



Spina Bifida and Hydrocephalus Across The Lifespan: Part 2 – Adult

Maureen Dennis

Opportunities for Hydrocephalus Research: Pathways to Better
Outcomes, Seattle, 9-11 July 2012



UNIVERSITY OF TORONTO
FACULTY OF MEDICINE



Healthier Children. A Better World.™

SickKids®
RESEARCH
INSTITUTE
Neurosciences
& Mental Health

Outline

1. Lifespan issues
 - a) Adult math and functional numeracy
 - b) Reaction time
 - c) Sleep and circadian rhythms
2. New adult challenges
 - a) Prospective memory
 - b) Depression
3. What does hydrocephalus add to adult profile?
4. Implications.



Lifespan issues



Healthier Children. A Better World.TM

SickKids
RESEARCH
INSTITUTE
Neurosciences
& Mental Health

Preschool, childhood numeracy

PRESCHOOLERS

- Counting
- Object-based addition, subtraction

SCHOOL-AGED CHILDREN

- Numeration and rational numbers
- Single digit addition, subtraction accuracy, speed
- Multi-digit addition, multiplication accuracy, speed
- Single digit addition speed, calculation strategies
- Multidigit subtraction
- Division
- Estimating and problem solving.



Healthier Children. A Better World.TM

Adult numeracy

- LONGITUDINAL
 - Children with spina bifida poor at computation, math problem-solving, grow into adults with same problems.
- CROSS-SECTIONAL
 - Young adults with spina bifida have poor computation accuracy, computation speed, math problem-solving.
 - Difficulties with functional numeracy (supermarket price comparisons, estimating quantities, prices, reading prescriptions).



Healthier Children. A Better World.TM

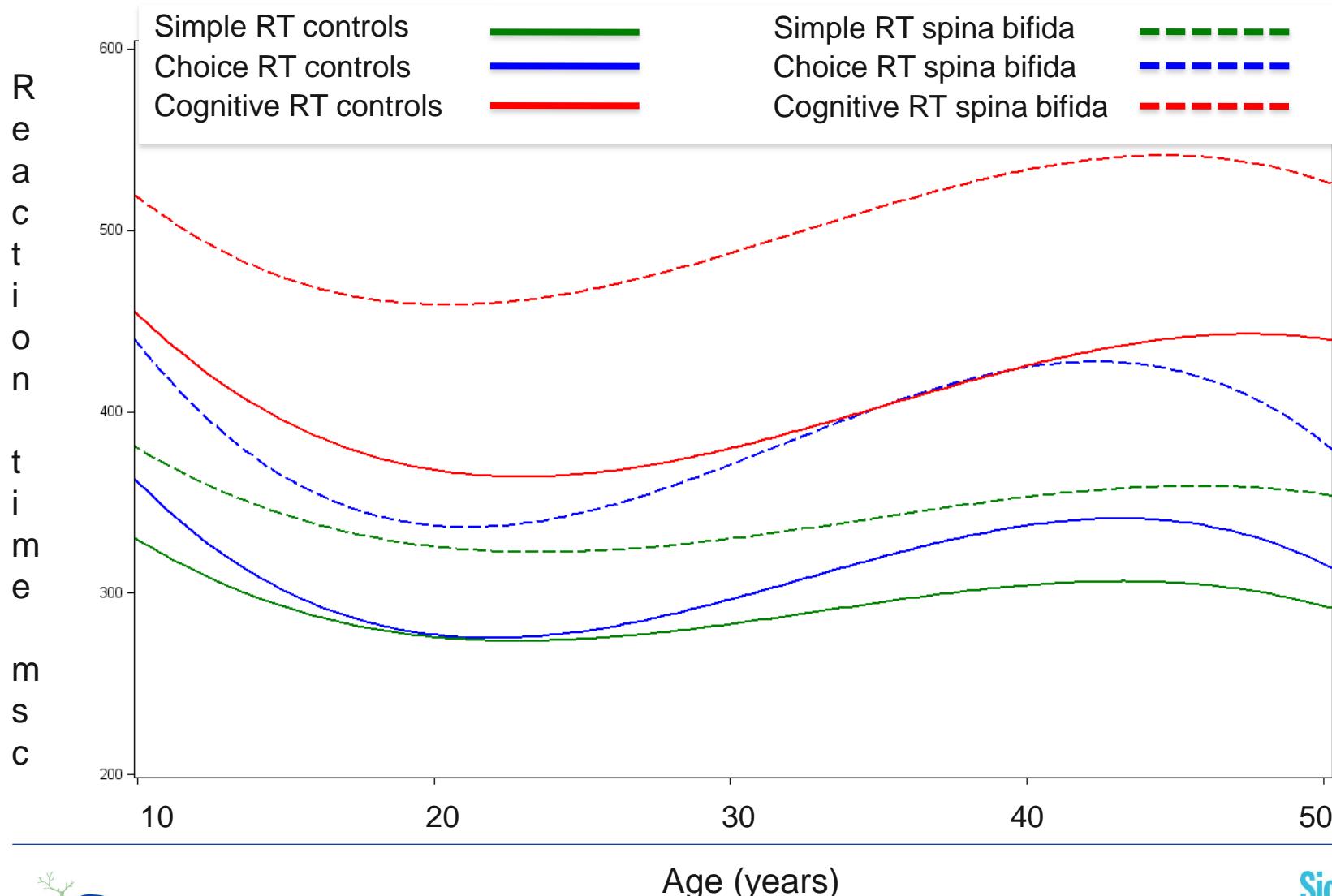
SickKids[®]
RESEARCH
INSTITUTE
Neurosciences
& Mental Health

