Long-term outcomes of traumatic brain injury in infancy and early childhood

Keith Owen Yeates, Ph.D., ABPP/CN

Center for Biobehavioral Health
Columbus Children's Research Institute

Department of Pediatrics
College of Medicine and Public Health
The Ohio State University

Objectives for presentation

- To summarize research concerning long-term outcomes of TBI in infancy and early childhood.
- To describe recent non-human animal and human research regarding the outcomes of early TBI
- To discuss practical implications of research on early TBI for clinical neuropsychologists

COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

Why study pediatric TBI?

- #1 cause of pediatric death and disability in U.S.
- Annual incidence
  200-300 head injuries/100,000 children
- Annual economic cost of
  pediatric TBI in the U.S. =
  $7.5 to $10 Billion

COLUMBUS Children's RESEARCH INSTITUTE

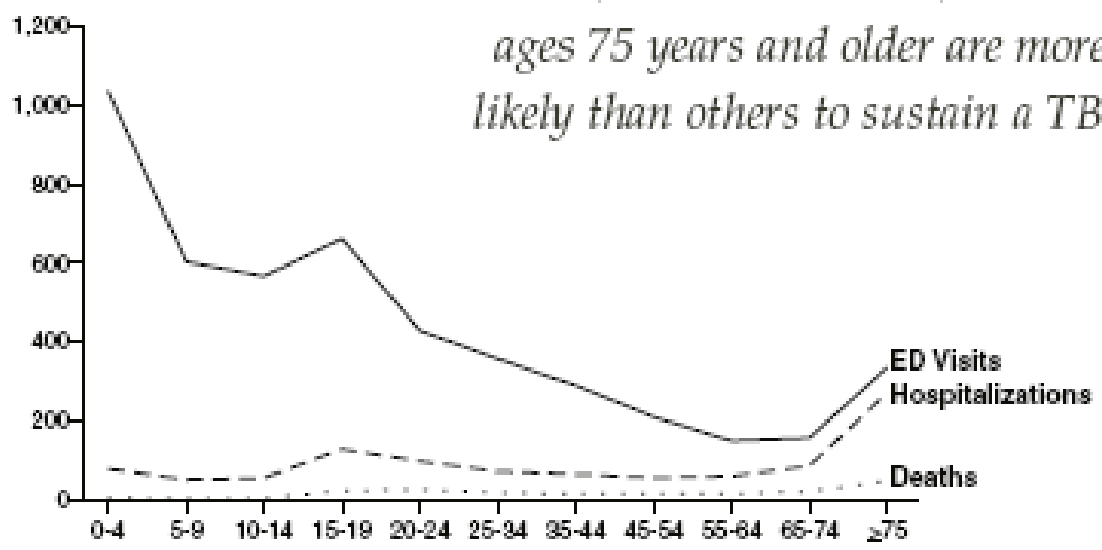
THE OHIO STATE COLLEGE OF MEDICINE AND PUBLIC HEALTH

Why be concerned about early TBI?

TBI by Age: Comparing the Rates

Figure 2. Average Annual Traumatic Brain Injury-Related Rates for Emergency Department Visits, Hospitalizations, and Deaths, by Age Group, United States, 1995–2001

Children, older adolescents, and adults ages 75 years and older are more likely than others to sustain a TBI.



COLUMBUS Children's® RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

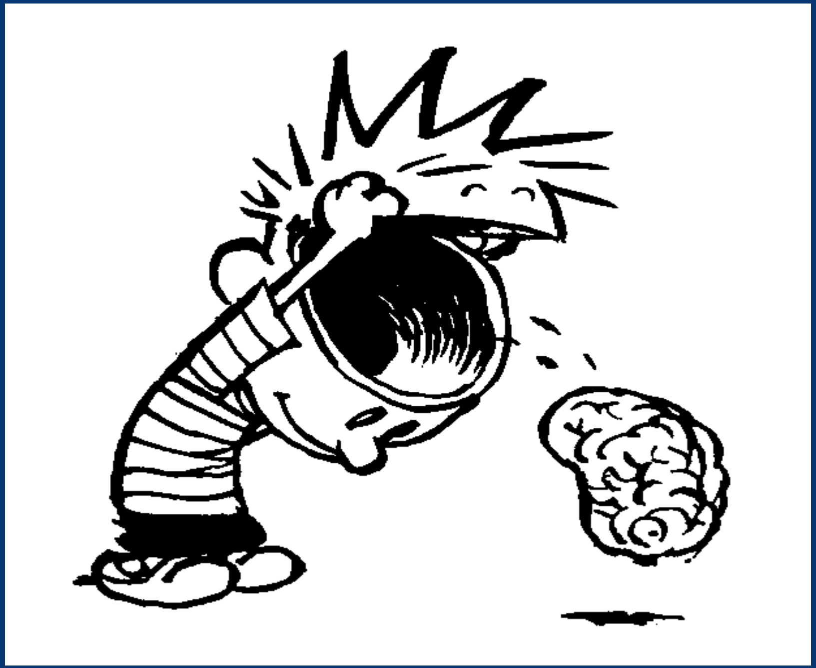
“Accidents” do happen!

But can
we explain
outcomes?

COLUMBUS Children's RESEARCH INSTITUTE

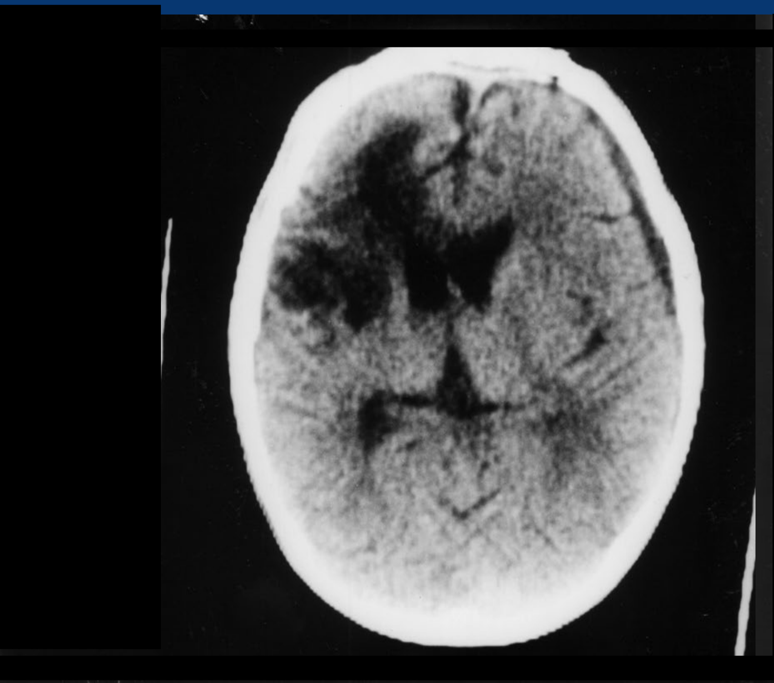
OHIO STATE
COLLEGE OF MEDICINE AND PUBLIC HEALTH

Is a younger brain a better brain?

