules

1. Horizontal Move
2. Diagonal Move
3. Vertical Move
4. Horizontal Move

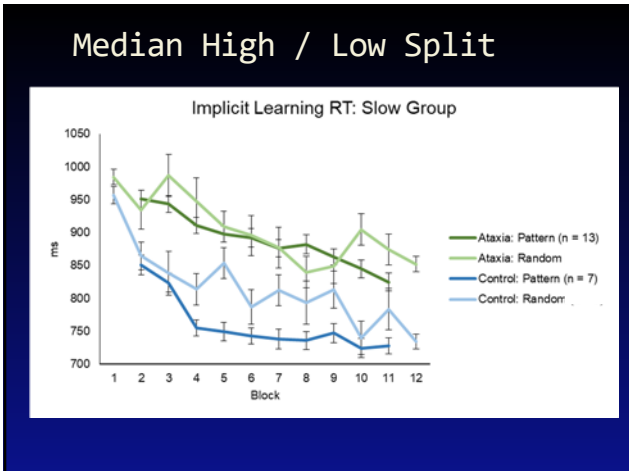
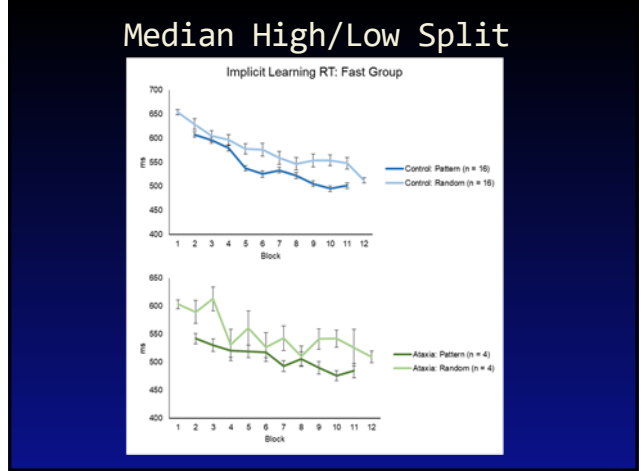
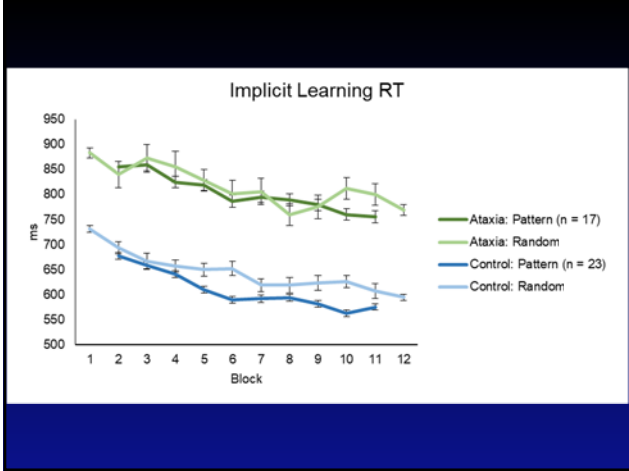


# Implicit Learning Task

- Trial order:
  - Random
  - Pattern
  - Pattern
  - Pattern
- Serial reaction time task:
  - Pattern faster than random



(Marvel, 2007)