Poor numeracy matters

- **EVERYDAY FUNCTION**
 - Difficulty using numbers in life.
 - Limits financial independence (holding bank accounts, taking medications, managing personal finances).
- Adult functional numeracy predicts independence:
 - Social
 - Personal
 - Community.



Reaction time



Healthier Children. A Better World.™

SickKids®
RESEARCH
INSTITUTE
Neurosciences
& Mental Health

Sleep and chronotype

- SLEEP

- Children with spina bifida report more problems than controls (daytime sleepiness; fatigue; poor energy).
- Adults with spina bifida report more problems than controls (trouble falling asleep; restless/disturbed sleep).

- CHRONOTYPE

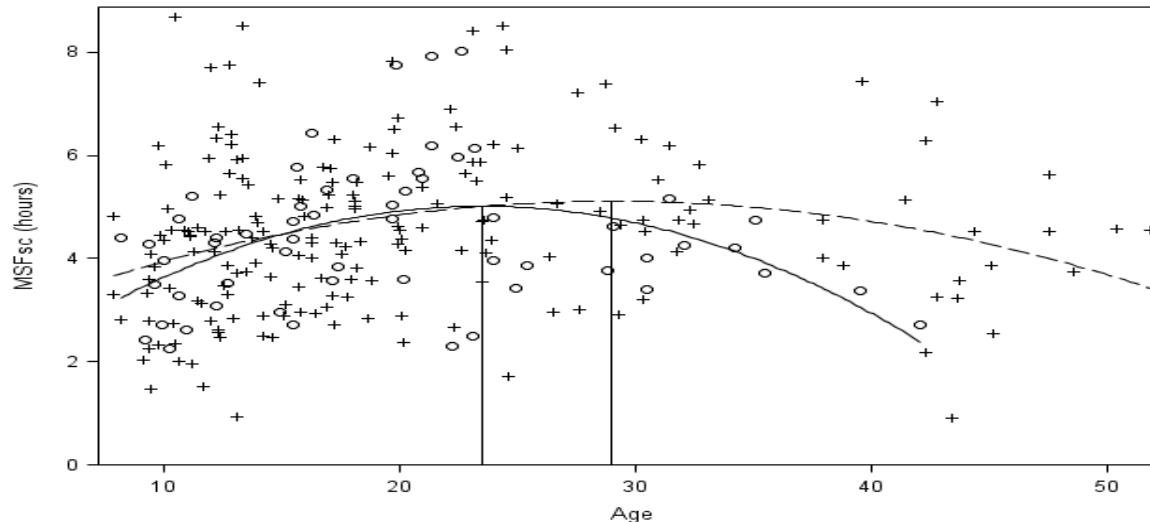
- Munich Chronotype Questionnaire measures phase relationship between timing of sleep and 24-hour day.
- Mid-point of sleep on “free” days, i.e., days without waking for school/work, corrected for sleep duration (MSFsc).
- MSFsc correlated with objective measures of circadian timing and sensitive to developmental changes, sleep pathologies.



