Cognitive and Emotional Aspects of Cerebellar Function and Dysfunction:

1. Anatomical Substrates

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Annual Meeting, Pacific Northwest Neuropsychological Society
University of Washington Faculty Club
Seattle, WA
March 6th, 2010
Nicolas Steno
(Niels Steensen, Niels Stensen,
Nicolaus Stenonis,
1638 – 1686)

Thomas Willis
1621-1675
Vincenzo Malacarne
(1744-1816)
Franz Josef Gall
(1758-1828)

Johann Gaspar Spurzheim
(1776-1832)
Marie Jean-Pierre Flourens
(1794 - 1867)
Lodewijk ('Louis') Bolk
(1866-1930)

www.inghist.nl/.../BWN/lemmata/bwn6/bolk
Diagram by Jan Voogd representing Bolk’s notion of functional localization in the cerebellum.

From Stein and Glickstein, 1992
Cerebellar clinical features – the cerebellar “motor” syndrome

- Gait ataxia
- Dysmetria of extremities
- Eye movement abnormalities
- Dysarthria
Cerebellum and Cognition

Snider, 1950

Schmahmann, 1997

Snider, 1950
Cerebellum - Essential anatomy
Anatomic Organization of the Cerebrocerebellar System
Cerebellar fissures in 3-D space
Right lateral view
Schmahmann et al., 2000
<table>
<thead>
<tr>
<th>VERMIS</th>
<th>FISSURE</th>
<th>HEMISPHERE</th>
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<tbody>
<tr>
<td>Lobule</td>
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<tr>
<td>I,II</td>
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<td>I,II</td>
</tr>
<tr>
<td>III</td>
<td>Precentral</td>
<td>III</td>
</tr>
<tr>
<td>IV</td>
<td>Preculminate</td>
<td>IV</td>
</tr>
<tr>
<td>V</td>
<td>Intraculminate</td>
<td>V</td>
</tr>
<tr>
<td>VI</td>
<td>Primary</td>
<td>VI</td>
</tr>
<tr>
<td>VII Af</td>
<td>Superior Posterior</td>
<td>Crus I</td>
</tr>
<tr>
<td>VII At</td>
<td>Horizontal</td>
<td>Crus II</td>
</tr>
<tr>
<td>VIIB</td>
<td>Ansoparamedian</td>
<td>VIIB</td>
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<td>VIII A</td>
<td>Prepyramidal/Prebiventer</td>
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<td>VIII B</td>
<td>Intrabiventer</td>
<td>VIII B</td>
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<tr>
<td>IX</td>
<td>Secondary</td>
<td>IX</td>
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<tr>
<td>X</td>
<td>Posterolateral</td>
<td>X</td>
</tr>
</tbody>
</table>
Makris et al., 2005
“Purkinje cell tree”
Santiago Ramon y Cajal
www.vocesdelaciencia.com.ar

Eccles, Ito, Szenthagotai, 1967

Cajal, 1911
Blood supply of human cerebellum.
Adapted from Tatu et al., 1996
Distributed neural systems comprise anatomic regions, or nodes. Unique architectural properties. Geographically arranged throughout cortical and subcortical areas. Linked anatomically in a precise and unique manner.
General principle of organization of cerebral connections: 5 major pathways

- Association fibers
- Striatal fibers
- Commissural fibers
- Projection fibers
  - Thalamic bundle
  - Pontine bundle

Schmahmann and Pandya, 2006
Diffusion spectrum imaging (DSI) - monkey


Wedeen, Wang, Schmahmann et al., NeuroImage 2008
Ex-vivo DSI Tractography of 80-90% of a Human Cerebral Left Hemisphere

Wedeen, Schmahmann, Dai, Wang, Frosch, 2009
Subcortical Nodes in Distributed Neural Circuits

- Basal Ganglia
- Thalamus
- Cerebellum
- Cerebral White Matter
The cerebrocerebellar circuit

Schmahmann, 1994
Schmahmann and Pandya, 1989, 1992

Cerebral cortex

Pons, low power

Pons, high power

WGA-HRP Isotope
Trajectory of corticopontine fibers in monkey.