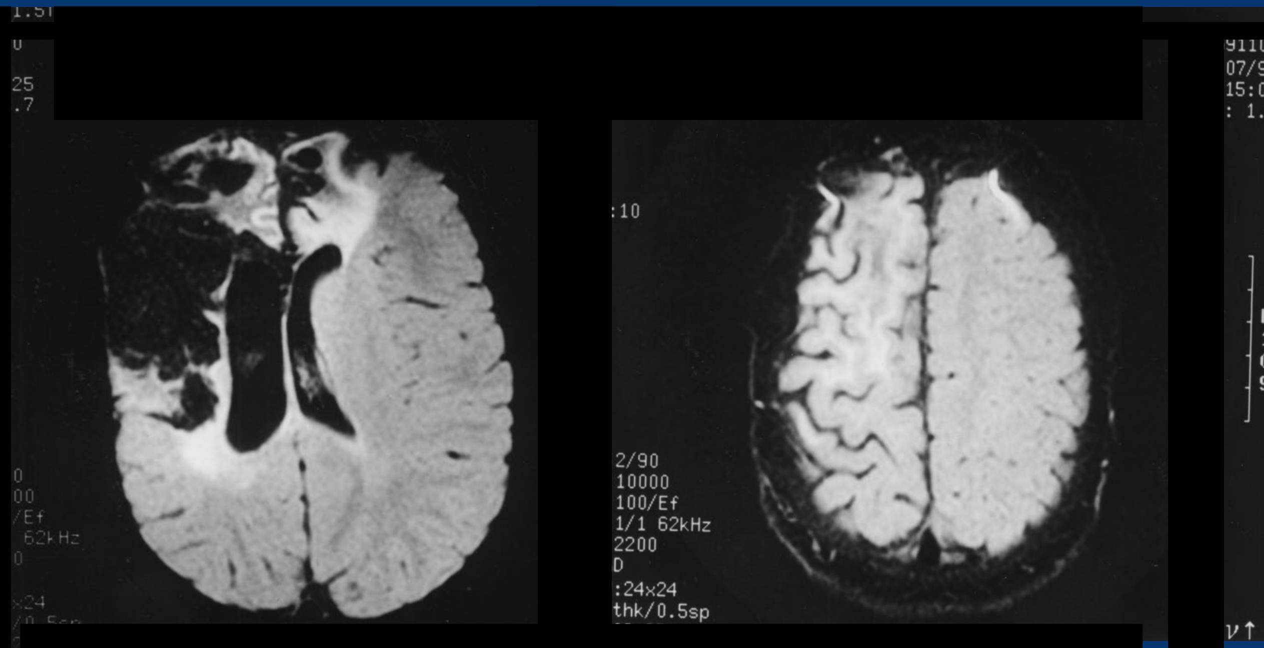


Effects of age-at-injury on recovery and outcome

Case example: 3 year old, penetrating TBI



Acute

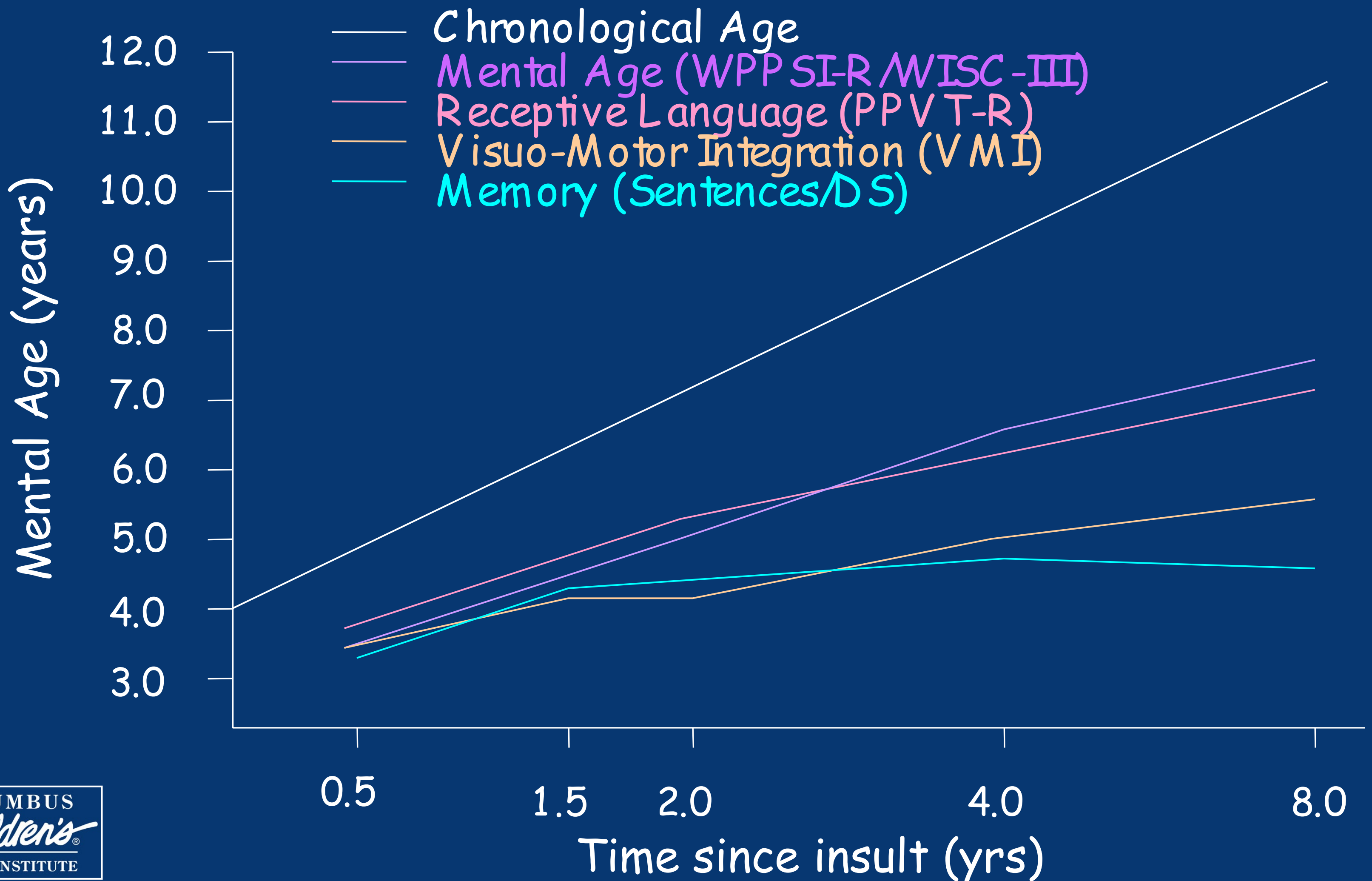


10 yrs post

COLUMBUS Children's RESEARCH INSTITUTE

OHIO STATE COLLEGE OF MEDICINE AND PUBLIC HEALTH

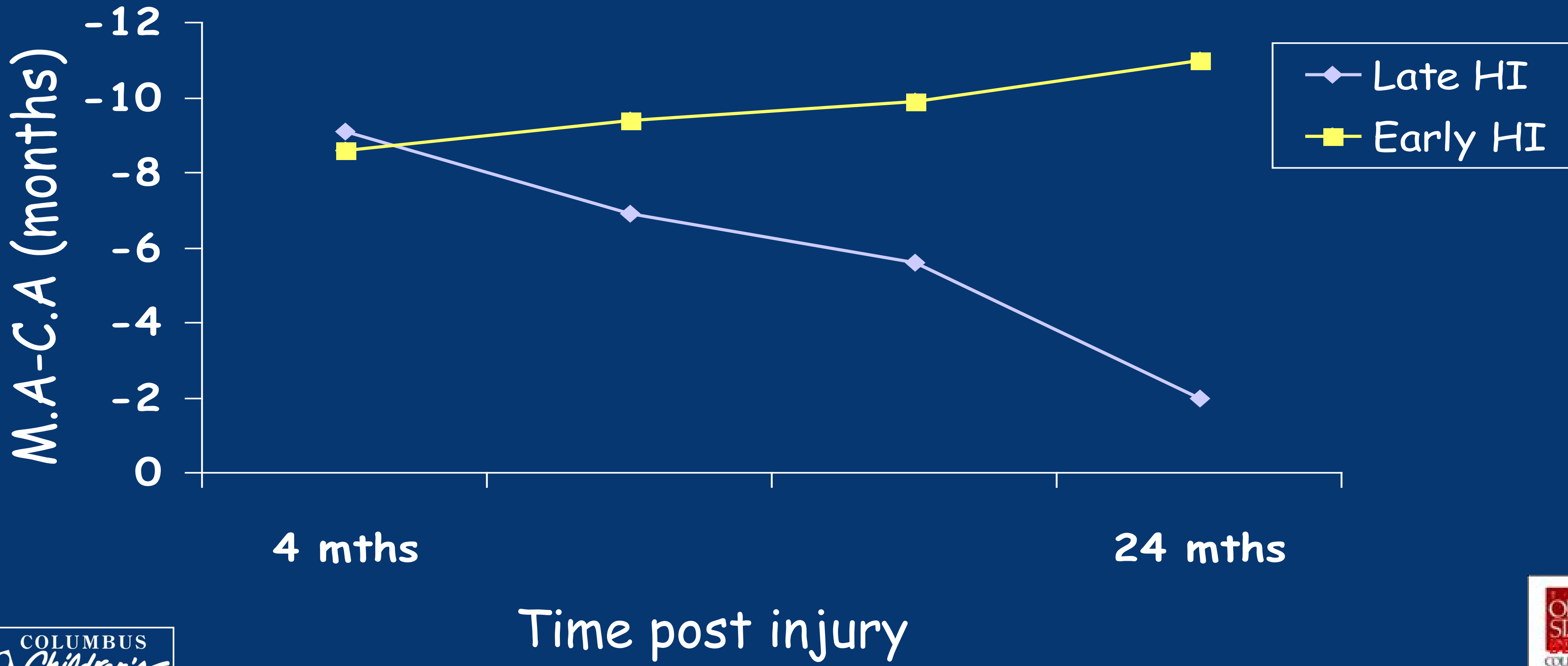
Progressive cognitive decline relative to age



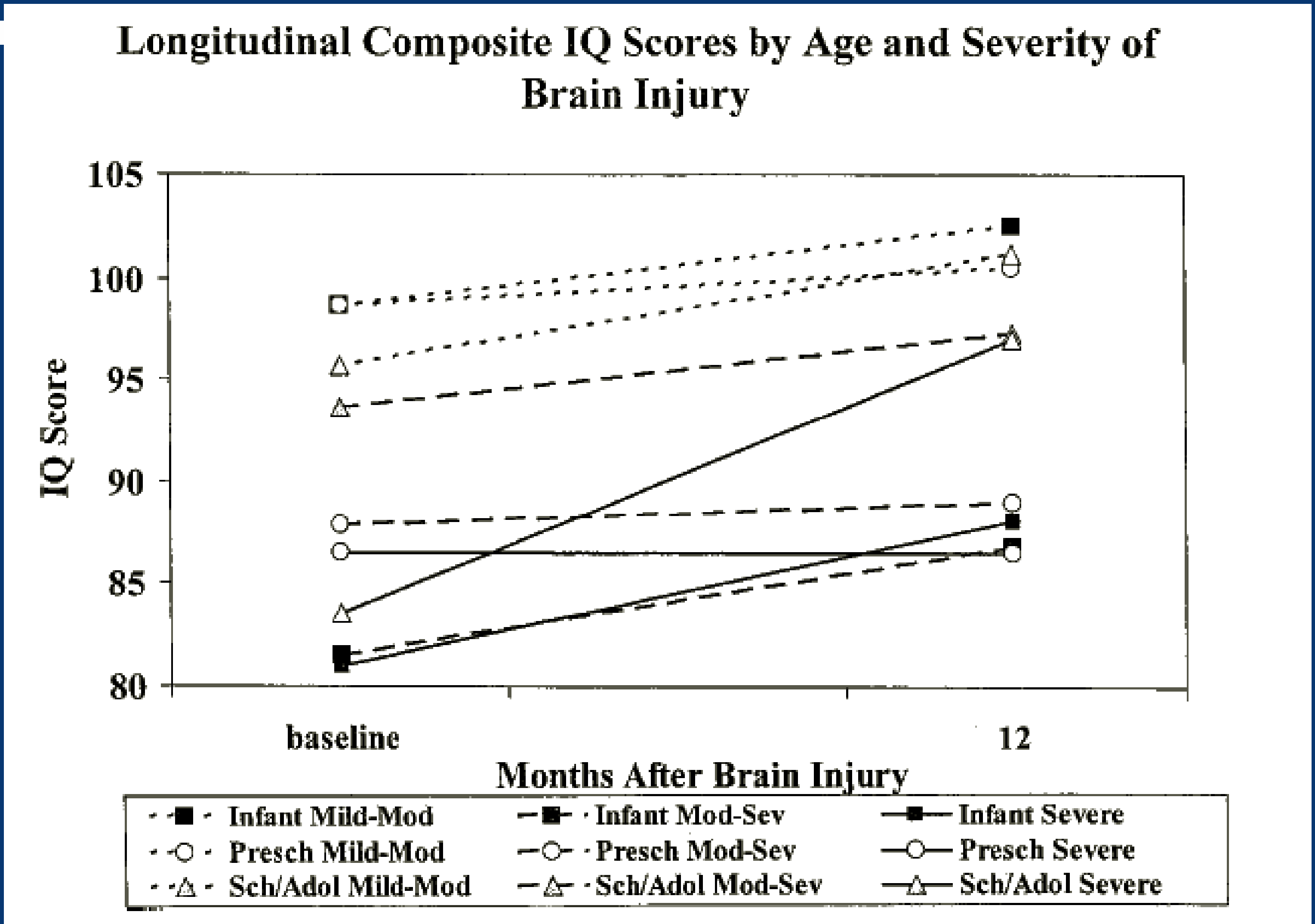
COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

