



Studying the cerebellum in sensory motor control

Chris Miall

Behavioural Brain Sciences
School of Psychology
University of Birmingham



Cerebellar-Cortical Control: Cells, Circuits, Computation, and Clinic

Training

C⁷ is an initial training network under the [FP7 Marie Curie Actions](#), starting in October 2009. It provides 17 young researchers with the opportunity to work in Europe's leading laboratories in cerebellar research.

Fellows across the network will work together in interdisciplinary research teams on cutting-edge questions.

Fellows will receive part of their training (3-6 months) at one or more of the other partner sites.

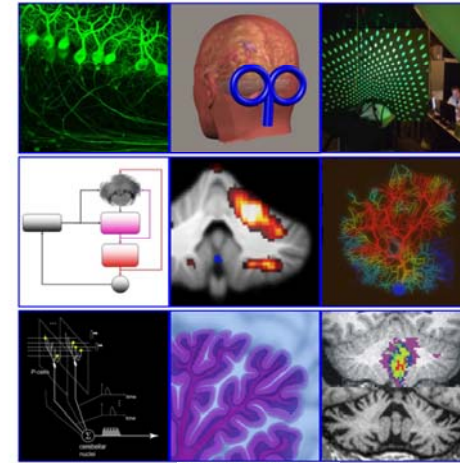
Fellows will have the opportunity to work with our industrial partners in the development of new technology for research, providing also opportunities outside of academia.

Level 1 Industry Partner

- [Alpha Omega/Alphabeta, Israel](#)

Associated Patient Organizations

- [DHDG](#)
- [EuroAtaxia](#)



Network

The C⁷ network brings together [9 research groups](#), [5 industrial partners](#), and [2 patient organizations](#) that form a European institute that conducts a truly interdisciplinary study of the cerebellum.

With electrophysiology, behavioural and clinical research, computational modelling and neuroimaging we will aim to answer three important questions:

1. What computation is performed in cerebellar networks?
2. How do distributed synaptic changes lead to learning?
3. How do cortico-cerebellar loops generate motor control and cognition?

Academic Partners

- [Jörn Diedrichsen \(London\)](#)
- [Maarten Frans \(Rotterdam\)](#)
- [Daphar Danchin \(Beer Sheva\)](#)
- [Dagmar Timmann-Baum \(Essen\)](#)
- [Chris Miall \(Birmingham\)](#)
- [Chris de Zeeuw \(Amsterdam\)](#)
- [Michael Hutter \(London\)](#)
- [Erik de Schutter \(Aachen\)](#)
- [Peter Thier \(Tübingen\)](#)

Associated Industry Partners

- [Chronos-Vision GmbH \(Berlin, Germany\)](#)
- [Noldus Information Technologies \(the Netherlands\)](#)
- [Industrial Development Ranger \(Bangor, Wales\)](#)
- [Brain Innovation B.V. \(Maastricht, the Netherlands\)](#)



Summary of my talk

1. Cerebellum:

Unique structure – unique function?

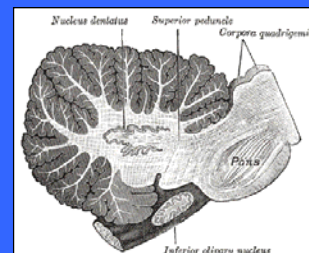
2. How do we study the cerebellum?

3. The idea of the cerebellum as a predictor

4. What next?



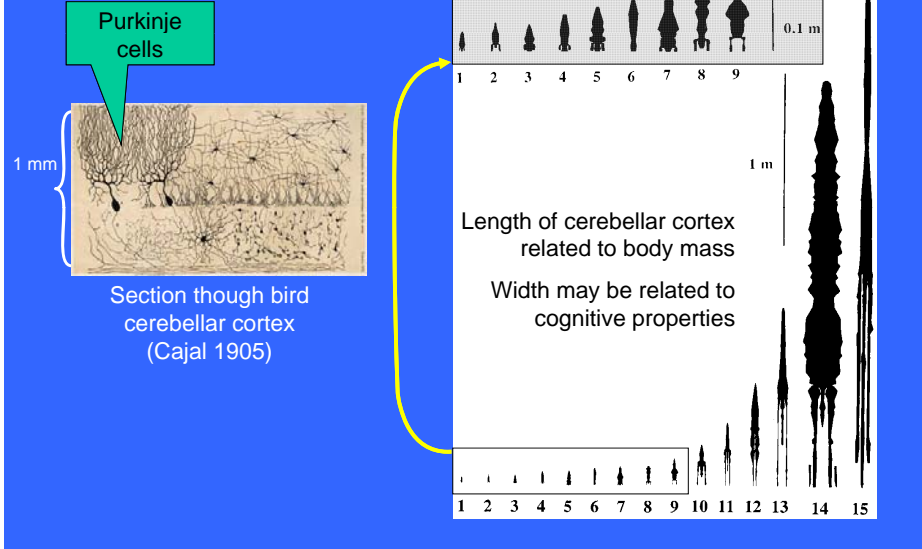
Cerebellum means “little brain” but a huge neural resource