Schmahmann and Pandya, 1992
Connectional neuroanatomy with diffusion spectrum imaging

Schmahmann, Wedeen, et al., 2006
Cerebro-cerebellar loops: Feedforward limb

Schmahmann, 1994, 1996
Schmahmann and Pandya, 1987, 1997
Motor corticopontine projections in rhesus monkey

Schmahmann, Rosene, Pandya, 2004
Prefrontopontine projections in rhesus monkey

Schmahmann and Pandya, 1997
Pontocerebellar projection in monkey

Brodal, 1979
Pontine projections to cerebellar crus I

Schmahmann and Pandya, (from Schmahmann 1996)
Cerebello-cerebral feedback circuit

Schmahmann, 1991
Cerebellar projections to frontal lobe

Middleton and Strick, 1997

Kelly and Strick, 2003
Reciprocal hypothalamocerebellar projections

Haines et al., 1997.
Sensorimotor vs. prefrontal and association area dichotomy in cerebrocerebellar interactions (fcMRI)

A. Motor cortex seeds label cerebellar anterior lobe
B. DLPFC seeds lobes cerebellar posterior lobe

Cerebellar anterior lobe seeds label sensorimotor cortex
Cerebellar posterior lobe seeds label association areas

Krienen and Buckner, 2009
Functional topography of human cerebrocerebellar connections as determined by fcMRI

Krienen and Buckner, 2009
Multiple tactile maps in the human cerebellum

Red - Hand  
Blue - Foot  
Bushara et al., NeuroReport 2001;12:2483-86

Representation of tactile maps for hand (red) and foot (blue) on semi-flattened map of cerebellum
Fiez et al., 1997

Speaking Aloud Visual Nouns minus Passively Viewing Nouns

Generating Verbs minus Speaking Aloud Visual Nouns

Z = -12  Z = -16  Z = -20

Fiez et al., 1997
Functional topography in the human cerebellum.

Motor
Mental Imagery
Language

Schmahmann et al., NeuroImage 1998
Activation in cerebral hemispheres and cerebellum in a silent verbal fluency task.
A: Right handed person with left cerebral and right cerebellar activation (Lobule VI).
B: Left handed person with right cerebral and left cerebellar activation (Crus I).
PAIN (Red) - vermal lobules III, IV, and V.
ANTICIPATION OF PAIN (Yellow) - lobule VI (vermis, paravermian).

Ploghaus et al. Science 1999;284:1979-81
Separate locations for sensorimotor and neurobehavioral functions

Stoodley and Schmahmann, 2009
Cerebellar functional topography. Single case fMRI

Key:
- Tapping = red-orange
- Verb generation = blue
- n-back = purple
- Mental rotation = green
- IAPS = yellow

Stoodley, Valera, Schmahmann, 2010
The associative and paralimbic incorporation into the cerebrocerebellar circuit is the anatomic underpinning of the cerebellar contribution to cognition, emotion and autonomic function.

Discretely organized anatomic sub-units subserve functional sub-systems (loops) within the cerebrocerebellar circuit.
Cognitive and Emotional Aspects of Cerebellar Function and Dysfunction: 2. Clinical Presentations

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Cerebellar clinical features – the cerebellar “motor” syndrome

- Gait ataxia
- Dysemetria of extremities
- Eye movement abnormalities
- Dysarthria
Clinical Reports - Cerebellum and Behavior: 1800’s