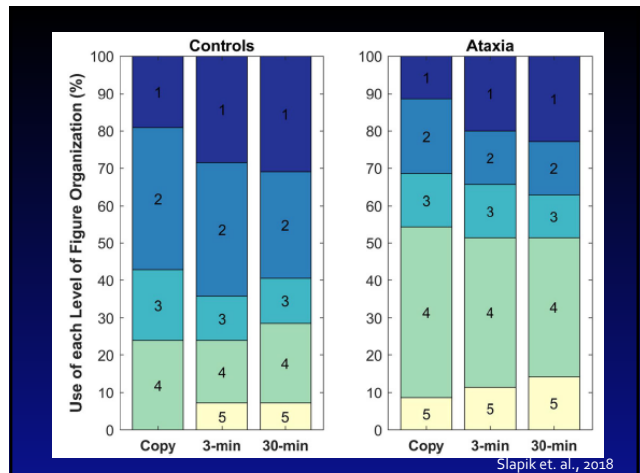
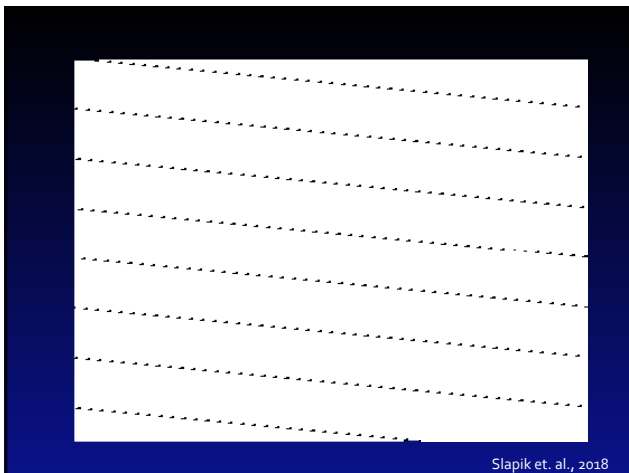
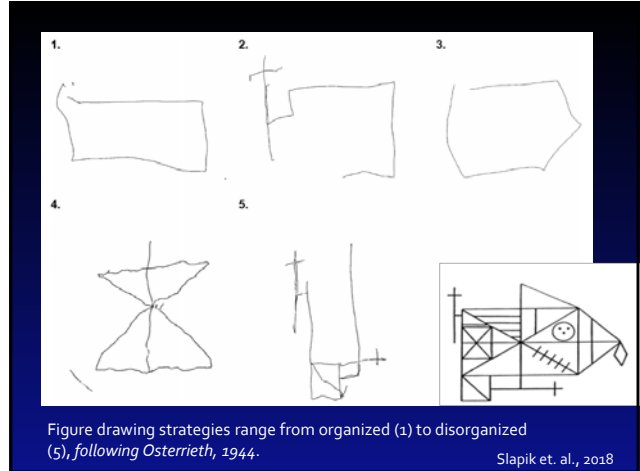
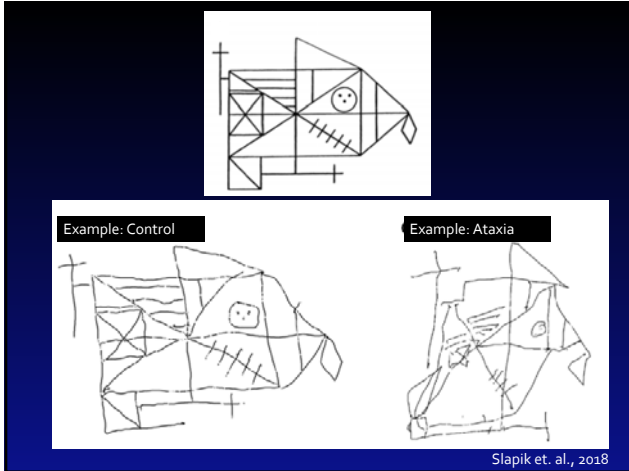


### Strategy Formation

- Rey Osterrieth Complex Figure (developed in 1941)

(Rey, 1941)






### Ordering: control condition

Click to pick up and place the cards in a logical order above.


Press ENTER when done.



### Ordering: Verbal condition

Click to pick up and place the cards in a logical order above.

Press ENTER when done.



### Ordering: Cartoon condition

Click to pick up and place the cards in a logical order above.


Press ENTER when done.



### Ordering: Spatial condition

Click to pick up and place the cards in a logical order above.

Press ENTER when done.