- maybe 30% of the total brain area
- more than 50% of all nerve cells
- highly conserved architecture across vertebrate species
- expanded in primates in parallel with neocortex

Cerebellar cortical sheet

F. SULTAN AND V. BOUTCHER: Shape of mammalian cerebellum 31



One role: sensory-motor prediction?

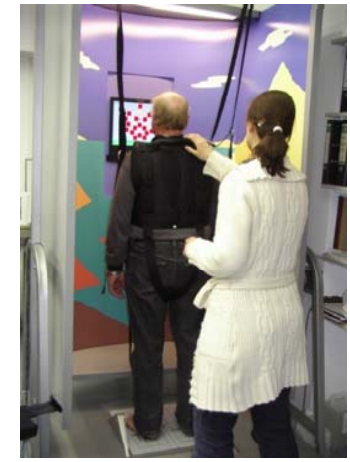


How do we study the cerebellum?

- Experiments with animals
 - Neuronal recording
 - Inactivation studies
- Theoretical models
- Experiments with normal volunteers
 - Brain stimulation
 - Brain imaging
- Experiments with patients
 - Behavioural measurements - eyes and limbs
 - Brain imaging

Effects of physiotherapy

Roxana Burciu and Dagmar Timmann
Department of Neurology, University Clinic Essen, Germany



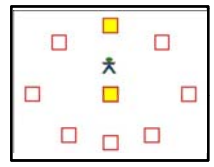
SMART Equitest NeuroCom

Our aims:

- To show that training improves ataxia
- To understand how training helps

Postural training:

- Move cursor on the screen by changing center of gravity
- One hour per day
- 14 days



Assessments:

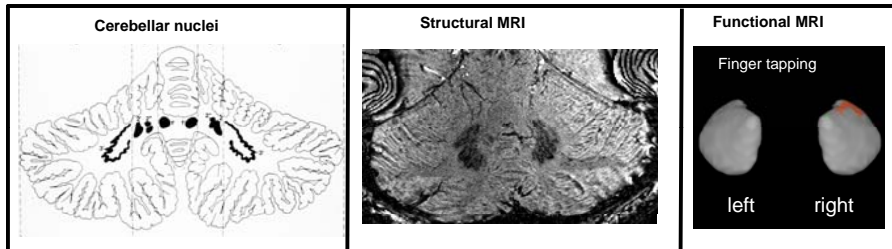
- Clinical ataxia scores and various postural measures
- Brain scans to show changes in gray matter density

Cerebellar nuclei in health and disease

Roxana Stefanescu and Dagmar Timmann
Department of Neurology, University Clinic Essen, Germany

Our aims:

- To better understand function and malfunction of the deep cerebellar nuclei



Experiments:

- Use a very strong magnet (7 Tesla) to do magnetic resonance imaging (MRI) of the cerebellum
- Measure size and activation of deep cerebellar nuclei
- Compare findings in participants with SCA3, SCA6, Friedreich's ataxia and no ataxia