Healthier Children. A Better World.TM

SickKids
RESEARCH
INSTITUTE
Neurosciences
& Mental Health

Spina bifida chronotype Age 7-55 Years



- Over lifespan, individuals with spina bifida (crosses, dotted line) show typical relationship between chronotype and age: as children, go to bed and wake early; as adolescents, sleep and rise times are later; as adults, sleep and rise earlier.
- Phase relationship between sleep-wake timing and 24 hour day in controls (circles, solid line); curve in controls trends downward when it peaks in SBM.
- **Aberrant synchronization of circadian rhythms to 24h day in SBM may contribute to reported sleep problems.**



New adult challenges



Healthier Children. A Better World.TM

SickKids[®]
RESEARCH
INSTITUTE
Neurosciences
& Mental Health

Prospective “TO DO” Memory

Event-based tasks

- tell examiner about 5 hidden objects when beeper goes off.
- hand examiner book after specific quiz question about TV program.

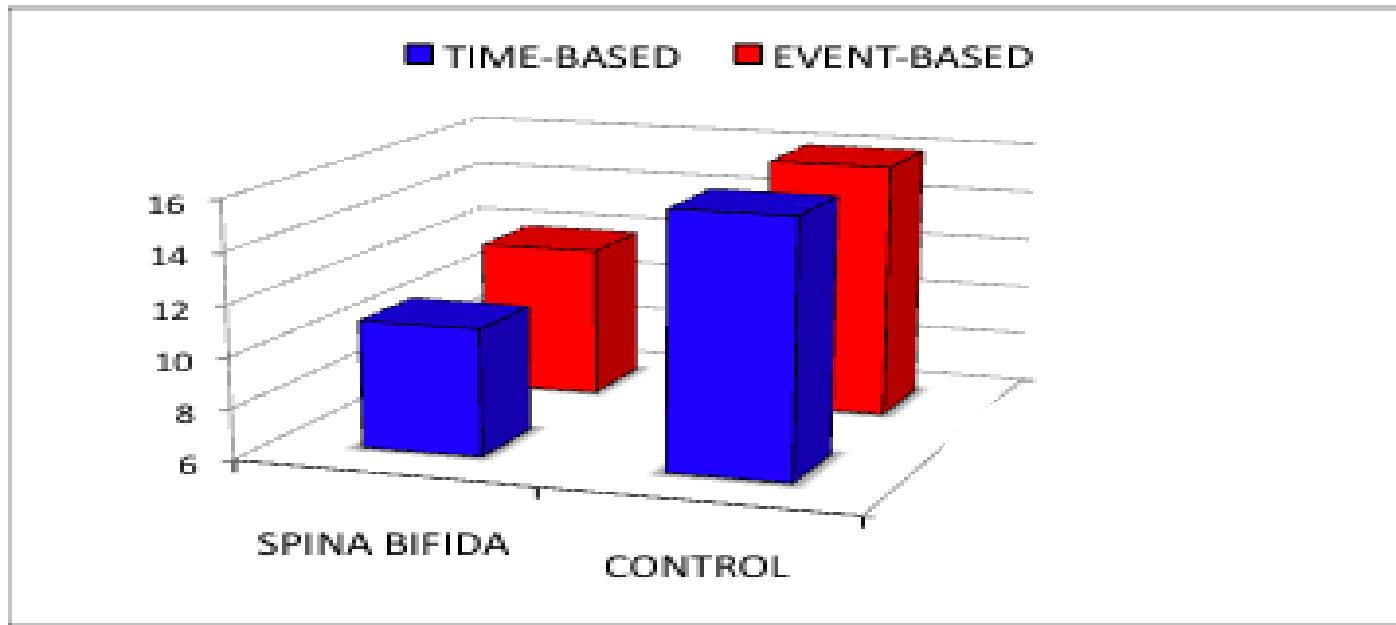


Time-based tasks

- tell examiner to make phone call at specific time cued by clock.
- remind examiner not to forget keys “when there are 7 min left” on timer.



Prospective memory in spina bifida



- Young adults with spina bifida score lower than age peers, for event- or time-based tasks.
- Poor prospective memory three times higher in older spina bifida group (over 32 years; 37.50%) than in younger spina bifida group (18-31 years; 12.50%).



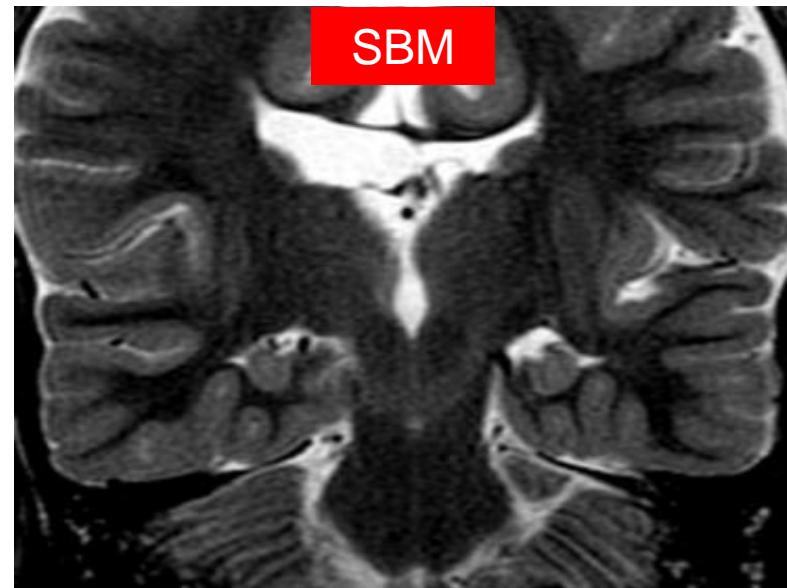
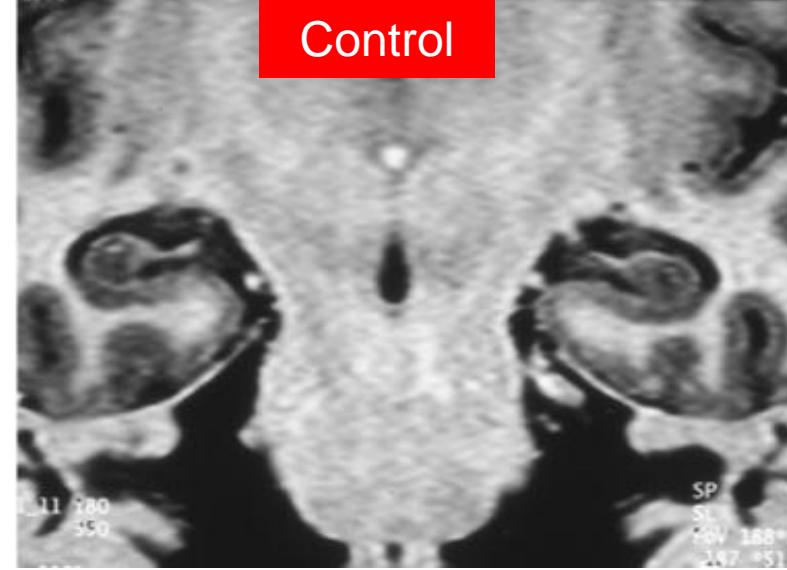
Neural basis of prospective memory