Progressive developmental gap

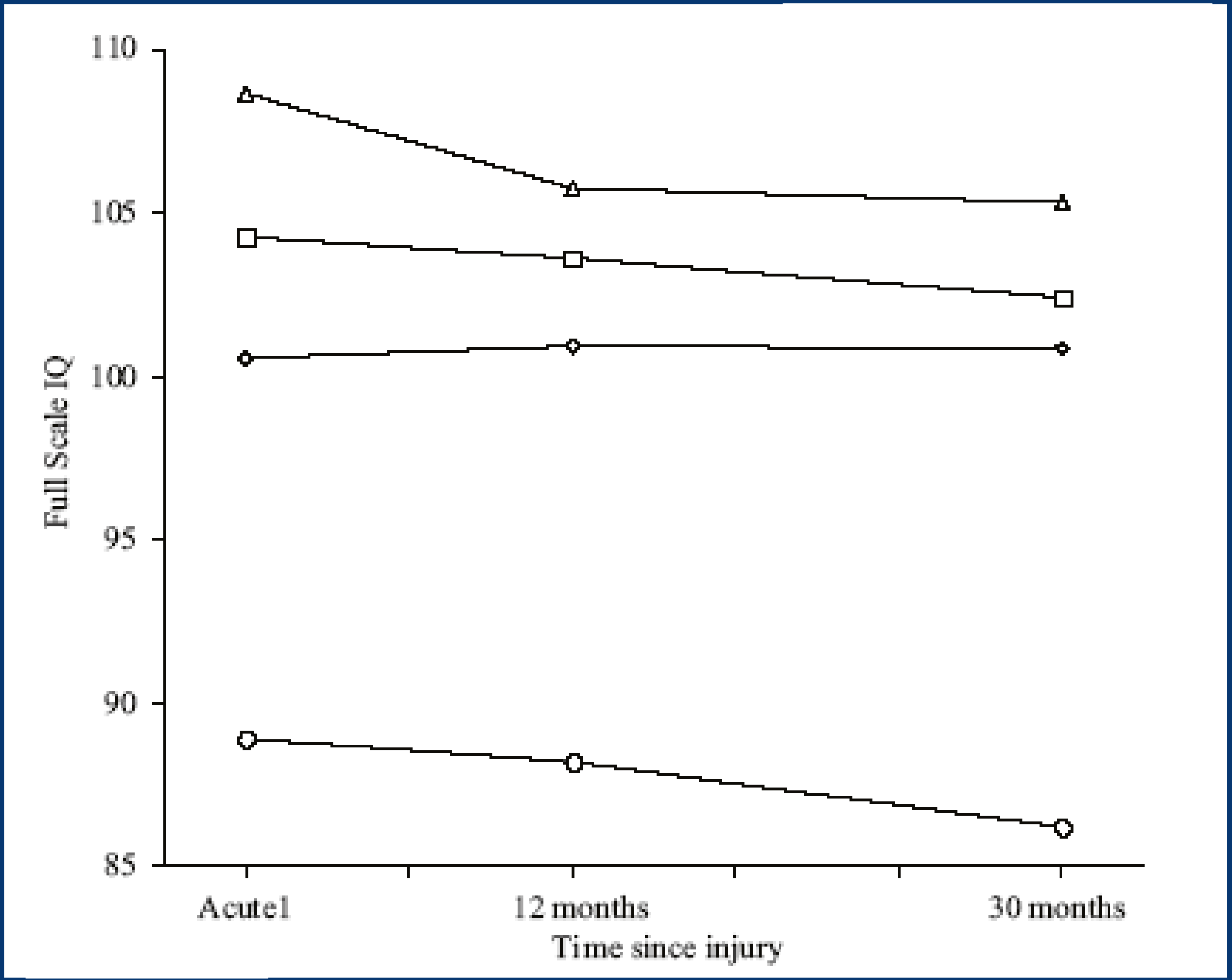


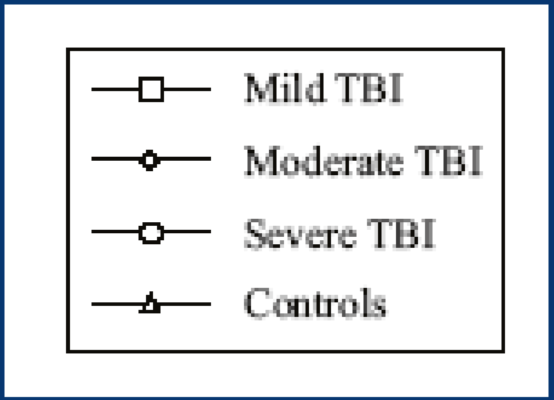
Differences in recovery



Ewing-Cobbs, Barnes, & Fletcher, *Developmental Neuropsychology*, 2003

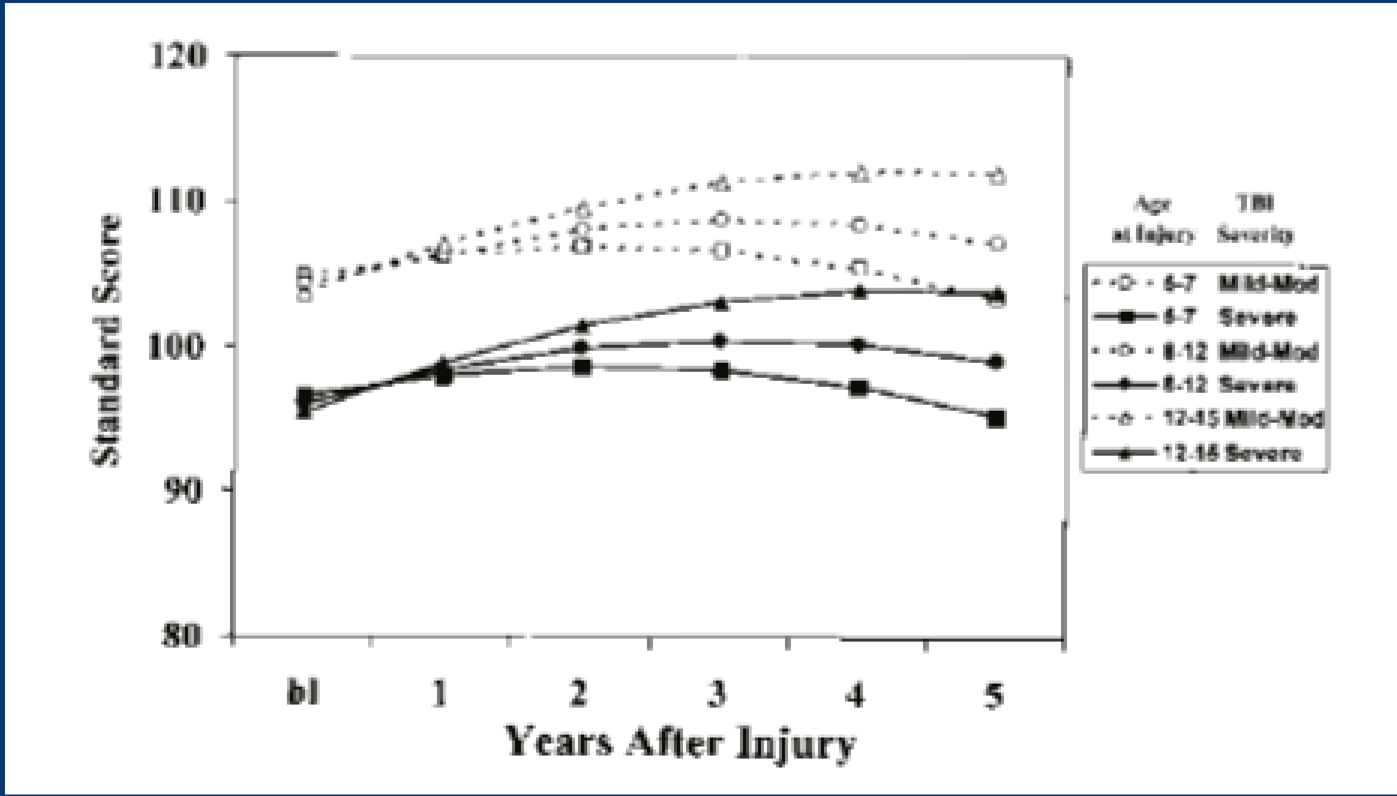
No long-term improvement in IQ





Anderson et al., *Brain*, 2004

Progressive lag in academic achievement



Ewing-Cobbs et al., *Developmental Neuropsychology*, 2004

What about long-term outcomes?