<table>
<thead>
<tr>
<th>INVESTIGATOR</th>
<th>LESION</th>
<th>BEHAVIOR</th>
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</thead>
<tbody>
<tr>
<td>Combettes, 1831</td>
<td>Agenesis</td>
<td>Delayed development, aberrant behavior</td>
</tr>
<tr>
<td>Andral, 1848</td>
<td>Agenesis, left</td>
<td>“Imbecile, weakness of character”</td>
</tr>
<tr>
<td>Vulpian, 1866</td>
<td>Atrophy</td>
<td>Aberrant behavior</td>
</tr>
<tr>
<td>Otto, 1873</td>
<td>Agenesis</td>
<td>Low intelligence, aberrant / deviant behavior</td>
</tr>
<tr>
<td>Ferrier, 1876</td>
<td>Agenesis</td>
<td>Feeble minded</td>
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<tr>
<td>Doursout, 1891</td>
<td>Atrophy</td>
<td>“Idiocy, irritability, brutality”</td>
</tr>
<tr>
<td>Fusari, 1892</td>
<td>Agenesis</td>
<td>Mental retardation (“grave imbecility”)</td>
</tr>
<tr>
<td>Neff, 1894</td>
<td>Atrophy</td>
<td>Mental deficiency</td>
</tr>
<tr>
<td>Bond, 1895</td>
<td>Atrophy</td>
<td>“Foolishness”</td>
</tr>
<tr>
<td>Londe, 1895</td>
<td>Spastic ataxia</td>
<td>Mental difficulties</td>
</tr>
<tr>
<td>Claasen, 1898</td>
<td>Atrophy</td>
<td>Mental deficiency</td>
</tr>
<tr>
<td>Whyte, 1898</td>
<td>Friedreich's ataxia</td>
<td>Mental impairment</td>
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<tr>
<td>INVESTIGATOR</td>
<td>LESION</td>
<td>BEHAVIOR</td>
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<td>------------------------------</td>
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<tr>
<td>Anton, 1903</td>
<td>Agenesis</td>
<td>Mental retardation</td>
</tr>
<tr>
<td>Batten, 1905</td>
<td>Agenesis</td>
<td>Mental retardation</td>
</tr>
<tr>
<td>Vogt, Astwazaturow, 1912</td>
<td>Hypoplasia</td>
<td>Mental retardation</td>
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<tr>
<td>Beyerman, 1917</td>
<td>“Congenital atrophy”</td>
<td>Mental retardation</td>
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<tr>
<td>Schob, 1921</td>
<td>“Congenital atrophy”</td>
<td>Mental retardation</td>
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<tr>
<td>Curschmann, 1922</td>
<td>Hereditary ataxia</td>
<td>Mental impairment</td>
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<tr>
<td>Koster, 1926</td>
<td>Hypoplasia</td>
<td>Mental retardation</td>
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<tr>
<td>Walter and Roese, 1926</td>
<td>Hereditary ataxia</td>
<td>Mental impairment</td>
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<tr>
<td>Santha, 1930</td>
<td>“Congenital atrophy”</td>
<td>Mental retardation</td>
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<tr>
<td>Scherer, 1933</td>
<td>“Congenital atrophy”</td>
<td>Mental retardation</td>
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<tr>
<td>Akelaitis, 1938</td>
<td>Cortical atrophy</td>
<td>Dementia (late stages)</td>
</tr>
<tr>
<td>Rubinstein, Freeman, 1940</td>
<td>Agenesis</td>
<td>Mild mental retardation, poor memory, delusions</td>
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# Clinical Reports - Cerebellum and Behavior: 1950-1975

<table>
<thead>
<tr>
<th>INVESTIGATOR</th>
<th>LESION</th>
<th>BEHAVIOR</th>
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<tbody>
<tr>
<td>Knoepfel, Macken, 1947</td>
<td>Degeneration</td>
<td>Psychosis</td>
</tr>
<tr>
<td>Jervis, 1950</td>
<td>“Congenital atrophy”</td>
<td>Mental retardation</td>
</tr>
<tr>
<td>Schut, 1950</td>
<td>OPCA</td>
<td>Intellectual difficulty (late)</td>
</tr>
<tr>
<td>Mutrux et al, 1953</td>
<td>“Congenital atrophy”</td>
<td>Mental retardation</td>
</tr>
<tr>
<td>Gillespie, 1965</td>
<td>Degeneration, aniridia</td>
<td>“Oligophrenia”</td>
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<tr>
<td>Carpenter, Schumacher 1966</td>
<td>Infantile atrophy</td>
<td>Mental retardation</td>
</tr>
<tr>
<td>Aguilar et al, 1968</td>
<td>Ataxia-telangiectasia</td>
<td>Mental deficiency (late)</td>
</tr>
<tr>
<td>Joubert et al, 1969</td>
<td>Vermal agenesis</td>
<td>Mental retardation</td>
</tr>
<tr>
<td>Keddie, 1969</td>
<td>Cortical atrophy</td>
<td>Paranoid psychosis</td>
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<tr>
<td>Hoffman et al, 1971</td>
<td>Degeneration</td>
<td>Impaired intellect (late)</td>
</tr>
<tr>
<td>Landis et al, 1974</td>
<td>OPCA</td>
<td>Mild cognitive impairment</td>
</tr>
</tbody>
</table>
If cerebellar action is exerted on cerebral centers either to potentiate or to dampen activity...then the cerebellum stands out as 'the great modulator of neurologic function' and new horizons of cerebellar action are introduced into neurology and psychiatry.