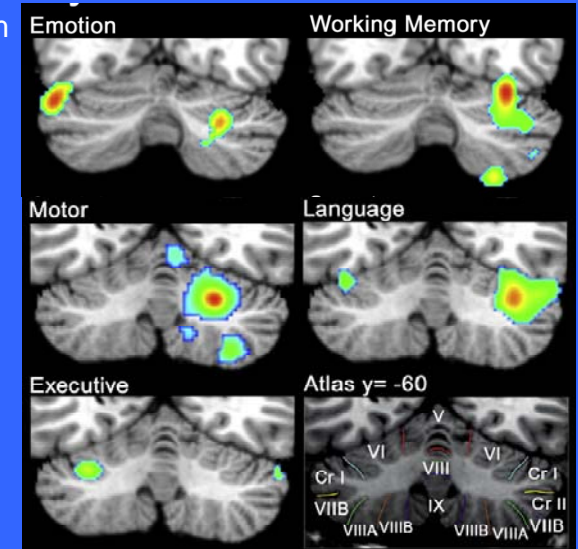
Imaging the cerebellum

Why is the cerebellum so active?

Movement tasks..

Potential roles in cognitive tasks (planning, attention, language)

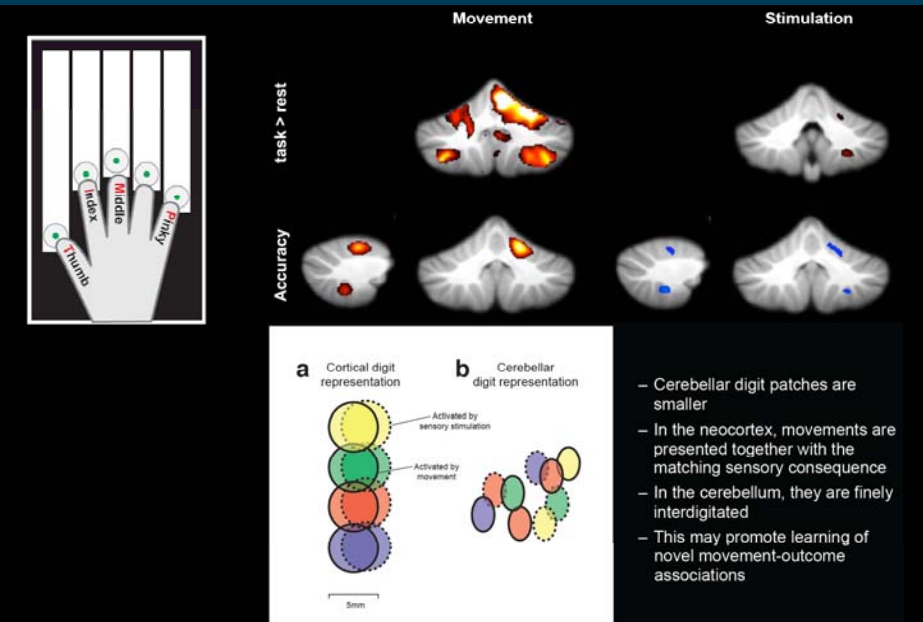
Links with affective disorders, autism, dyslexia.



Joern Diedrichsen, UCL London

- Cerebellum plays a prominent role in motor learning.
- Are there finger representations in the cerebellum?
- How are they different from the neocortical counterparts?
- How is sensory and motor integrated here?

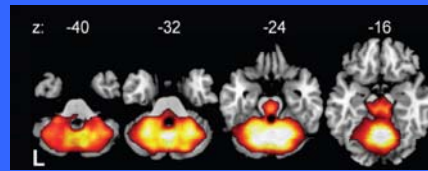
Cerebellar maps of the digits



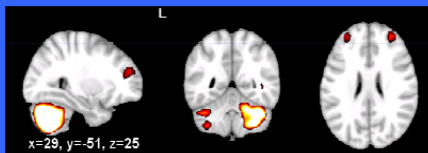
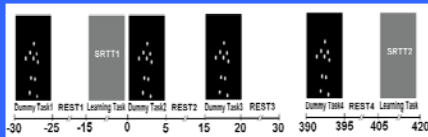
Cerebellar resting activity and motor memory

The cerebellum may be active at rest to consolidate previous learning experiences into memories (skills)

1. Visuomotor adaptation
2. Serial Reaction Time Task



Albert, Robinson & Miall, *Curr Biol* 2009



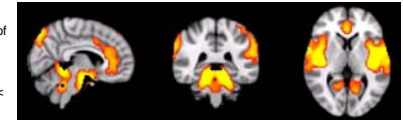
Patients with focal cerebellar damage recruit cerebral cognitive resources

Resting-state fMRI to investigate changes in functional connectivity patterns in cerebellar stroke patients and normal age/gender-matched controls

Default Mode Network and a cerebellar network are weaker in patients than in controls

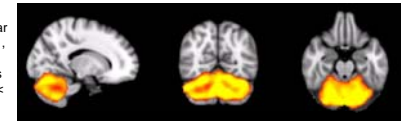
Interaction between the anterior cingulate cortex and the cerebellum is stronger in patients than controls

Fig. 1. Co-activation between sub-regions of the DMN ($p < 0.001$, $n=26$) is significantly reduced in patients relative to controls ($p < 0.05$).