- Involves frontal, temporal lobe.
- Spina bifida involves:
 - atypical development of frontal lobes
 - thinning of key white matter tracts like uncinate fasciculus connecting inf. frontal, ant. temporal
 - hippocampi rotated outward and laterally dislocated
 - elevation of medial parahippocampal gyri
 - abnormal sulcation in mesiotemporal cortex.



Temporal lobe

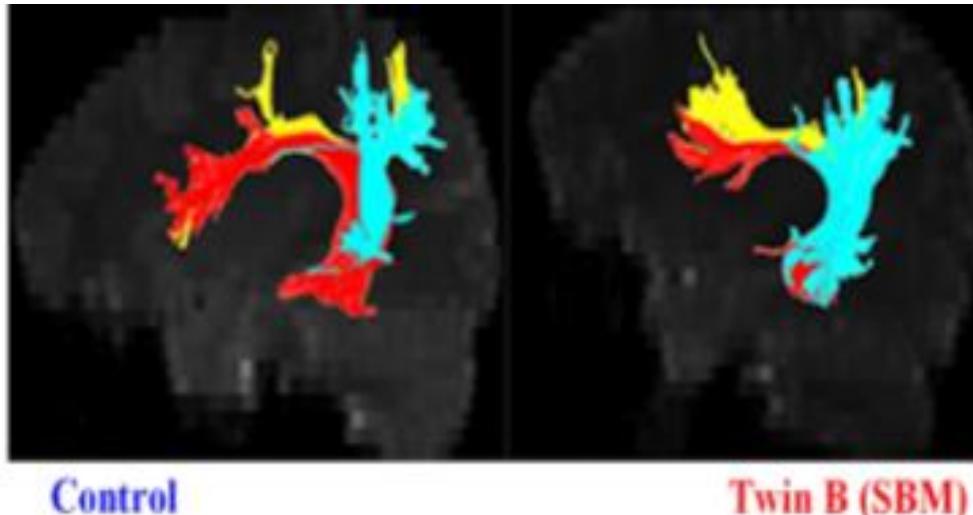
- Mesial temporal cortex abnormal in size, shape 85-93%
- Hippocampi rotated outward, laterally dislocated
 - Primary hypoplasia + hydrocephalus effects on hippocampus, connecting fibres
 - Parahippocampal gyri elevated medial to hippocampus, not inferior



Beak: Fimbria
Head: Hippocampus
Neck: Horizontal subiculum
Torso: Parahippocampal gyrus

Healthier Children. A Better World.TM

Arcuate fasciculus in spina bifida



ARCUATE FASCICULUS
Segments: **fronto-temporal (AFT),
fronto-parietal, temporo-parietal**

