

The Cerebellum in Clinical Disorders

December 5, 2017

Cherie Marvel, PhD
Associate Professor
Depts. of Neurology & Psychiatry



Overview

- Neurological Damage
 - Motor signs
 - Cognitive deficits
- Developmental Disorders
 - Range of evidence
- Environmental Contributors
- How does the cerebellum work? (i.e., how does it contribute to clinical disorders?)
- Pilot studies in cognition in cerebellar ataxia

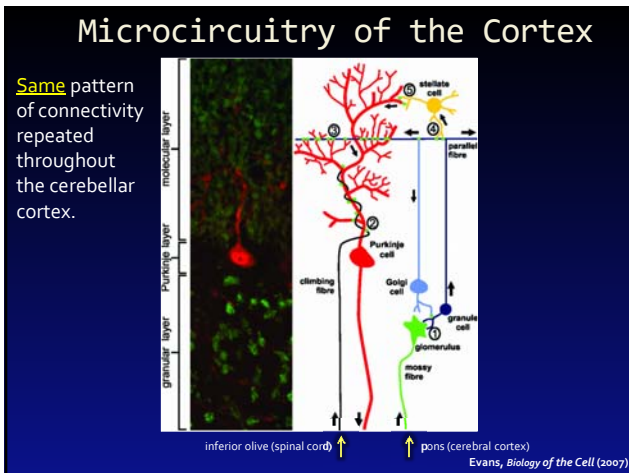
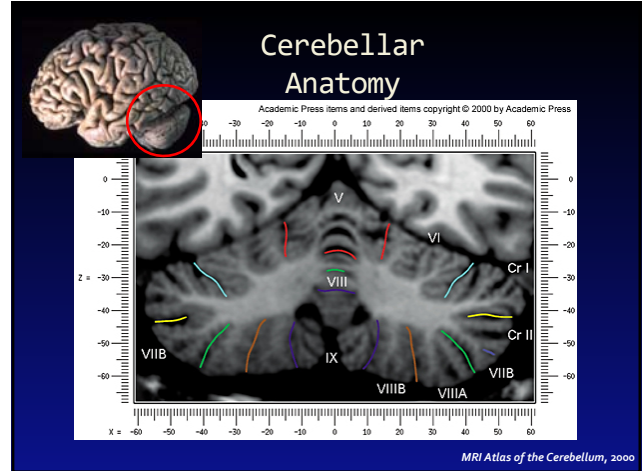
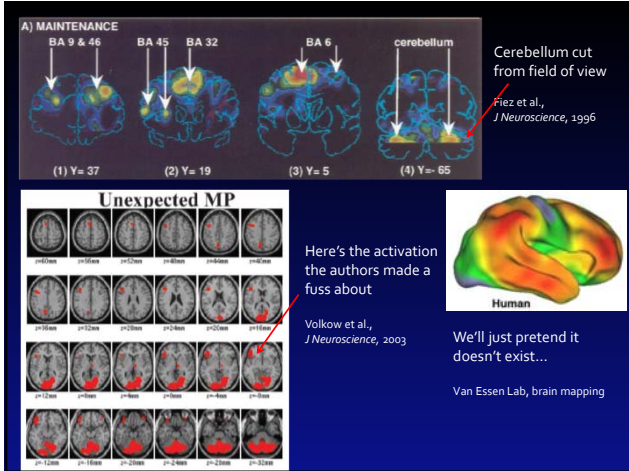
The Cerebellum



The Cerebellum



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



Historical Perspective: Henrietta Leiner

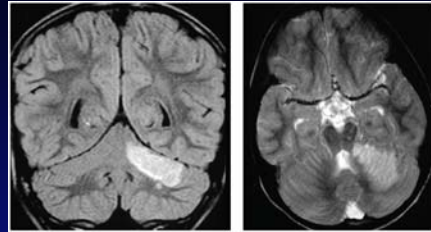
1. Had a background in computers prior to studying neuroanatomy (1940s!)
2. Suggested that the homogeneous, parallel circuitry of the cerebellum allows rapid information processing (like a computer)
 1. Phylogenetically older parts = controlled motor function
 2. Newer parts = controlled cognition