MNI coordinates: $x=6$, $y=-38$, $y=4$ mm

Fig. 2. Co-activation across L & R cerebellar hemispheres ($p < 0.01$, $n=26$), is also reduced significantly in patients relative to controls ($p < 0.05$).



MNI coordinates: $x=16$, $y=62$, $y=22$ mm

Fig. 3. The cerebellum is more strongly correlated with the anterior cingulate cortex in patients relative to controls. This may suggest a greater use of cognitive resources in this group after stroke.



MNI coordinates: $x=0$, $y=16$, $y=32$ mm

Transcranial magnetic stimulation



Silvanus Phillips Thompson depicted with the device he had used

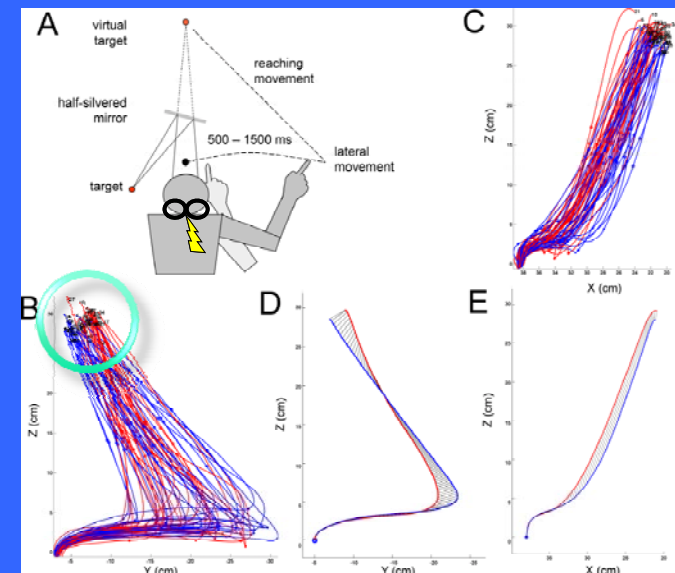


magnetic coils used by Magnusson and Stevens. Additional



TMS disruption of state estimation

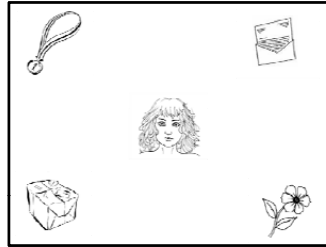
Miall, Christensen, Cain & Stanley
PLoS Biology 2007





A predictive role for the cerebellum in language processing

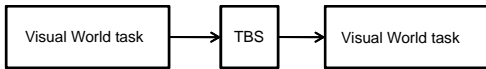
- The right cerebellum is involved in language tasks
 - **Visual World Task**
 - Subjects look at scenes and listened to sentences
 - Target (object) can (or cannot) be predicted from the verb (**predictive vs non-predictive condition**)
 - eye-movements are recorded
- Target is fixated earlier in the predictive condition
Paradigm can be used to study prediction in language



Predictive: The girl will **write** the letter

Non-predictive: The girl will **receive** the letter

- **Hypothesis:** cerebellum is involved in predictive language processing
- rTMS will perturb predictive eye gaze shift
⇒ predictive effect will decrease or disappear