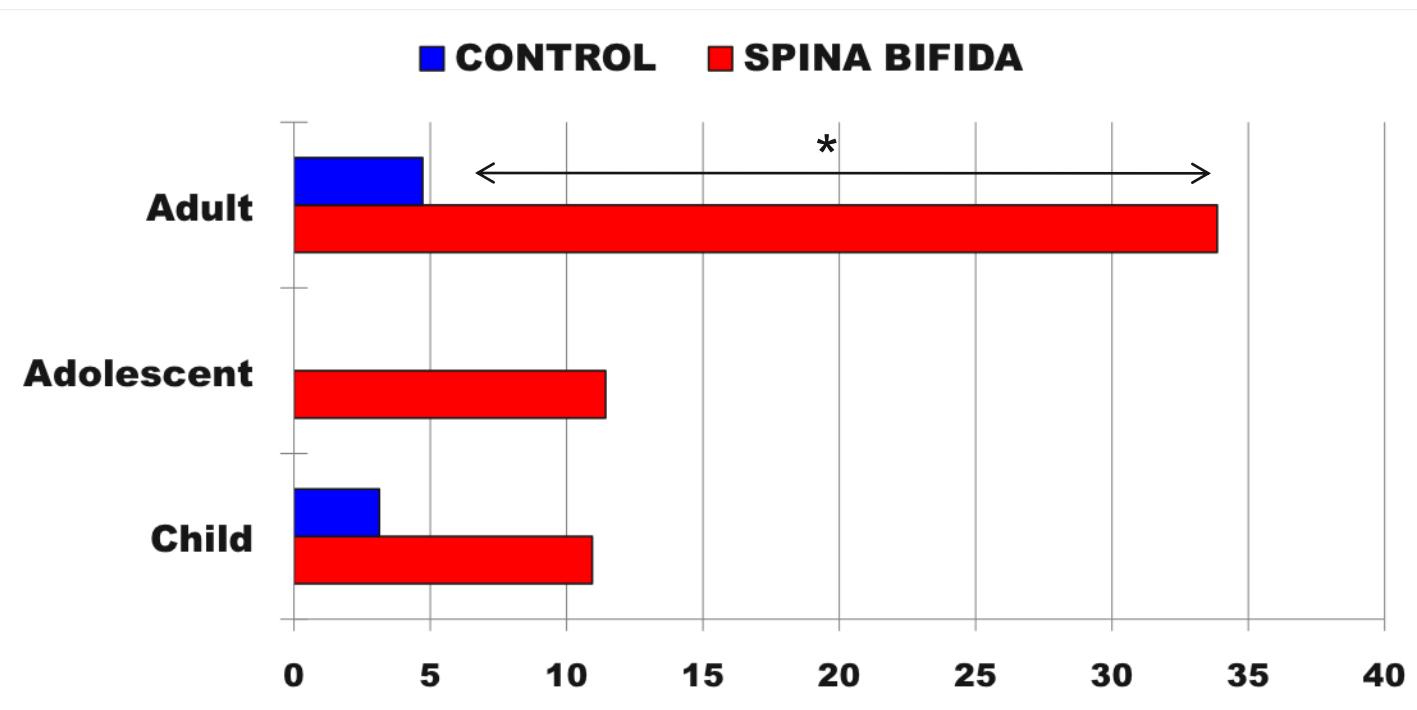
- Abnormal development in spina bifida
- **LEFT Arcuate AFT segment less myelinated.**



(Hasan, Eluvathingal, Kramer, Ewing-Cobbs, Dennis, Fletcher *et al*, *J. Magnetic Res Imag*, 2008)

Healthier Children. A Better World.TM

Depression



% at or above cut-off for clinical depression (SBM N=229; CON N=96)



Healthier Children. A Better World.TM

SickKids[®]
RESEARCH
INSTITUTE
Neurosciences
& Mental Health

What does hydrocephalus add to adult profile?



Healthier Children. A Better World.TM

SickKids[®]
RESEARCH
INSTITUTE
Neurosciences
& Mental Health

Hydrocephalus in spina bifida

- Affects brain development, contributes to dysmorphologies.
 - The Chiari II malformation
 - Corpus callosum hypoplasia.
- Contributes to abnormalities of association fibres:
 - macrostructure (poor visualization)
 - microstructure (\downarrow fractional anisotropy, \uparrow diffusivities)
 - impaired myelination (\uparrow transverse diffusivity)
 - abnormal axonal features (\uparrow axial diffusivity).
- ~50 studies of no association IQ and shunt revisions. But:
 - Small N
 - No separation of type of shunt revisions, spina lesion level (thoracic vs. lumbar)
 - Simple linear correlations, no statistical modeling.