Neuropsychology Review, 2010



Cerebellum: Neurological Damage

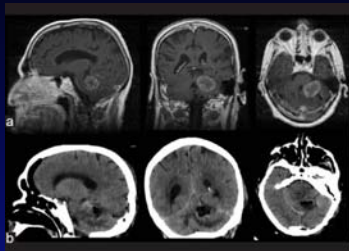
- Stroke



Left superior cerebellum
Stroke Research and Treatment, 2011

Cerebellum: Neurological Damage

- Tumor or tumor resection

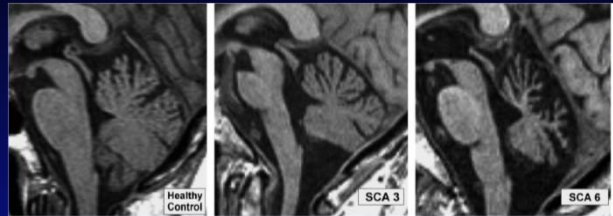


a) Cerebellar tumor

b) Tumor resection
Surgical Neurology International (2012)

Cerebellum: Neurological Damage

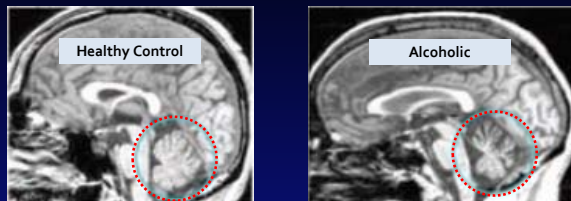
- Degeneration due to endogenous factors (e.g., inherited disease of spinocerebellar ataxia, SCA)



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

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



© 2004 Wright State University

Cerebellar Ataxia



©NEUROPASS

Cerebellar Ataxia



Cognitive Deficits

- Verbal working memory impairments
 - e.g., digit span
- Verbal fluency (especially phonemic)
- Executive function (Trails B, card sorting)
- Effects may be subtle, in the low-normal range, but significantly lower than well-matched controls.

J Neurol Neurosurg Psych, 2000; Brain, 2006; Behav Neurol, 2008; 2010

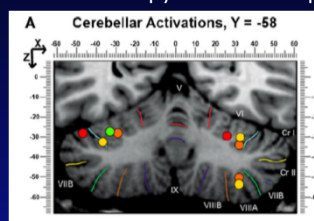
Cerebellum: Developmental Disorders

- 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

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

How does the Cerebellum Work?

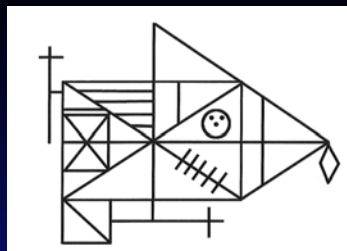
- Uniform circuitry = whatever the cerebellum is doing, it does it the same way for every computation
- Difference in outcome-- depends upon the connections: where is information coming from and where is it going to?
- Outcome may also depend upon when the disruption occurred (pre-natal, developmental,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

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.

Working Hypothesis

- The cerebellum controls the timing and sequencing of movements
- Results in:
 - Coordinating finely timed movements
 - Initiating a procedural approach to problem solving
 - Automatizing the process at hand--more "room" available to concentrate on other things (boosts multi-tasking ability)

Rey Osterreith Complex Figure Task



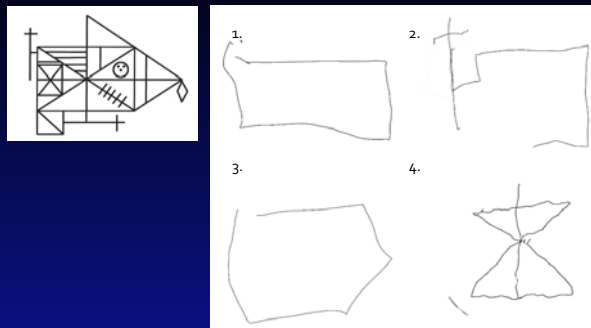
1. Copy figure as shown
2. 3 min: With figure out of view, draw all the part you can remember
3. 30 min: Draw again from memory

Rey, 1941

Drawn on a Tablet- records all aspects of the drawing (where lines are placed, sequence of drawing figure pieces, speed, velocity, etc.)