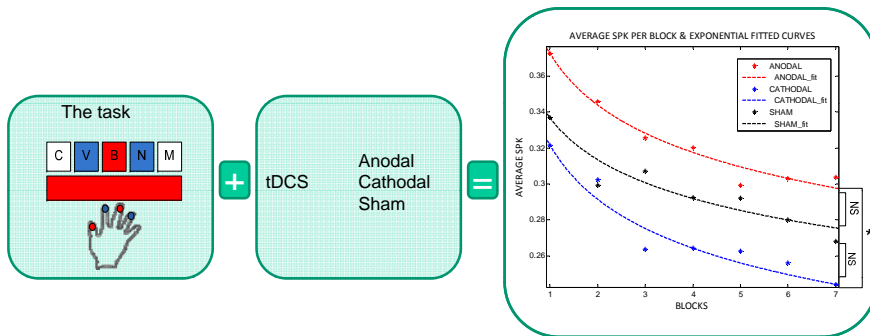


Transcranial direct current stimulation



Polarity-specific effect of cerebellar tDCS in a novel motor task

- ✓ tDCS can modulate in a focal and polarity-specific manner cerebellar excitability
- ✓ How does tDCS affects **learning**?



- Results:
- ✓ Anodal tDCS slowed down performance
 - ✓ Cathodal tDCS enhanced performance



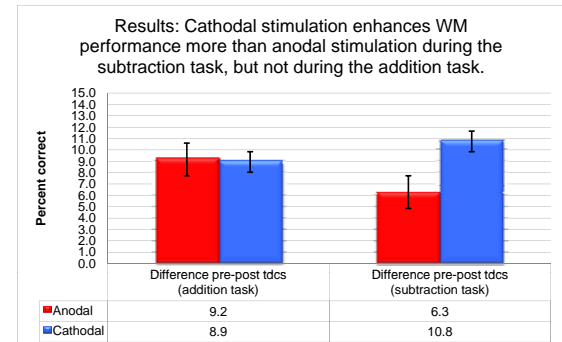
Cerebellar stimulation & working memory in tasks with high cognitive demand

The cerebellum sends and receives information from areas of the prefrontal cortex that are involved in cognition

Paced Auditory Serial Addition Task (PASAT) versus Paced Auditory Serial Subtraction Task (PASST)

- The PASAT and PASST share the same covert speech operations but require different levels of cognitive skill - subtraction is more difficult than addition

| | | | | | | | | | |
|-----|----|----|----|----|----|----|----|----|----|
| 1+4 | 8 | 1 | 5 | 1 | 3 | 7 | 2 | 6 | 9 |
| 5 | 12 | 9 | 6 | 6 | 4 | 10 | 9 | 8 | 15 |
| 4 | 7 | 3 | 5 | 3 | 6 | 8 | 2 | 5 | 1 |
| 13 | 11 | 10 | 8 | 8 | 9 | 14 | 10 | 7 | 6 |
| 5 | 4 | 6 | 3 | 8 | 1 | 7 | 4 | 9 | 3 |
| 6 | 9 | 10 | 9 | 11 | 9 | 8 | 11 | 13 | 12 |
| 7 | 2 | 6 | 9 | 5 | 2 | 4 | 8 | 3 | 1 |
| 10 | 9 | 8 | 15 | 14 | 2 | 6 | 12 | 11 | 4 |
| 8 | 5 | 7 | 1 | 8 | 2 | 4 | 9 | 7 | 9 |
| 9 | 13 | 12 | 8 | 9 | 10 | 6 | 13 | 16 | 16 |
| 3 | 1 | 5 | 7 | 4 | 8 | 1 | 3 | 8 | 2 |
| 12 | 4 | 6 | 12 | 11 | 12 | 9 | 4 | 11 | 10 |



Motor role(s) of the cerebellum

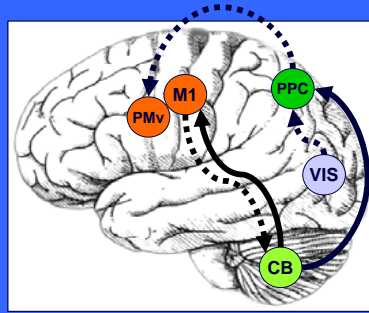
Coordination of eye & hand
modulates cerebellar activity
signal

Skilful movement depends on
prediction

Cerebellum provides a “forward”
prediction of movement outcome

Spatial pattern of cerebellar
activation suggests a modular
arrangement

Cerebellum is brain’s “virtual
reality machine”



The cerebro-cerebellar challenges

- Does the cerebellum “predict”
cognitive processes?

- How does the cerebellum
perform these calculations?

- What are the effects of
cerebellar disease on the
cerebral cortex?

- How does the brain
reorganize after cerebellum
damage?