Ray S. Snider
Amelioration of aggression in monkeys by cerebellar lesions.

Berman et al., 1978.
Demonstration of cerebellar – limbic physiological interactions.

The midline cerebellum (vermis and fastigial nucleus) is an integral part of the neural network for emotional expression and asserts a unique modulating effect on brain sites where physiological activity correlates with pathological behavior and epilepsy.

Robert G. Heath et al.

Essential brain circuitry involved in eyeblink conditioning.

Thompson et al., 1997
Something important seems to happen to convulsive phenomena, to a variety of vegetative functions, to emotional behavior and perhaps even to the highest level of intellectual function when a cerebellar influence is introduced into the nervous system. Whatever it does to modify the activity of other parts of the brain, it probably does the same thing in all its possible varied roles. Its uniformity of structure throughout vertebrates and within its various subdivisions in higher mammals makes this most likely.

Robert S. Dow

Cerebellar histopathology in Autism

Bauman and Kemper, 1997
5-days following cerebellar midline ganglioglioma resection
A Journey Through
Emotions

The times used to be so different.
Although I know there were so
Many good times, I can only seem
to remember the bad ones....

Why is that the case,?

Years ago, the tears rolled down
My cheeks as if it were a once in
A lifetime journey to the edge of
My face. Now, it is as though that
Journey has turned into a routine.
Performed weekly.

How can one's life be ever changing
At each moment if it is looked upon?
And who can say that tomorrow's trauma
Will not be better or worse than yesterday's?

I wonder who controls these emotions
Felt day after day, year from year.
Is it God? Me? Or some being unknown
to these eyes I call my own? I wonder....
Table 1 *Patient characteristics*

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Education (years)</th>
<th>Diagnosis</th>
<th>Interval: onset–examination</th>
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<tr>
<td>1</td>
<td>23</td>
<td>16</td>
<td>Midline/paravermis resection</td>
<td>1 week</td>
</tr>
<tr>
<td>2</td>
<td>44</td>
<td>12</td>
<td>Bilateral PICA stroke</td>
<td>1 month</td>
</tr>
<tr>
<td>3</td>
<td>57</td>
<td>20</td>
<td>Bilateral PICA stroke</td>
<td>2 weeks</td>
</tr>
<tr>
<td>4</td>
<td>32</td>
<td>16</td>
<td>Right PICA stroke</td>
<td>2 weeks</td>
</tr>
<tr>
<td>5</td>
<td>62</td>
<td>18</td>
<td>Right PICA stroke</td>
<td>2 weeks</td>
</tr>
<tr>
<td>6</td>
<td>74</td>
<td>12</td>
<td>Right PICA stroke</td>
<td>2 weeks</td>
</tr>
<tr>
<td>7</td>
<td>56</td>
<td>12</td>
<td>Right PICA (medial) stroke</td>
<td>1 month</td>
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<tr>
<td>8</td>
<td>58</td>
<td>18</td>
<td>Right PICA (branch) stroke</td>
<td>2 years</td>
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<tr>
<td>9</td>
<td>67</td>
<td>12</td>
<td>Left PICA stroke</td>
<td>1 week</td>
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<tr>
<td>10</td>
<td>66</td>
<td>9</td>
<td>Left PICA stroke</td>
<td>2 weeks</td>
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<tr>
<td>11</td>
<td>58</td>
<td>12</td>
<td>Left PICA stroke</td>
<td>2 weeks</td>
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<tr>
<td>12</td>
<td>50</td>
<td>16</td>
<td>Right AICA stroke</td>
<td>1 week</td>
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<tr>
<td>13</td>
<td>58</td>
<td>12</td>
<td>Left SCA stroke</td>
<td>2 weeks</td>
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<tr>
<td>14</td>
<td>36</td>
<td>12</td>
<td>Right SCA stroke</td>
<td>1 week</td>
</tr>
<tr>
<td>15</td>
<td>22</td>
<td>16</td>
<td>Postinfectious cerebellitis</td>
<td>1 month</td>
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<tr>
<td>16</td>
<td>12</td>
<td>Grade 6</td>
<td>Postinfectious cerebellitis</td>
<td>1 month</td>
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<td>17</td>
<td>42</td>
<td>12</td>
<td>Postinfectious cerebellitis</td>
<td>3 months</td>
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<td>18</td>
<td>24</td>
<td>12</td>
<td>Cerebellar cortical atrophy</td>
<td>6 years</td>
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<td>19</td>
<td>31</td>
<td>16</td>
<td>Cerebellar cortical atrophy</td>
<td>4 years</td>
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<tr>
<td>20</td>
<td>56</td>
<td>12</td>
<td>Cerebellar cortical atrophy</td>
<td>5 years</td>
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</tbody>
</table>