- Few studies lasting into adulthood
- Research challenges
  - Retrospective designs
  - Measurement of severity
  - Selective attrition
  - Non-standardized outcome measures
- Nonetheless, bulk of evidence shows poor outcomes for young children with severe TBI

Asikainen et al., *Brain Injury*, 1996

- 496 S with TBI, followed for at least 5 years, admitted to rehabilitation program
- Age at injury correlated with outcome
  - S aged 7 yrs or less at time of injury suffered severe disability as measured by Glasgow Outcome Scale more often than older age groups
  - Less capable of independent employment than children injured at 8-16 years of age

Cattelani et al., *Brain Injury*, 1998

- 20 adults (ages 18-29) initially referred for TBI between 8 and 14 years of age
- IQ scores in low-average to average range
- On GOS
  - 20% severe disability
  - 25% moderate disability
- Social maladjustment prominent

Klonoff et al., *J Neurol Neurosurg Psychiatry*, 1993

- 23-year follow-up of 159 adults with mean age at injury of 8 years
  - Injuries relatively mild
- Composite measure of neurological status best predictor of outcome
  - Post-acute IQ also was reliable predictor
- Unemployment rate low (4%)
- 30% report leisure restricted

Jonsson et al., *Brain Injury*, 2004

- 8 patients with severe TBI, mean age of injury at 14 years, assessed at 1, 7, and 14 years post injury
- Verbal IQ declines over time
- Poor attention and working memory
- Verbal learning most impaired

Koshkiniemi et al.,
Arch Pediatr Adolesc Med, 1995

- 39 children with severe brain injury at less than 7 years of age, evaluated in adulthood (> 21 years of age)
- Only 59% able to attend typical school
- IQ low-average to average in 70% (mean 85)
- IQ and injury severity predict outcomes
- Only 23% able to work full-time
  - 0% if injured < 4 years of age

Nybo et al.,
J Inter Neuropsych Society, 2004

- 27 children with severe TBI < 7 years of age, evaluated in later adulthood (mean 40 years), from Koshkiniemi et al.
- 89% independent in ADLs
- 33% working full-time
  - 74% unchanged in vocational status
- Cognitive flexibility (CANTAB Intradimensional/ Extradimensional Shift Test) predicted full-time employment

McKinlay et al.,
J Neurol Neurosurg Psychiatry, 2002

- Prospective study of birth cohort
- Examined effect of mild head injury < age 10
  - Divided according to outpatient/inpatient treatment
  - Compared to non-injured cohort
- Inpatients show increased inattention and conduct disorder at ages 10 to 13
  - Most often apparent in those injured before age 5
- No clear effects for cognitive/academic measures

Anderson, Newitt, & Brown (unpublished)

- Long-term functional outcome in adults following childhood TBI
  - Retrospective study of adults with a history of mild/moderate and severe TBI in childhood
  - Issues investigated: education, employment, relationships and social skills, leisure, mental health

Sample inclusion criteria

- 2-16 years at time of injury
  - Diagnosis of traumatic brain injury, including period of altered consciousness
- Currently 18-30 years of age

COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

Sample recruitment

- 251 individuals contacted
- 99 participants and parents completed study
  - Mild/moderate TBI, N = 70
  - Severe TBI, n = 30

COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

Measures

- Demographic questionnaire
  - SES, medical and developmental history, education/employment, interventions, family/social history
  - Parent report
- NEO Personality Inventory-Revised
  - Self report
- WAIS-III

COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

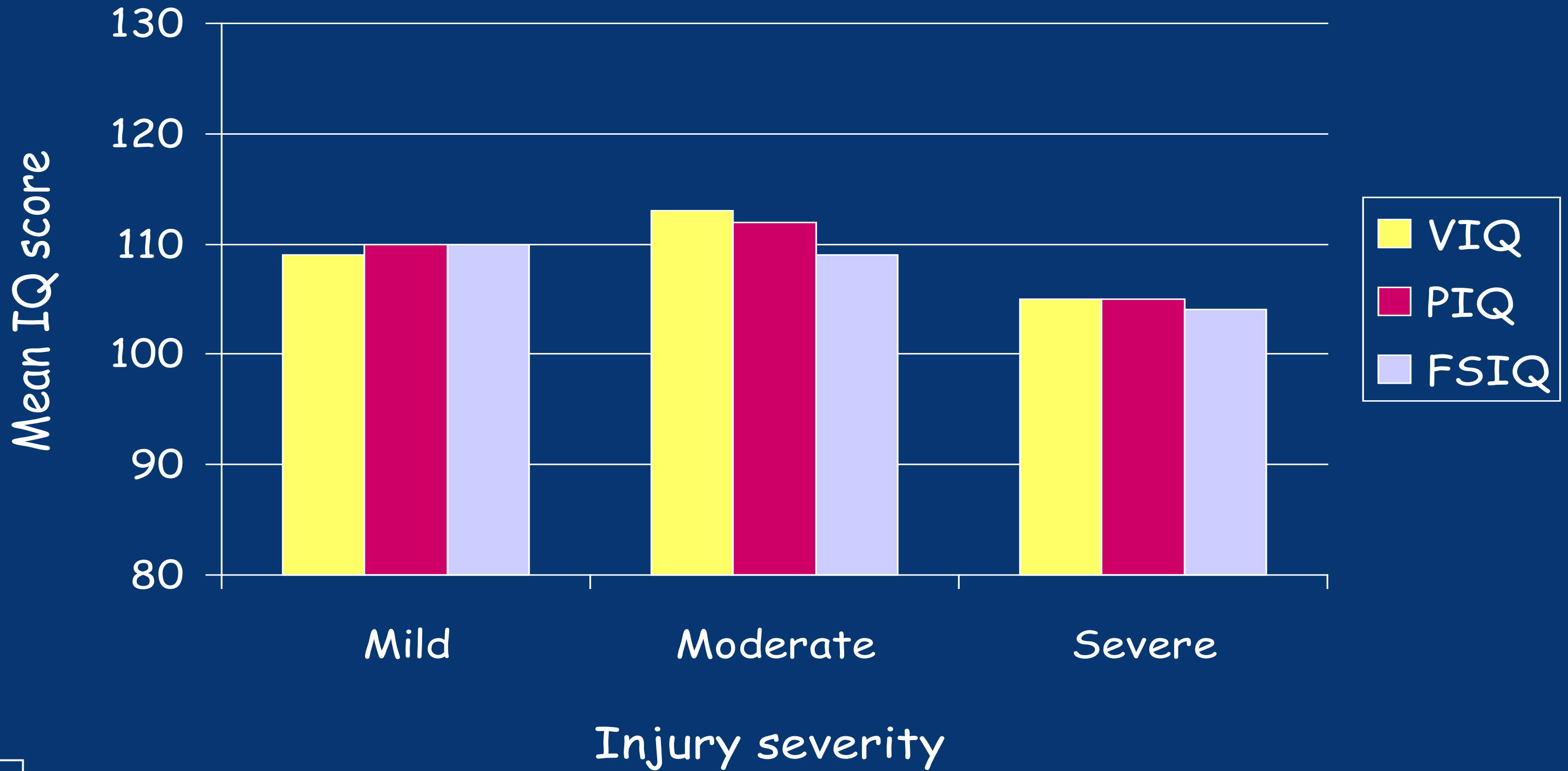
Measures

- Modified Sydney Psychosocial Reintegration Scale
  - Parent/self report
  - Domains
    - Work and lesiure
    - Relationships
    - Living skills

NEO Personality Inventory – Revised

- Mean T scores for all domains in average range
- No relationships found with gender, injury severity, disability, or age at injury