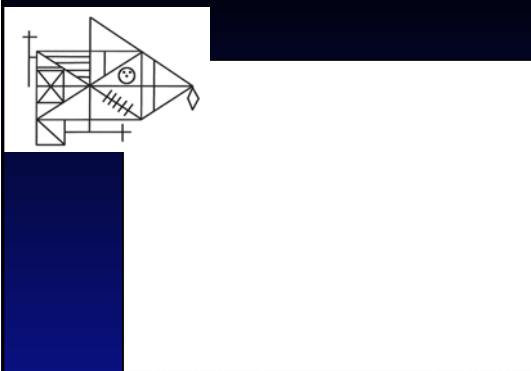


Figure Drawing Strategies



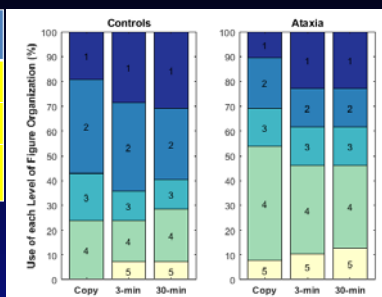
Strategy Score	Criteria
1	Participant begins by drawing the large rectangle.
2	Participant begins by drawing a detail attached to the large rectangle, and then proceeds to the rectangle.
3	Participant begins by drawing the overall contour of the shape, and then adds internal details.
4	Participant draws details one x one, without an organizing structure.
5	Participant copies discrete parts of the figure with no semblance of organization.
6	Participant substitutes a similar object, such as a boat or a house.
7	Participant creates an unrecognizable scrawl.

Example: Ataxia Patient using strategy #5



Strategy Ratings

Figure Drawing Condition	Group	Strategy Mean	p-value
Copy	Control	2.6	.004
	Ataxia	3.5	
3 min recall	Control	2.3	.004
	Ataxia	3.3	
30 min recall	Control	2.4	.007
	Ataxia	3.3	



Studies have shown...

- Using a better organized strategy (starting with outside and working on details inside) == > leads to higher memory recall for the figure

Figure Recall Accuracy

- Maximum score = 36; * = score correlated with strategy

Figure Drawing Condition	Group	Strategy Mean	p-value
Copy	Control	29.9	.000
	Ataxia	25.6	
3 min recall	Control	15.0*	.90
	Ataxia	14.8	
30 min recall	Control	15.0*	.98
	Ataxia	15.0	

Poor Strategy but Normal Recall

- How do patients adapt?
- Better accuracy in ataxia was related to faster processing speed (how quickly information is transmitted within the brain)
- When motor starts to fail, cognition helps maintain function. Those with high neuronal integrity are better at compensating.

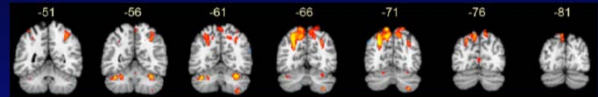
Question

If the cerebellum is involved in timing/ sequencing/ automatizing of motor and cognition . . .

What happens when motor and cognition rely on the cerebellum at the same time?

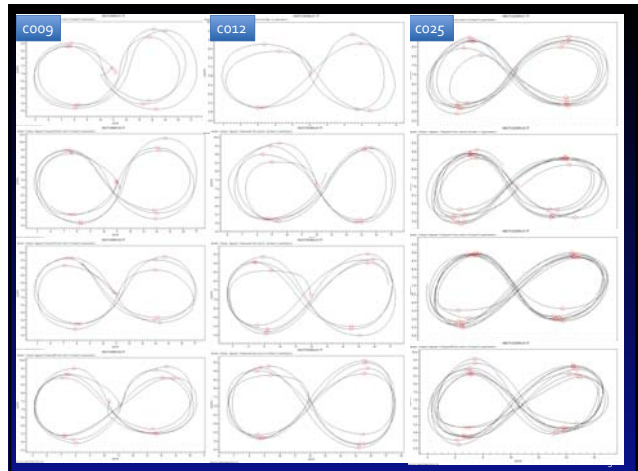
Pilot Study in Cerebellar Ataxia

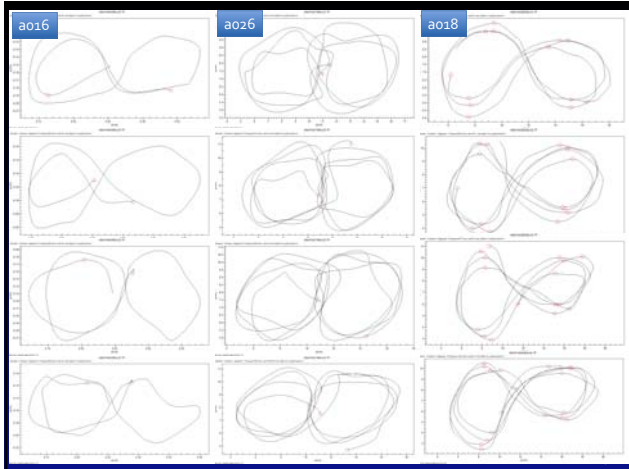
- Tests:
 - Drawing figure 8s
 - Letter recall (involves cerebellum, as shown in Marvel & Desmond, 2012)