AICA = anterior inferior cerebellar artery; PICA = posterior inferior cerebellar artery; SCA = superior cerebellar artery.
Clinical impairments in patients with cerebellar lesions

Deficit Scores by Test Category

- Executive Function
- Reasoning
- Calculation
- Affect
- Visual Spatial
- Verbal Memory
- Language
- Visual Memory
- Arousal
- Remote Recall
- Apraxia
62.-yr man with R-PICA infarction.
57-yr man with bilateral PICA and right SCA infarction. Perseverative copying of a 2-loop diagram

Schmahmann and Sherman, 1998
Reasoning and Abstraction

Visual-spatial / Visual Construction

Post-infectious (EBV) cerebellitis

Rey copy during illness

Taylor copy after recovery
Intellectual Function

Z SCORE DISTRIBUTIONS

The Cerebellar Cognitive-Affective Syndrome

- Executive Function
  Planning, set-shifting, verbal fluency, abstract reasoning, working memory
- Spatial Cognition
  Visual spatial organization and memory
- Language Deficits
  Agrammatism and apraxia
- Personality Change
  Blunting of affect, disinhibited and inappropriate behavior

Schmahmann and Sherman, 1998
Cognitive overshoot?

Hi, my name is [Architect, actually, I'm very good at it. Even though I was born in the States, I was raised in [how I'm living in right now, I'm in Boston, in the Mass. General where they are trying to find out what is happening with me...]

Schmahmann, 1998
CCAS in children

- 19 children (3-3 to 14-10)
- Surgical excision of tumors
- 11 medulloblastoma, 7 astrocytoma, 1 ependymoma
- Evaluated 1 to 22 months post-operatively
- Behavioral deficits more apparent in older children

Levisohn, Cronin-Golomb, Schmahmann, Brain, 2000
CCAS following tumor resection in children

5-yr-old boy. Medulloblastoma

Rey figure.
6-yr-old boy.
Left cerebellar
cystic astrocytoma
CCAS in children after tumor resection

- **Problem-solving**
  Failure to organize verbal or visual-spatial material

- **Visual-spatial**
  Impaired planning and organization

- **Expressive language**
  Long latencies, poor initiation, brief responses, lack of elaboration, word finding, confrontation naming

- **Memory**
  Impaired for stories; better with multiple-choice

- **Regulation of affect (vermis lesions)**
  Irritable, impulsive, disinhibited, labile affect

Levisohn, Cronin-Golomb, Schmahmann
Brain 2000;123 :1041-50
Cerebellar agenesis

Sensorimotor impairments

Abnormal eye movements - impaired saccades, pursuit, VORC
Oral motor apraxia
Gross and fine motor delay; Mild clumsiness and ataxia
Cerebellar agenesis

Rey Figure

Rey Figure

COPY

DELAY
Cerebellar Agenesis
Behavioral observations (n=6)

• Executive impairments
  Perseveration, disinhibition, impaired abstract reasoning, working memory and verbal fluency

• Spatial cognition
  Poor perceptual organization, copying and recall

• Language
  Expressive language delay – requiring sign language in two. Impaired prosody. Over-regularization of past tense verbs

• Psychiatric/affective
  Autistic-like stereotypical performance, obsessive rituals, difficulty understanding social cues. Tactile defensiveness

Chheda, Sherman, Schmahmann, 2002
Cerebellar growth in 3rd Trimester

% increase in volume

Cerebellar Volume  ICC Volume  Brain Volume

p<0.001

% increase between 28-40 weeks PCA

Limperopoulos et al, Pediatrics 2005
Premature Birth
(Before 33 weeks gestation)

• Reduced cerebellar volume compared to controls
• Associated with deficits in:
  Executive and visual-spatial function
  Block design, object assembly subtests of WISC-R

Language skills
  Schonnel reading age, Similarities subtest of WISC-R, Riddle interpretation, Reading – decoding and understanding subtests of K-ABC