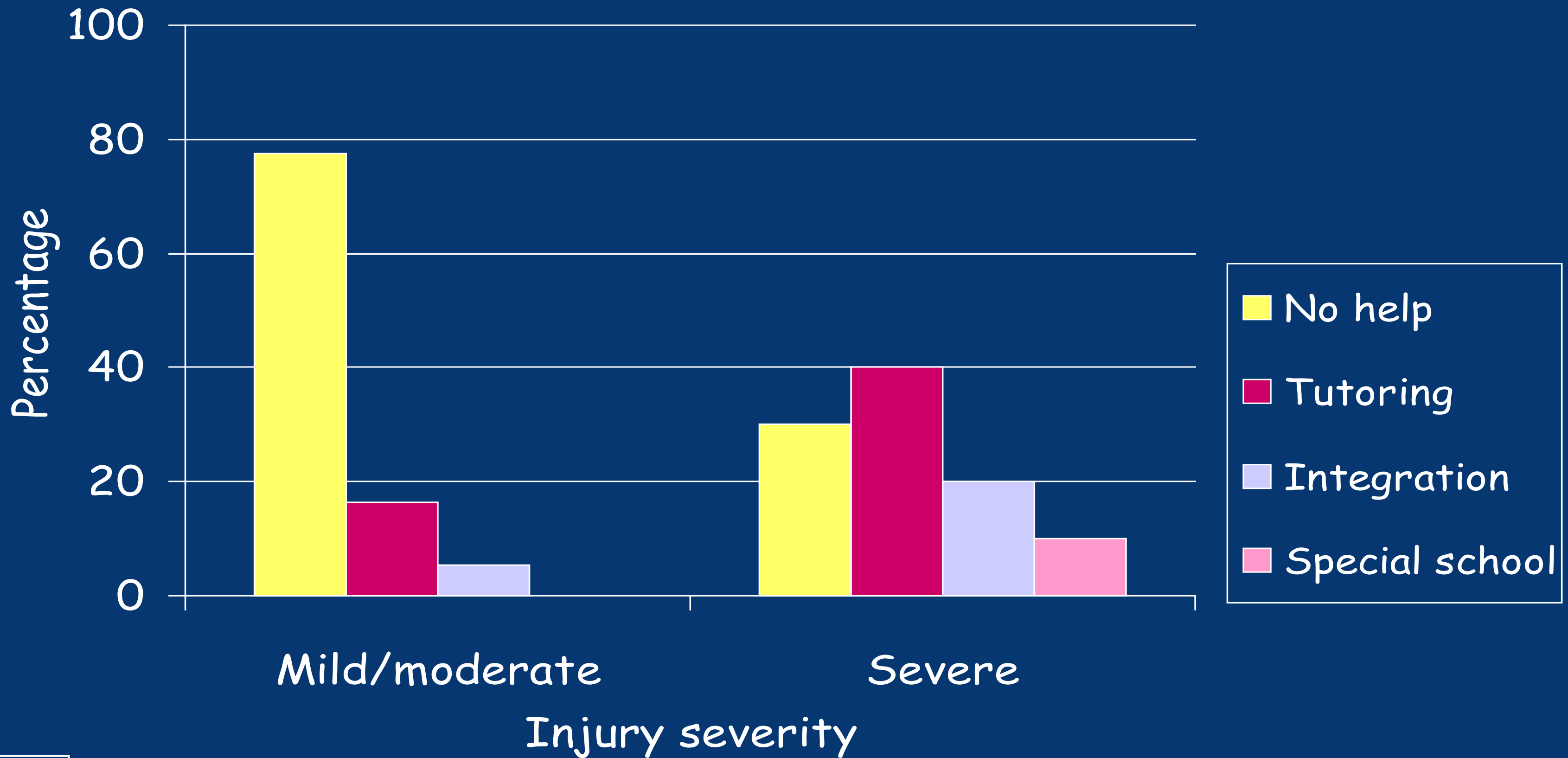
Intellectual function



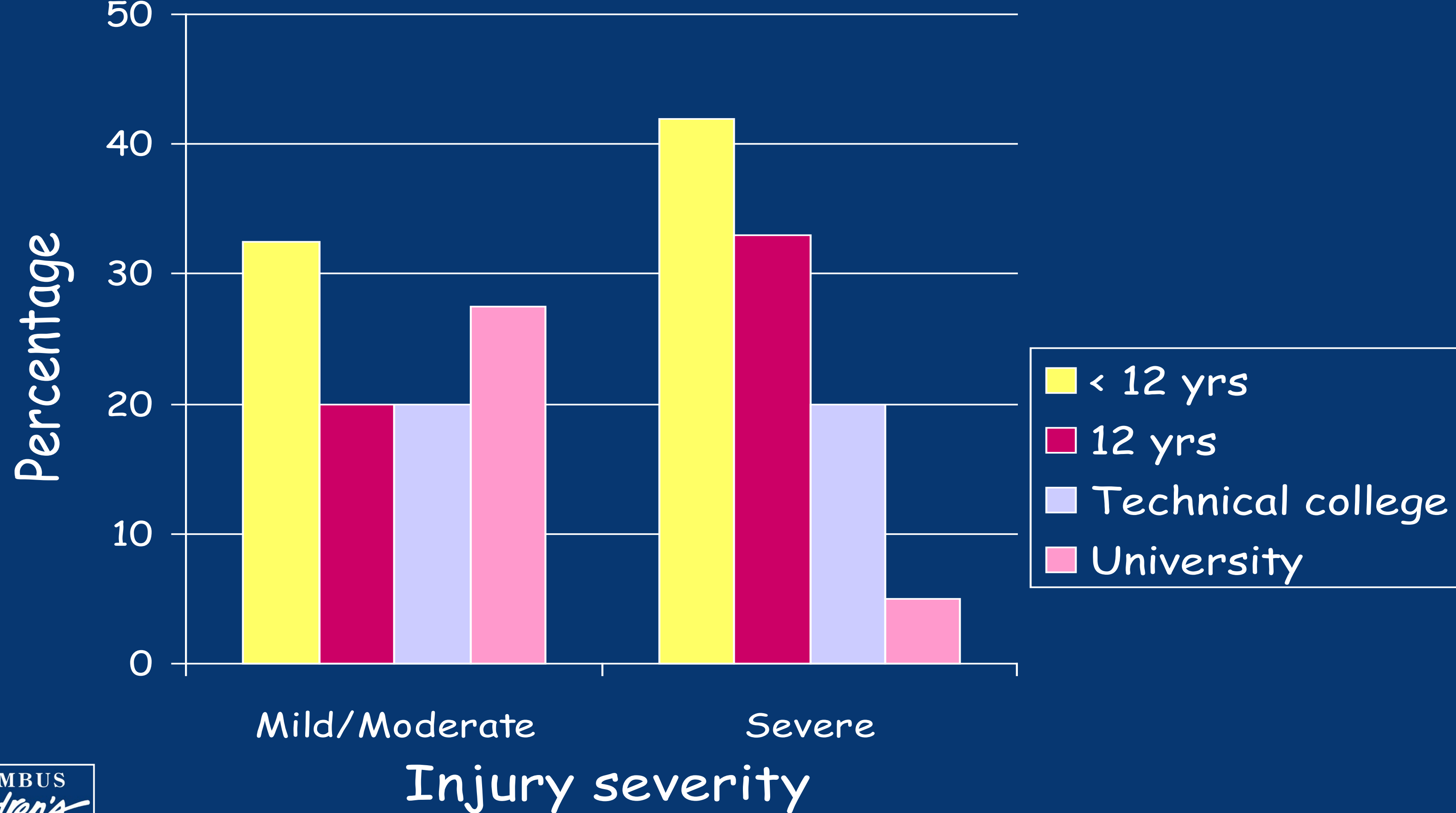
Initial conclusion

- Few deficits on standardised psychological measures (NEO, WAIS-III)
- Measures may not capture functional impairments (education, employment, psychosocial) identified in adults following childhood TBI

Educational help required post-TBI



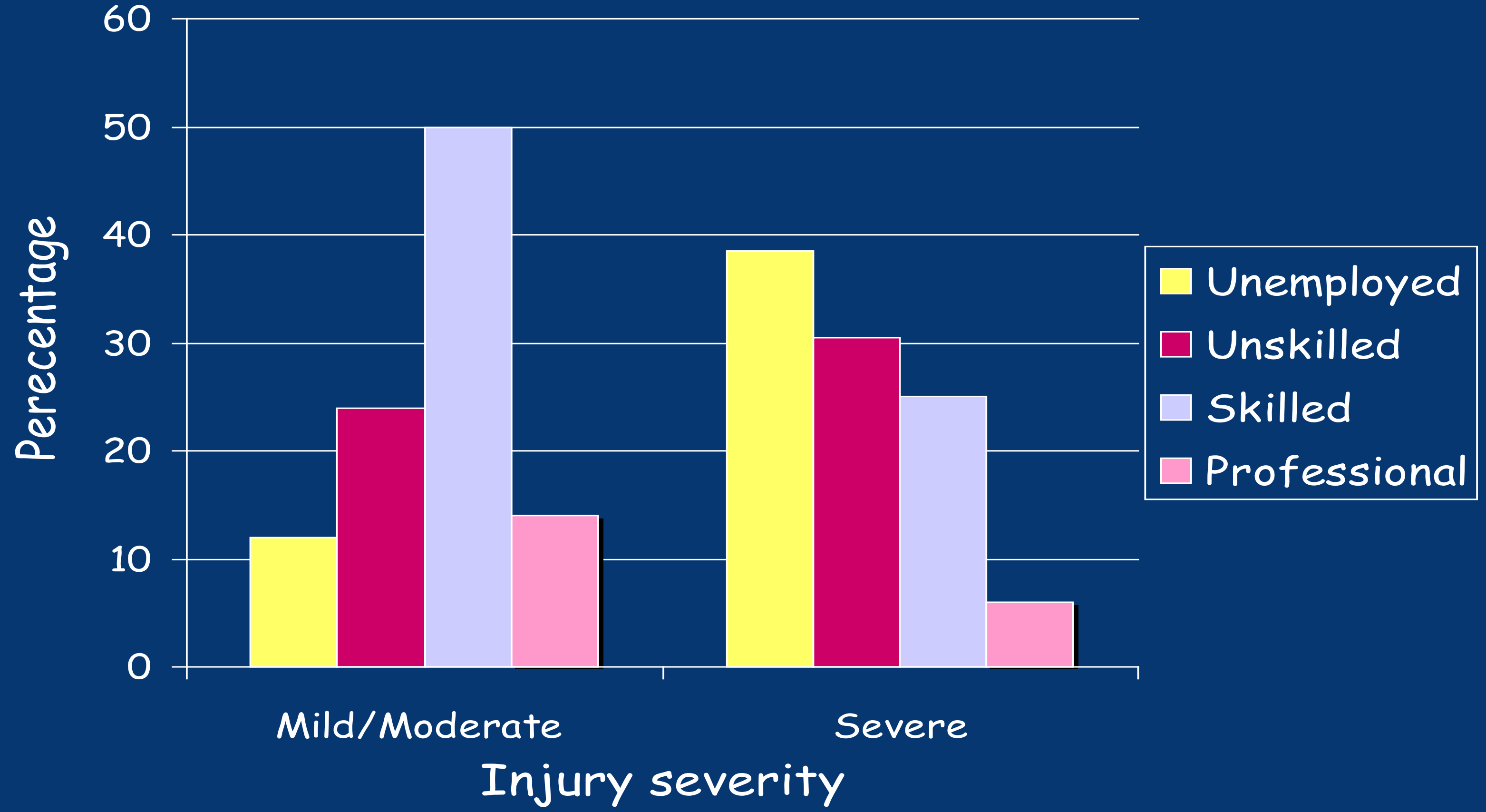
Educational levels post-TBI



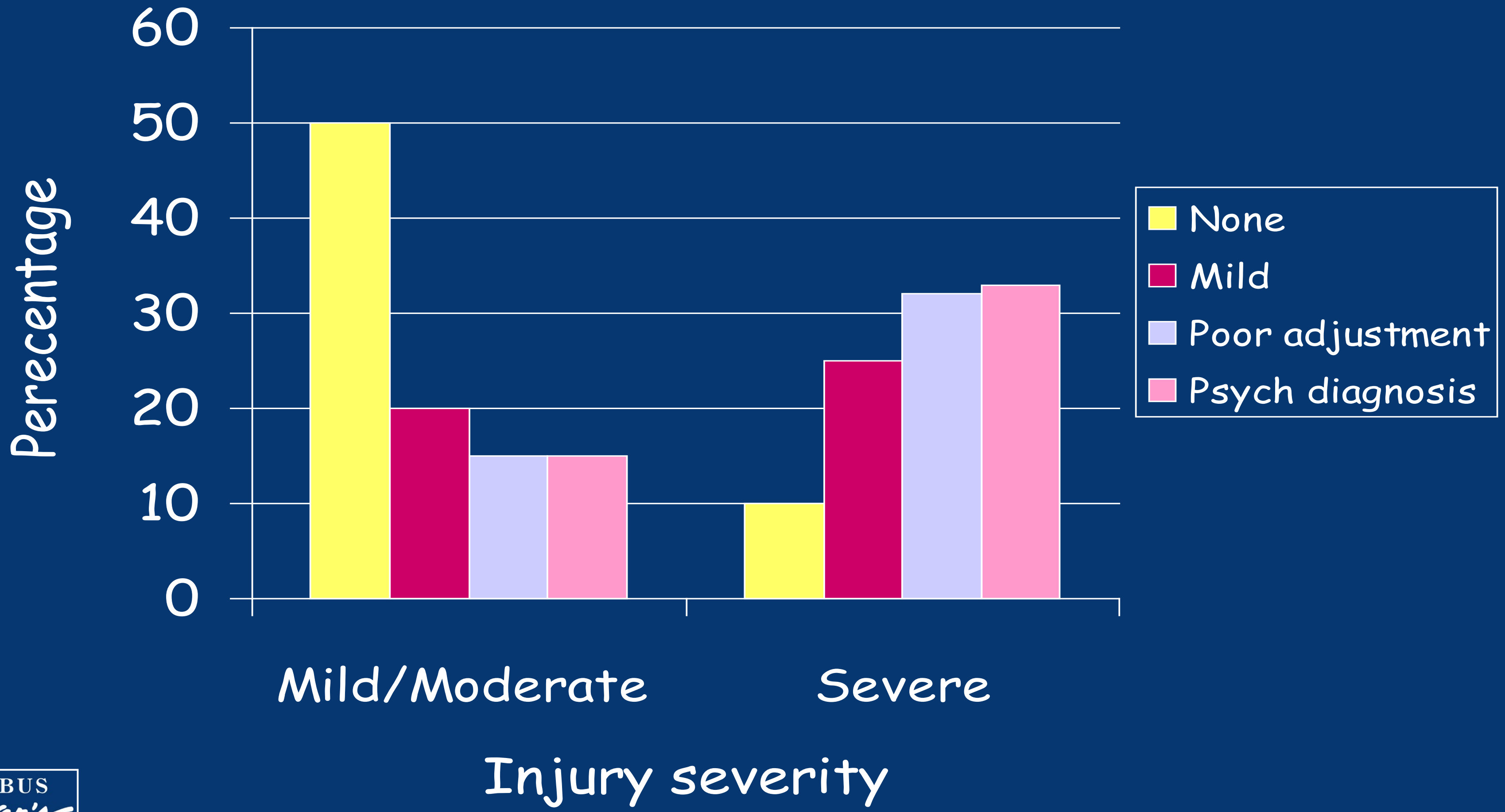
COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