Motor Learning in Ataxia:

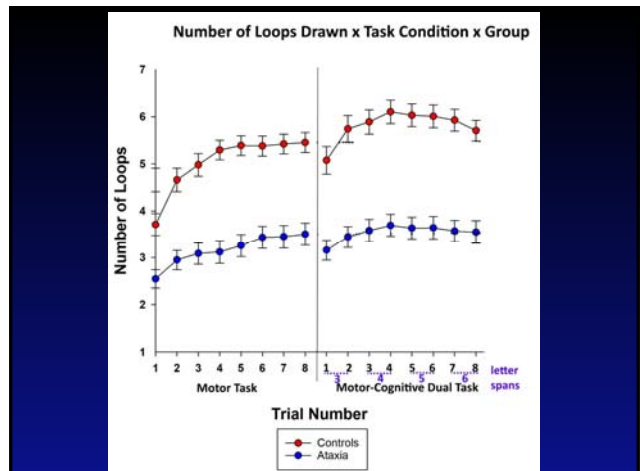
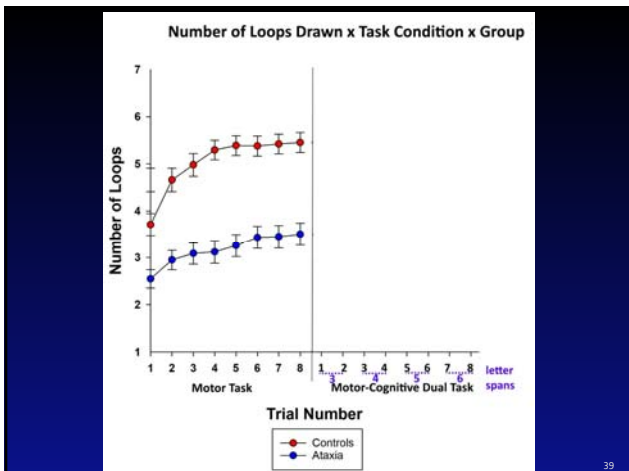
Subjects used stylus to "draw" figure 8 patterns on a tablet

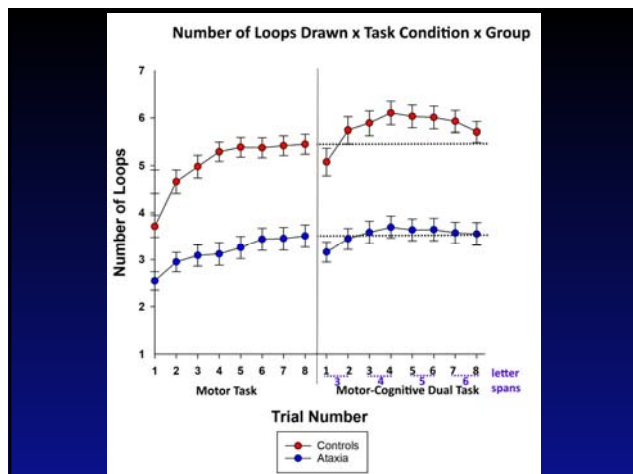




Single and Dual Task Conditions

- Single task: draw figure 8s for 5 sec
- Dual task: while drawing figure 8s, also rehearse a set of letters (read aloud by the experimenter beforehand -- 5 sec)
 - Number of letters spanned 3-6 in length
 - Letter span increased across trials





Cerebellar Ataxia: Motor-Cognitive Interactions

- Letter recall was normal in ataxia (data not shown)
- Rate of motor learning was slow
- Rate of motor learning was further disrupted by adding a cognitive load (even though cognitive performance was spared)

Taken together, data suggest...

- In ataxia –
 - Patients rely on cognitive strategies to compensate for loss of cerebellar motor function
 - Processing speed in complex figure recall
 - Working memory when drawing loops

Taken together, data suggest...

- In ataxia –
 - Patients rely on cognitive strategies to compensate for loss of cerebellar motor function
 - Processing speed in complex figure recall
 - Working memory when drawing loops
 - When cognitive demands are high, cognition is less available to aid motor function → motor function suffers
 - Rate of loop drawing flatlined early during letter recall

Summary

- Cerebellum is fundamental to many motor and cognitive functions, depending upon input/output.
- Cerebellar function is, therefore, related to a wide variety of movement and cognitive disorders.
- When primary motor functions of the cerebellum begin to fail, cognitive processes help to maintain normal function (up to a point).

Leiner movie - out take!