Allin et al., Brain 2001; 124: 60-66.
Cerebral lesions with secondary cerebellar growth impairment

Mean Cerebellar volume (cc)

VM | PVL | PVHI | Term

p<0.001

Limperopoulos et al, Pediatrics 2005
Transtentorial diaschisis

Ipsilateral
10.4 cc

Contralateral
7.1 cc

Limperopoulos et al, Pediatrics 2005
Cerebellar hemorrhage in preterm infants n = 35

NICU - Hemorrhage on ultrasound Evaluation at 32.1 +/- 11.1 months

- Severe motor disability 48%
- Cognitive deficits 40%
- Language delay
  - expressive 42%
  - receptive 37%
- Autistic features 37%
- Behavioral problems 34%
- Vermis involvement – more severe global developmental, functional, social-behavioral deficits

Limperopoulos et al., Pediatrics 2007; 120, 584-593
Cerebellar development during childhood and adolescence (n = 50)
Supporting studies - adults

Stroke

Cerebellar degenerative disease

Superficial siderosis
Cerebellar Psychopathology

Degenerative Cerebellar disease (31 patients)

- Non-cognitive psychiatric disorders 77%
- Mood disorders 68%
- Personality change 26%
- DSM-IV criteria for dementia 19%

Leroi et al., Am. J. Psychiatry 2002; 159:1306-14
Supporting studies - children

Tumors


Development

Behaviorally Defined Disorders with Cerebellar Anomalies

- **Attention Deficit Hyperactivity Disorder**
  - Berquin et al., Neurology, 1998; 50: 1087-93
  - Castellanos et al., Arch. Gen. Psychiatry 2001; 58: 289-95

- **Dyslexia**
  - Nicolson et al., Lancet 1999; 353: 1662-7

- **Cognitive deficits in infants born very pre-term**
  - Allin et al., Brain 2001; 124: 60-66

- **Autism**
  - Bauman and Kemper, 1997

- **Schizophrenia**
  - Nopoulos et al., Biol Psychiatry 1991; 46: 703-11
  - Loeber et al., Am J Psychiatry 2001; 158: 952-4
Neuropsychiatry of the Cerebellum

• 23 patient case reports
  – Tumor
  – Non-progressive cerebellar ataxia
  – Focal hypoplasia (vermis)
  – Agenesis (partial or complete)
  – Post-infectious cerebellitis
Langerhans cell histiocytosis of the cerebellum
Neuropsychiatry of the Cerebellum

- Attentional Control
- Emotional Control
- Autism Spectrum Disorders
- Psychosis Spectrum Disorders
- Social Skill Set

Positive (exaggerated) symptoms
Negative (diminished) symptoms in each category reflecting cognitive / emotional dysmetria

Schmahmann, Weilburg, Sherman
<table>
<thead>
<tr>
<th><strong>Attentional Control</strong></th>
<th><strong>Positive (exaggerated) symptoms</strong></th>
<th><strong>Negative (diminished) symptoms</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Inattentiveness</td>
<td>Ruminativeness</td>
</tr>
<tr>
<td></td>
<td>Distractibility</td>
<td>Perseveration</td>
</tr>
<tr>
<td></td>
<td>Hyperactivity</td>
<td>Difficulty shifting focus of attention</td>
</tr>
<tr>
<td></td>
<td>Compulsive and ritualistic behaviors</td>
<td>Obsessional thoughts</td>
</tr>
<tr>
<td><strong>Emotional control</strong></td>
<td>Impulsiveness, disinhibition</td>
<td>Anergy, anhedonia</td>
</tr>
<tr>
<td></td>
<td>Lability, unpredictability</td>
<td>Sadness, hopelessness</td>
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<tr>
<td></td>
<td>Incongruous feelings, pathological laughing / crying</td>
<td>Dysphoria</td>
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<tr>
<td></td>
<td>Anxiety, agitation, panic</td>
<td>Depression</td>
</tr>
<tr>
<td><strong>Autism spectrum</strong></td>
<td>Stereotypical behaviors</td>
<td>Avoidant behaviors, tactile defensiveness</td>
</tr>
<tr>
<td></td>
<td>Self stimulation behaviors</td>
<td>Easy sensory overload</td>
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<tr>
<td><strong>Psychosis spectrum</strong></td>
<td>Illogical thought</td>
<td>Lack of empathy</td>
</tr>
<tr>
<td></td>
<td>Paranoia</td>
<td>Muted affect, emotional blunting</td>
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<tr>
<td></td>
<td>Hallucinations</td>
<td>Apathy</td>
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<tr>
<td><strong>Social skill set</strong></td>
<td>Anger, aggression</td>
<td>Passivity, immaturity, childishness</td>
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<tr>
<td></td>
<td>Irritability</td>
<td>Difficulty with social cues and interactions</td>
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<tr>
<td></td>
<td>Overly territorial</td>
<td>Unawareness of social boundaries</td>
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<tr>
<td></td>
<td>Oppositional behavior</td>
<td>Overly gullible and trusting</td>
</tr>
</tbody>
</table>
Motor Assessment