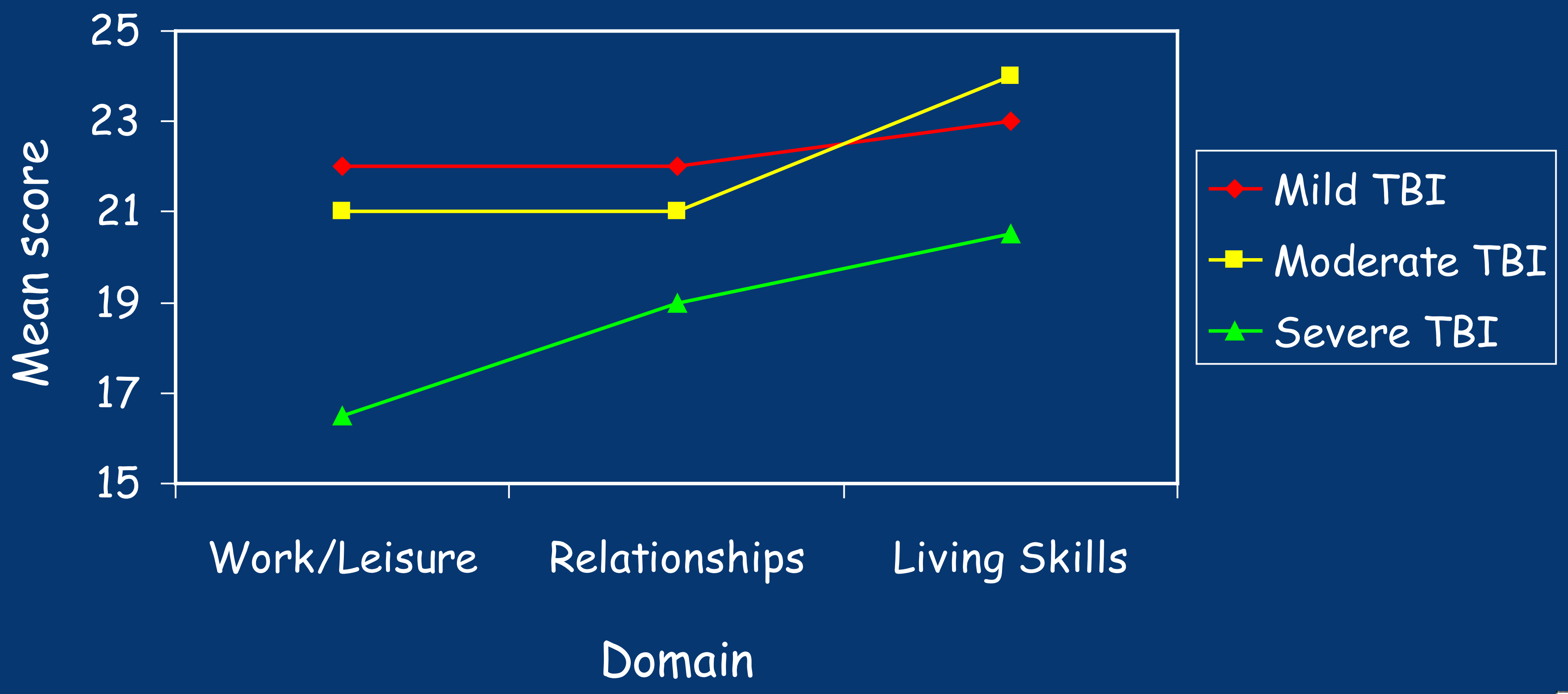
Employment status post-TBI



Psychological problems post-TBI



Quality of life post-TBI



Final conclusion

- More severe TBI in childhood is associated with:
  - Need for more educational support
  - Poor educational achievement
  - Low employment status
  - Poor psychological function
  - Poor quality of life
  - High frequency of social isolation

COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

Are we asking the wrong question?

- Not whether TBI matters, but for whom
- Group differences are less interesting than individual differences
  - Who has poor outcomes (and why)?
- Search for mediators and moderators of outcomes
  - Injury-related factors
  - Non-injury-related factors

Age-related differences in causes of TBI

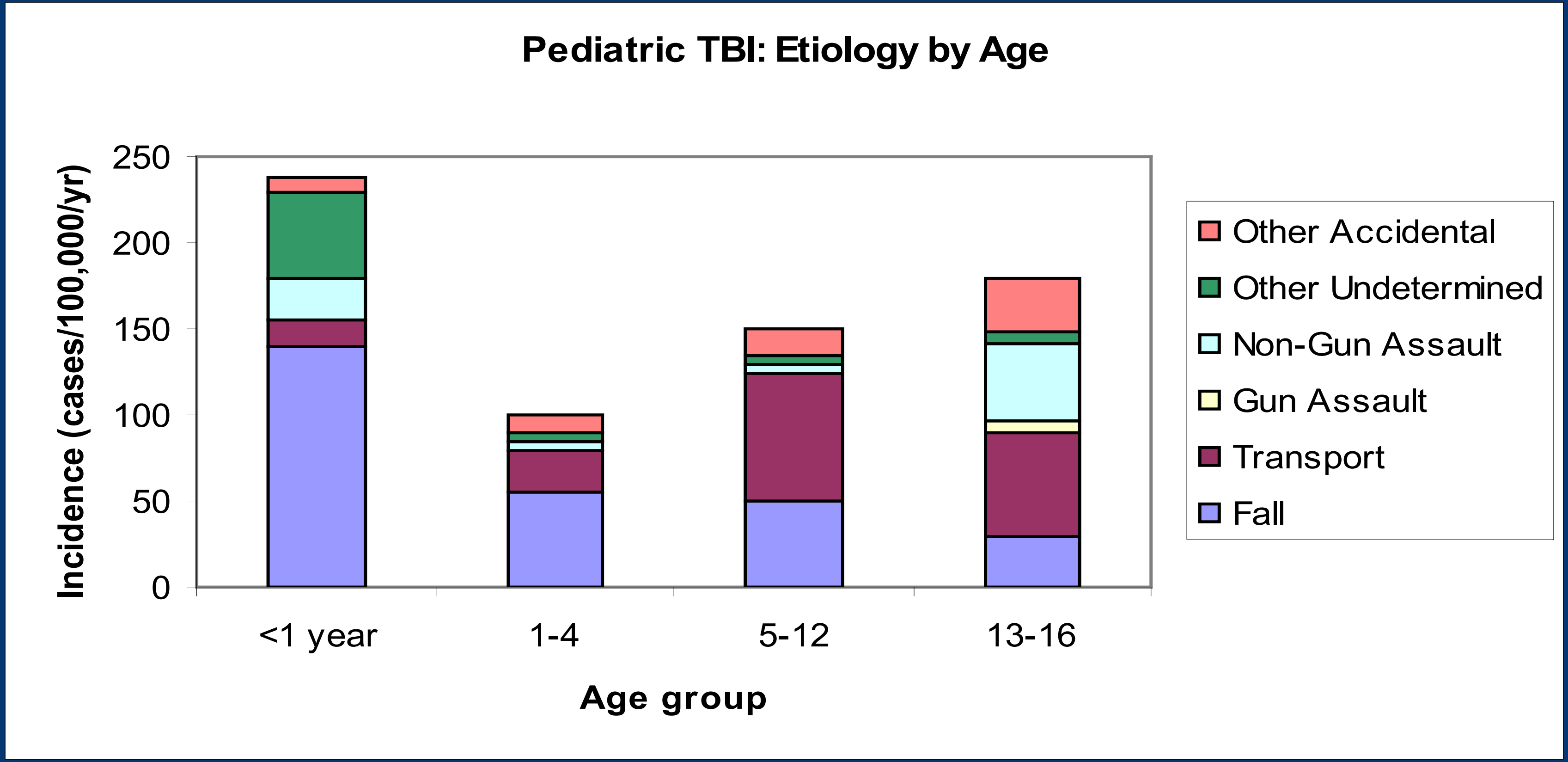
TBI by External Cause: Comparing the Rates

Figure 4. Average Annual Traumatic Brain Injury-Related Rates for Emergency Department Visits, Hospitalizations, and Deaths, by Age Group and External Cause, United States, 1995–2001

COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

Age differences in incidence & etiology

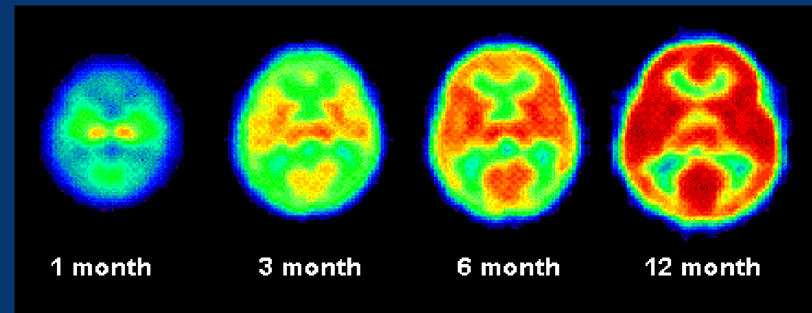


Durkin MS, et. al. 1998

COLUMBUS Children's RESEARCH INSTITUTE

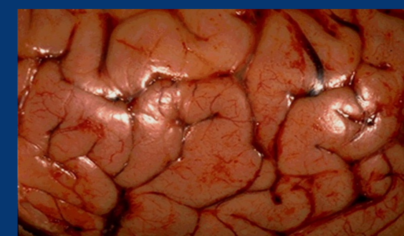
THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

Physiological distinctions in childhood TBI



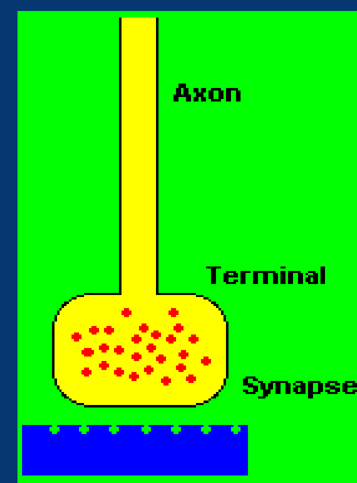
Biomechanics
- -Thinner skull
- -Greater proportional cranial mass

Energy metabolism
- -Increased cerebral glucose metabolism

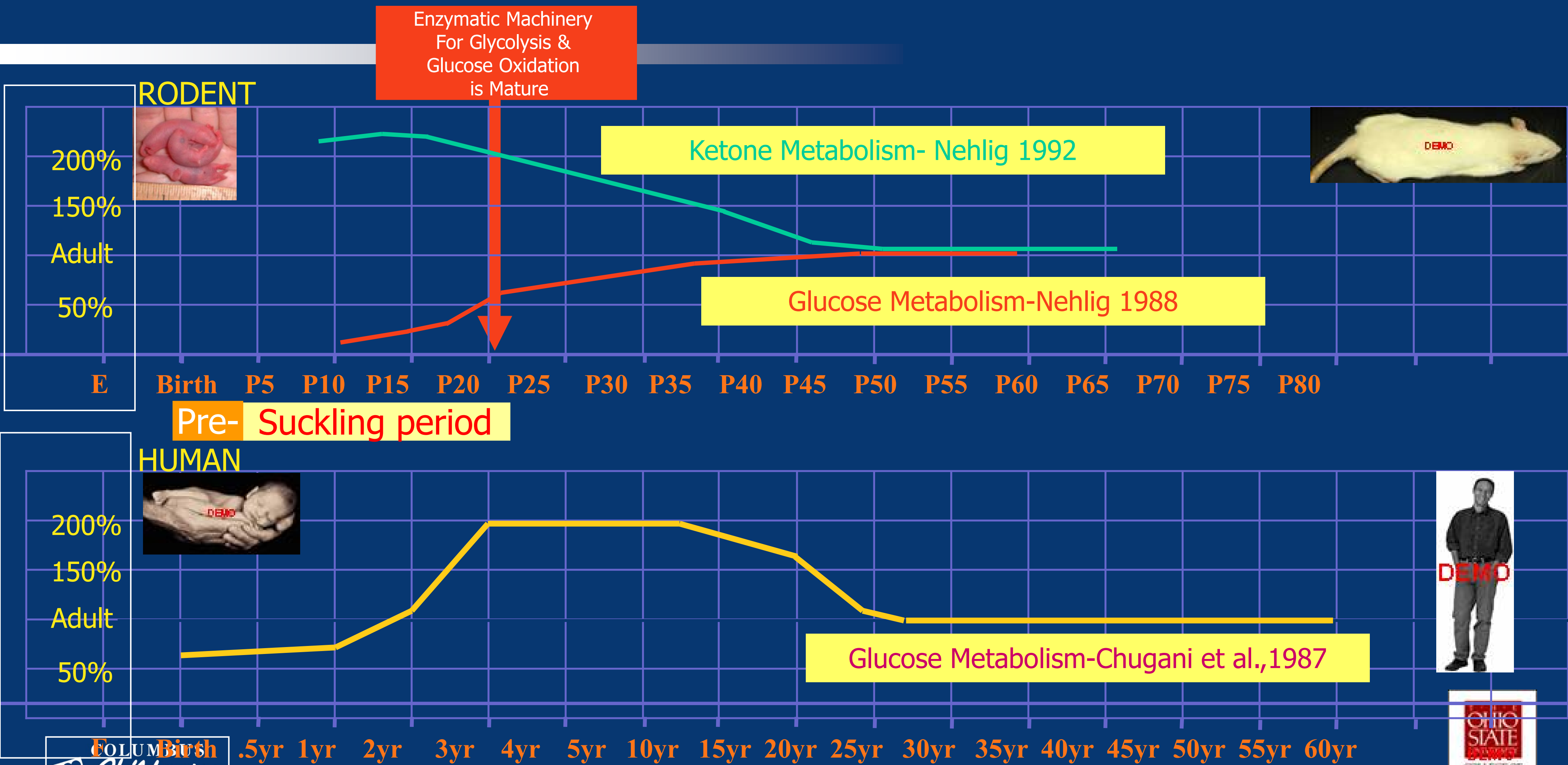


Vascular reactivity and autoregulation
- -Greater brain water content
- -Increased susceptibility to cerebral edema