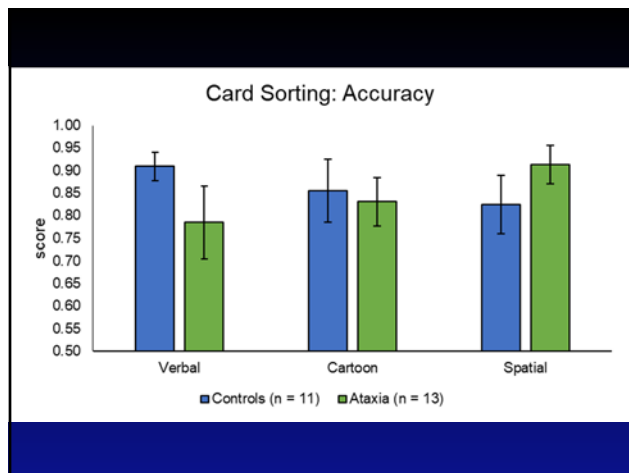
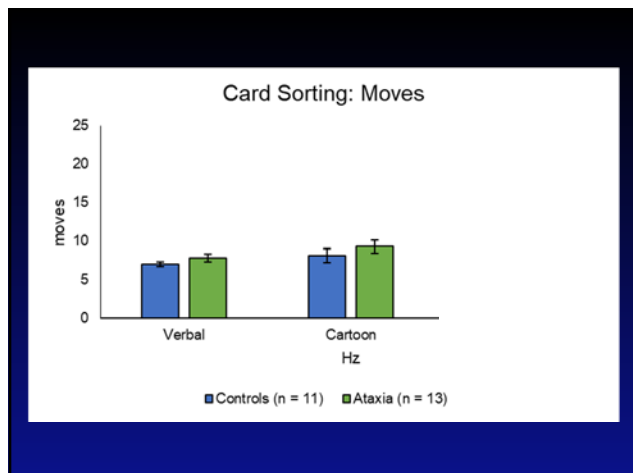
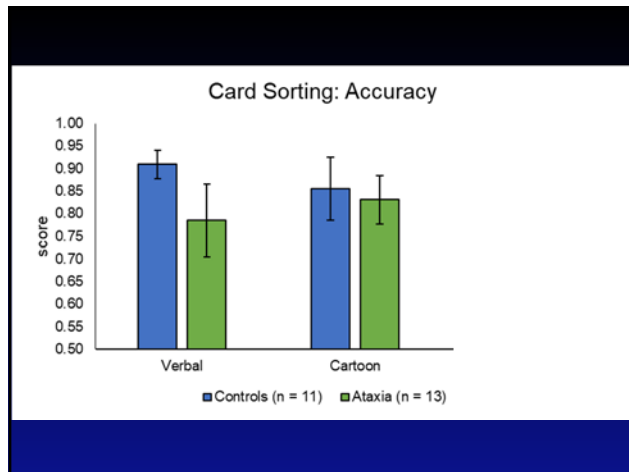


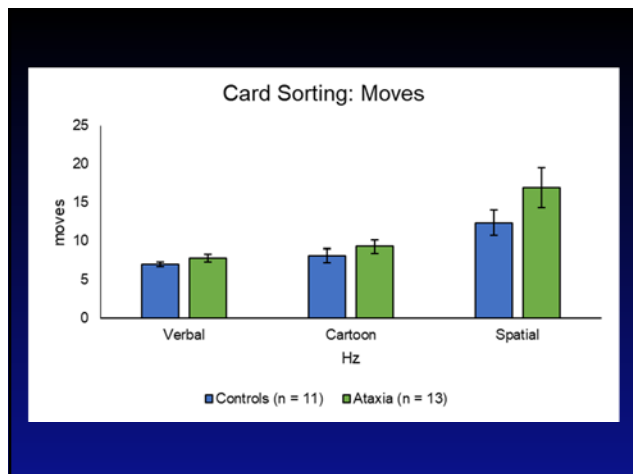
## Scoring: Accuracy & # of Moves

Accuracy based on formula following Leggio et al., 2008

$$RR = \frac{(\text{Correctly sequenced cards}) - (\text{Correct sequence fragments})}{\text{Total number of cards} - 1}$$

Total number of moves were recorded by the computer. Experimenters observed and marked # of moves that appeared unintentional --> these were subtracted from total # of moves.





## Taken together, data suggest...

- In ataxia –
  - Cerebellar role in timing and sequencing extends to cognitive domain
    - Implicit sequencing
    - Strategy formation
    - Logical ordering

## Summary

- Cerebellum structure is uniform throughout, contributing to its fundamental role in diverse motor and cognitive functions
  - Role is define by *input & output connections* with the rest of the brain.
- Cerebellar activity is, therefore, related to a wide variety of movement and cognitive functions and dysfunctions.

## Leiner movie – out take!