Kuypers’ motor task before and after DN lesions (Lawrence and Kuypers, 1968)

Kuypers’ testing board

![Motor Task](chart.png)
Conceptual Set Shifting Task (CSST)

Red

Shift

Triangle

CSST - Shift Conditions

Group

Errors to Criterion

Control
Cerebellar

* p = 0.01

371.3

432.3
CSST – Perseverative Errors

Perseverative errors compared to chance

Total number

* P = 0.006

Control  Cerebellar

190.75  329.50

Percent

* P < 0.007

Control  Cerebellar

52%  78%
There are regions of the cerebellum devoted to cognitive processing rather than to motor coordination.

The cerebellum appears to be a critical modulator of prefrontal systems mediating executive function.

<table>
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<th>Section</th>
<th>Points</th>
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<td>I. POSTURE AND GAIT</td>
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<td>Walking capacity</td>
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<tr>
<td>Gait speed</td>
<td></td>
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<tr>
<td>Standing, eyes open</td>
<td></td>
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<tr>
<td>Spread of feet in natural position, eyes open</td>
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<tr>
<td>Body sway with feet together, eyes open</td>
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<tr>
<td>Body sway with feet together, eyes closed</td>
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<td>Quality of sitting position</td>
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<td>II. KINETIC FUNCTIONS</td>
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<tr>
<td>Knee-tibia test</td>
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<tr>
<td>Action tremor in heel-to-knee test</td>
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<tr>
<td>Decomposition of leg movement</td>
<td></td>
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<tr>
<td>Decomposition of leg tapping</td>
<td></td>
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<tr>
<td>Finger-to-nose test: decomposition and dysmetria</td>
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<tr>
<td>Finger-to-nose test: intention tremor of the finger</td>
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<tr>
<td>Finger-finger test (action, tremor and/or instability)</td>
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<tr>
<td>Pronation-supination alternating movements</td>
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<tr>
<td>Rebound of the arms</td>
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<td>Overshoot of the arms</td>
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<tr>
<td>Drawing of Archimedes’ spiral on a predrawn pattern</td>
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<tr>
<td>III. SPEECH DISORDERS</td>
<td>10</td>
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<tr>
<td>Dysarthria: fluency of speech</td>
<td></td>
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<tr>
<td>Dysarthria: Clarity of speech</td>
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<tr>
<td>Dysarthria: Alternating syllables</td>
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<td>IV. Oculomotor Disorders</td>
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<tr>
<td>Abnormal eye movements at rest</td>
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<tr>
<td>Gaze-evoked nystagmus</td>
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<td>Abnormalities of the ocular pursuit</td>
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<tr>
<td>Dysmetria of the saccade</td>
<td></td>
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<tr>
<td>Saccadic intrusions into vestibulo-ocular reflex cancellation</td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>120</td>
</tr>
</tbody>
</table>
Blood supply of human cerebellum.
Adapted from Tatu et al., 1996

Schmahmann, MacMore, Vangel
Motor deficit (MICARS score) following Cerebellar Stroke

Groups 1+2+5: 20.5 +/- 11.8

versus

Group 4: 3 +/- 2.0

* p < 0.0001

All lobules              I-V                I-V, +VI            VII-X, +VI       VII-X only

Group  5 1 2 3 4

n=11                 n=1                     n=4                     n=4                  n=13

Motor deficit (MICARS score) following Cerebellar Stroke

Schmahmann, MacMore, Vangel, 2009
CEREBELLAR STROKE WITHOUT MOTOR DEFICIT: CLINICAL EVIDENCE FOR MOTOR AND NON-MOTOR DOMAINS WITHIN THE HUMAN CEREBELLUM

J. D. SCHMAHMANNA,∗ J. MACMOREA AND M. VANGELB

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Key words: cerebellum, ataxia, motor control, functional topography.