Healthier Children. A Better World.™

Hydrocephalus and adult outcome

- In adults, number of shunt revisions negatively related to:
 - functional numeracy
 - some memory functions
 - independent living
 - employment.
- Young adults with spina bifida and nonfunctioning shunts or non-shunted ventriculomegaly show improved memory after shunt treatment.



Implications



Healthier Children. A Better World.TM

SickKids[®]
RESEARCH
INSTITUTE
Neurosciences
& Mental Health

Implications

1. Recognize lifespan challenges that affect daily life more in adulthood than in childhood.
 1. For individuals 18 years and older, encourage continuing education in life skills mathematics.
 1. Encourage awareness and strategies (note taking helped spina bifida with prospective memory tasks).
 2. Access to appropriate care (e.g., for depression).
 3. Hydrocephalus affects function more in adulthood than in childhood, so childhood shunt management and adult shunt function continue to be important.



Groups vs. individuals

- Group research helps to:
 - Write journal articles, get tenure, adopt position.
 - Hope University will provide chair to adopt position in.
- But intervening to create a more positive medical, physical, or cognitive lifetime outcome requires individual prediction of ecologically salient function.



Healthier Children. A Better World.TM

SickKids[®]
RESEARCH
INSTITUTE
Neurosciences
& Mental Health

Grant Support

- US National Institutes of Health Program Project Grants (1998-2010) P01 HD35946 P01 HD35946-06
- National Cancer Institute of Canada

Colleagues (Houston & Toronto)

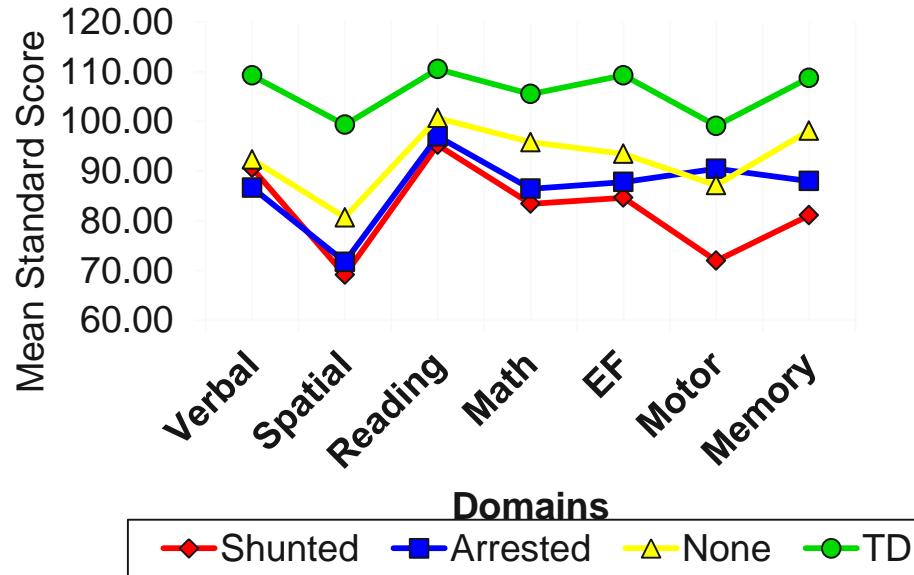
- Marcia Barnes
- Paul Cirino
- James Drake
- Kim Edelstein
- Jack Fletcher
- David Francis
- Lyla Hampson
- Ross Hetherington
- Jenifer Juranek
- Michael Salman
- Amery Treble



Healthier Children. A Better World.TM

SickKids
RESEARCH
INSTITUTE
Neurosciences
& Mental Health

Hydrocephalus status and outcome

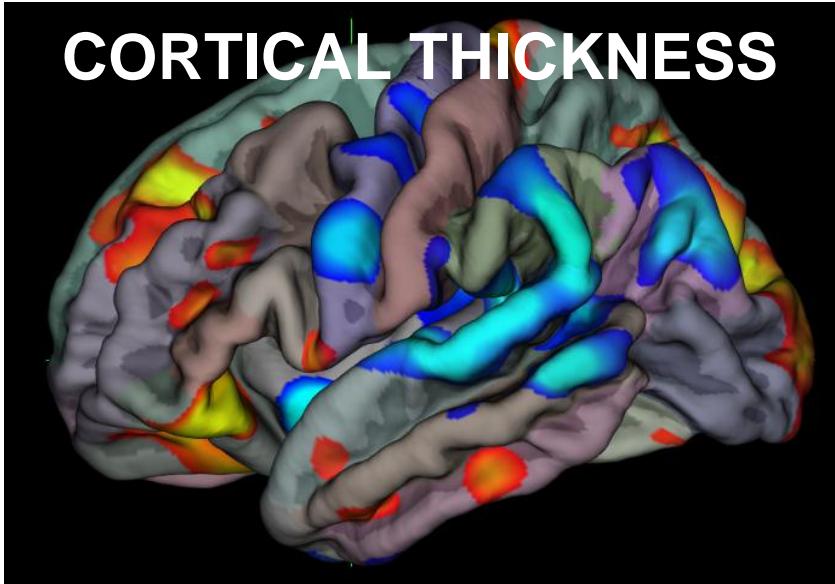


- Neurocognitive function in typically developing (N=61) children, children with spina bifida and shunted hydrocephalus (N=166), arrested hydrocephalus (N=18), or no obvious hydrocephalus (N=24).

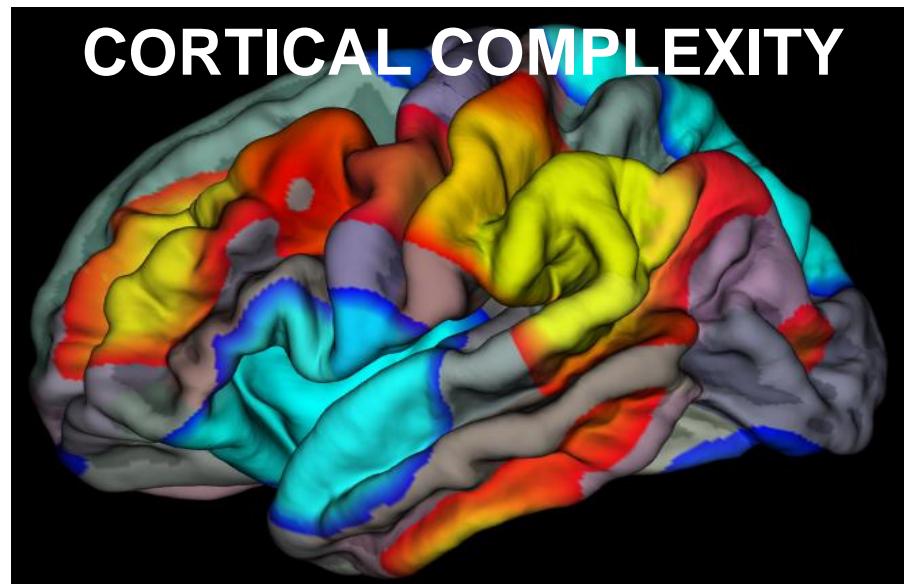


Healthier Children. A Better World.TM

CORTICAL THICKNESS



CORTICAL COMPLEXITY



- ‘Hot’ colors indicate cortical thickness or complexity GREATER in the SBM group relative to age peers; “cold” indicate LESSER in the SBM group.

- **ALTERED PATTERNS OF LOCAL AND LONG-RANGE CORTICAL CONNECTIVITY**
- **SOME CORTICAL REGIONS TOO FAT, SOME TOO THIN.**



Healthier Children. A Better World.TM