The notion that the cerebellum is devoted purely to the coordination of gait, extremity and oculomotor movement, and articulation has been deeply entrenched in medical and neurological texts. Evidence pointing to
Cerebellar functional topography. Single case fMRI

Key:
Tapping = red-orange
Verb generation = blue
n-back = purple
Mental rotation = green
IAPS = yellow

Stoodley, Valera, Schmahmann, 2010
Dysmetria of Thought Theory

Cerebellum is an integral node in the distributed neural circuits subserving sensorimotor, cognitive, autonomic and affective processing.

The cerebellar cortex is anatomically homogeneous, but different cerebellar regions modulate different functional domains i.e., functional topography.

- Sensorimotor
- Cognitive
- Limbic

Makris et al., 2005
Dysmetria of Thought Theory

In the same way that the cerebellum regulates the rate, rhythm, force, and accuracy of movements, so does it regulate the speed, consistency, capacity, and appropriateness of mental or cognitive processes

Dysmetria of Thought Theory

The cerebellum detects, prevents, and corrects mismatches between intended outcome and perceived outcome of interaction with the environment. It facilitates actions harmonious with the goal, appropriate to context, and judged accurately and reliably according to the strategies mapped prior to and during the behavior.

Dysmetria of Thought Hypothesis

Topography anterior – posterior

**Sensorimotor** –
- predominantly anterior lobe (I - V), VI
- “secondary” representation in lobule VIII
- vestibulocerebellum in lobules IX and X

**Cognitive, affective** –
- predominantly neocerebellum (vermal and hemispheric components of lobules VI and VII)

Makris et al., 2005
Dysmetria of Thought Hypothesis

Topography medial - lateral

Vermis and fastigial nucleus -
autonomic regulation, affect, emotionally important memory

Cerebellar hemispheres and dentate nucleus -
executive, visual-spatial, linguistic, learning and memory

Makris et al., 2005
Dysmetria of Thought

Postulated fundamental function distributed throughout the cerebellum - the **Universal Cerebellar Transform (UCT)**

that cerebellum utilizes to optimize performance by modulating behavior around a homeostatic baseline automatically and according to context

Anatomic specificity in cerebrocerebellar loops permits cerebellum to contribute to multiple domains
By corollary, there is a **Universal Cerebellar Impairment (UCI)** that is hypothesized to be **dysmetria**

This includes dysmetria of movement (**ataxia**); and dysmetria of thought and emotion (**the cerebellar cognitive affective syndrome**)
Conclusions

• topographic organization in human cerebellum of sensorimotor function, cognition and emotion

• cerebellar lesions disrupt cerebellar modulation of anatomical-functional subunits within the cerebrocerebellar system

• clinical deficits reflect the domain of function in the cerebral hemisphere that has been deprived of its cerebellar influence

• therapeutic implications of the modulating influence of cerebellum in behavioral neurology and psychiatry
Implications for therapy

• The need-to-know imperative
• Window for cognitive rehabilitation and cross modal therapies
• Implications for behavioral neurology and neuropsychiatry in children
• Potential for novel treatment strategies in psychiatric illness
Collaborators

Neuroanatomy
Deepak Pandya

Cerebellar Atlas
Julien Doyon
Alan Evans
David McDonald
Michael Petrides
Arthur Toga

Clinical investigations
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Milan Chheda
Alice Cronin-Golomb
Stefanie Freeman
Matthew Frosch
Tessa Hedley-Whyte
Raquel Gardner
Amy Hurwitz
Lisi Levisohn
Jason MacMore
Josef Parvizi
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Kathie Sims
Mark Vangel
Jeffrey Weilburg

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David Kennedy
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Bruce Rosen
Catherine Stoodley
Eve Valera

Diffusion Spectrum Imaging
George Dai
Helen D’Arceuil
Alex de Crespigny
Ruopeng Wang
Van Wedeen

Cerebellar TMS
Asli Demirtas-Tatlidede
Alvaro Pascual Leone

Primate behavior
Ronald Killiany
Tara Moore
Mark Moss
Douglas Rosene

National Institutes of Mental Health
McDonnell-Pew Program; National Library of Medicine;
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Photo by Jinny Sagorin