Neurotransmission
- -Increased excitatory amino acid receptors



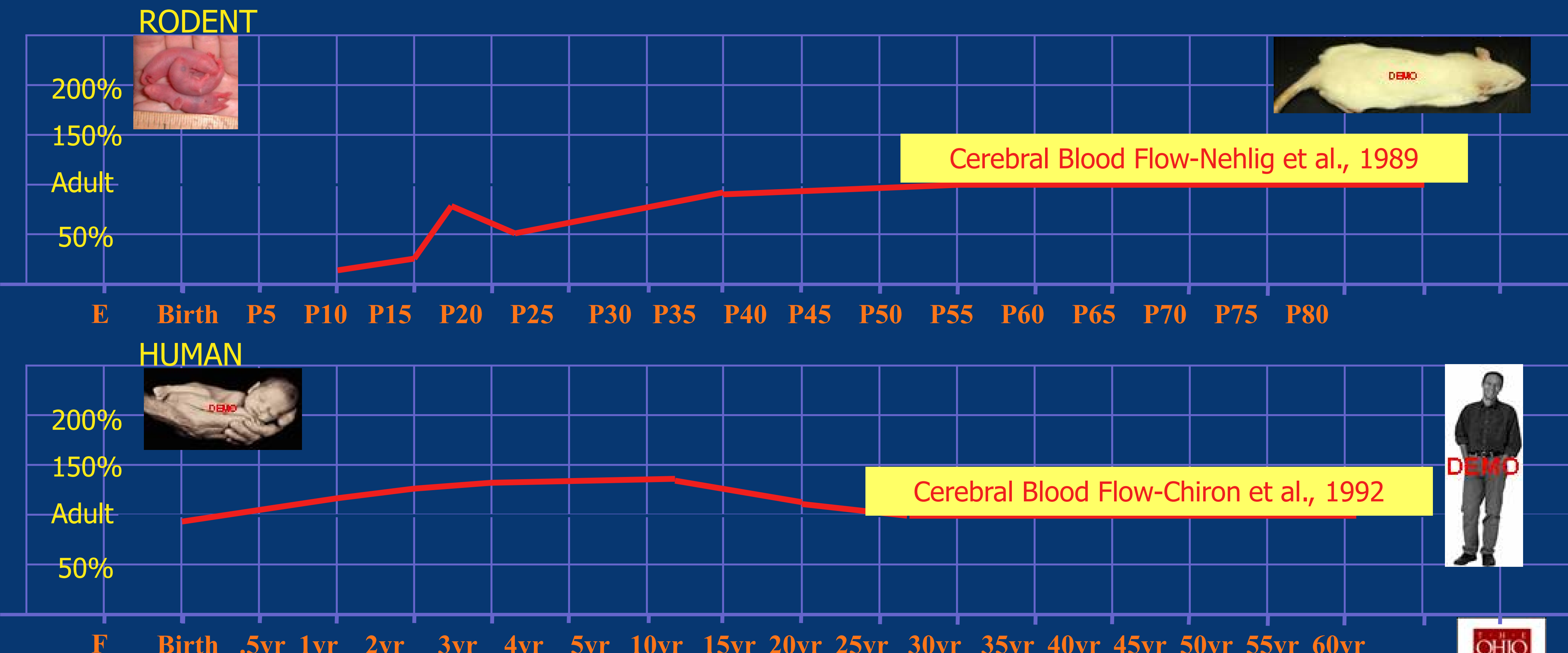
Changes in brain metabolism with age



COLUMBUS Children's RESEARCH INSTITUTE

OHIO STATE COLLEGE OF MEDICINE AND PUBLIC HEALTH

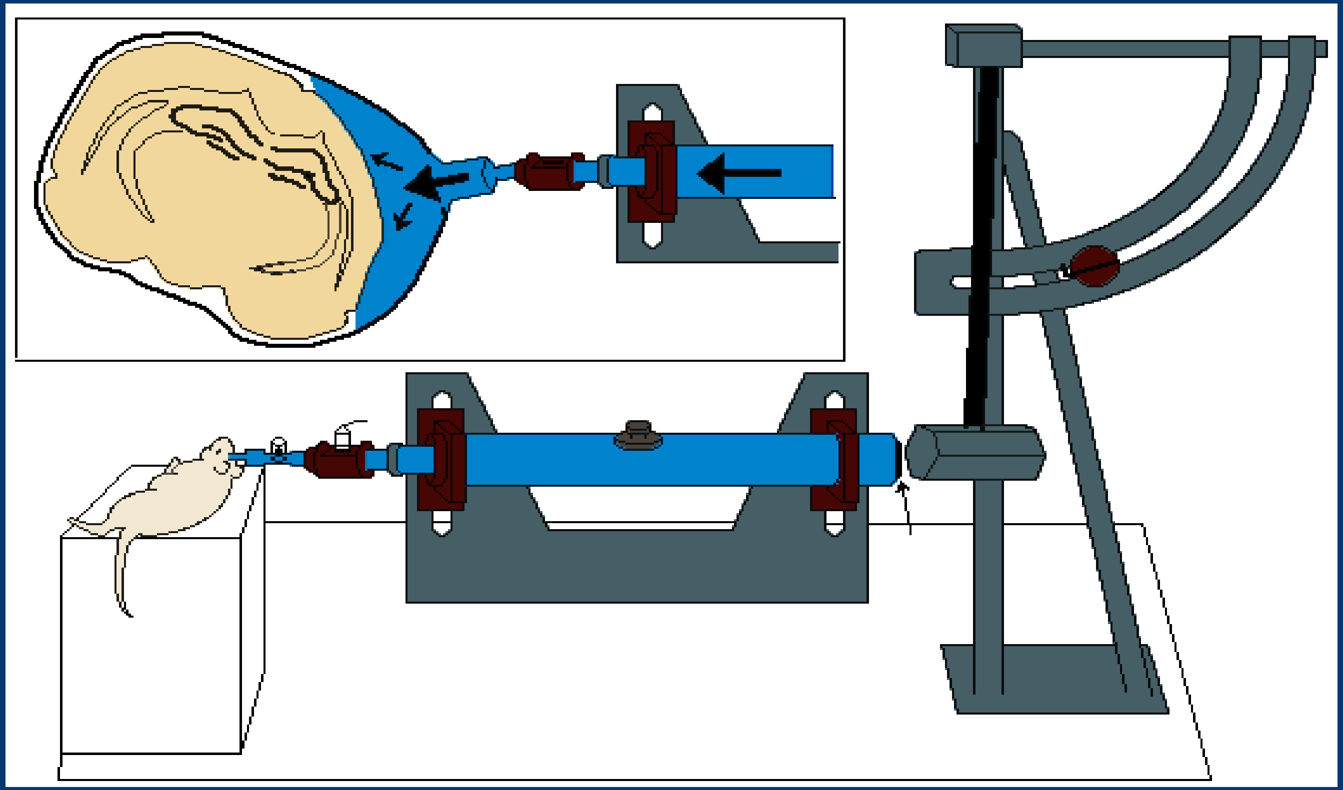
Changes in cerebral blood flow with age



COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE COLLEGE OF MEDICINE AND PUBLIC HEALTH

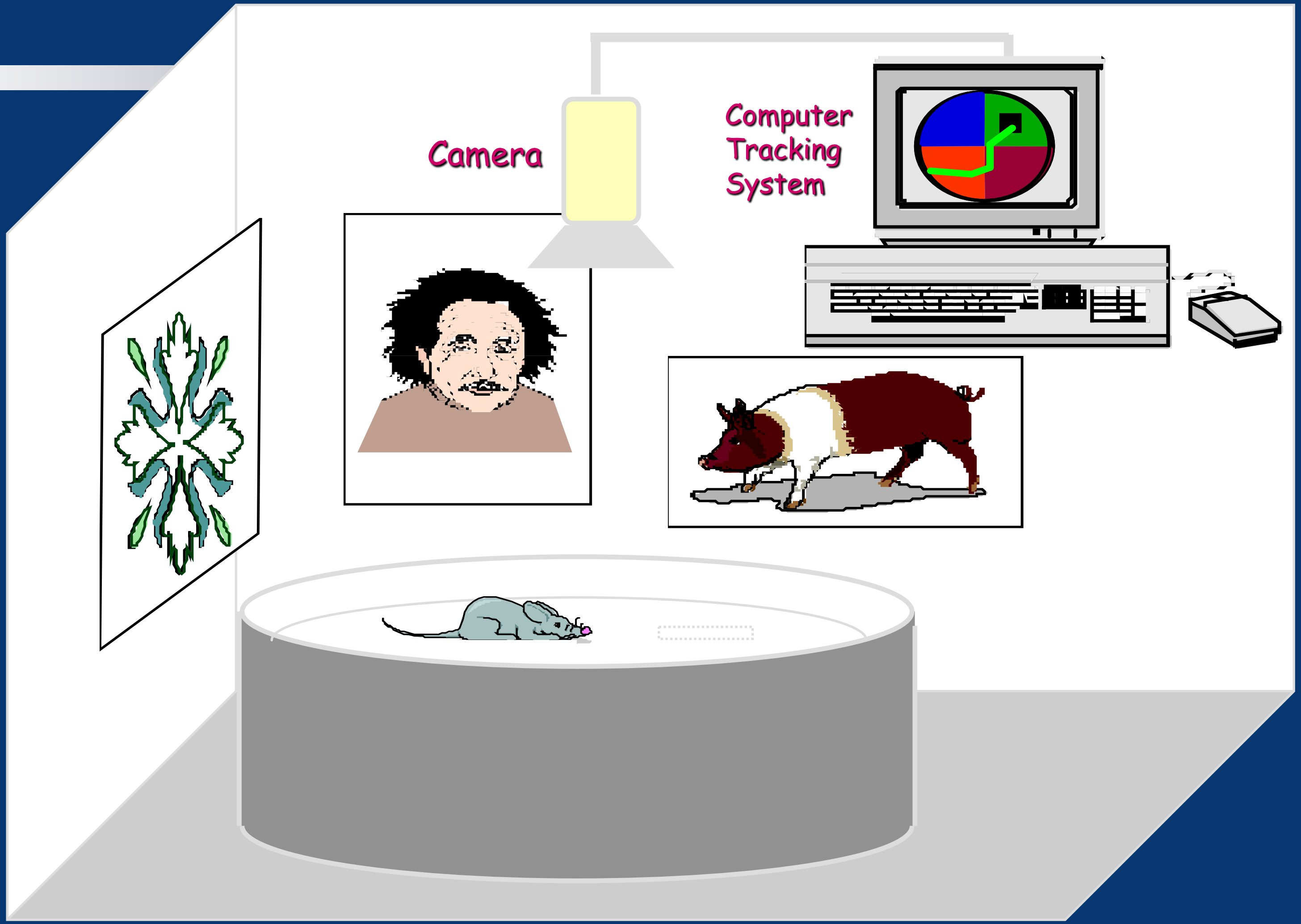
Fluid percussion injury model



COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

Morris Water Maze

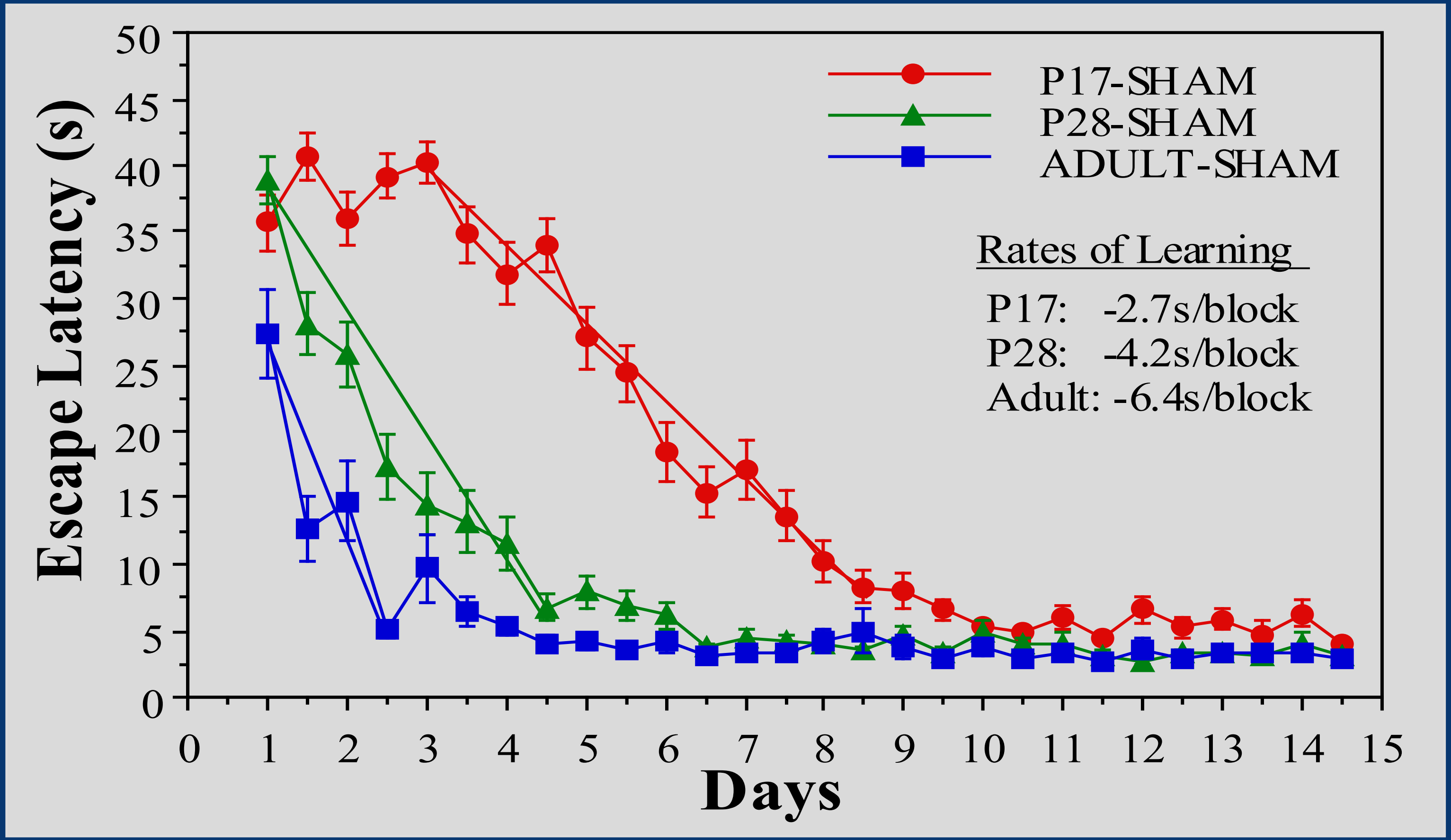


M.L. Prins, UCLA Division of Neurosurgery

COLUMBUS Children's RESEARCH INSTITUTE

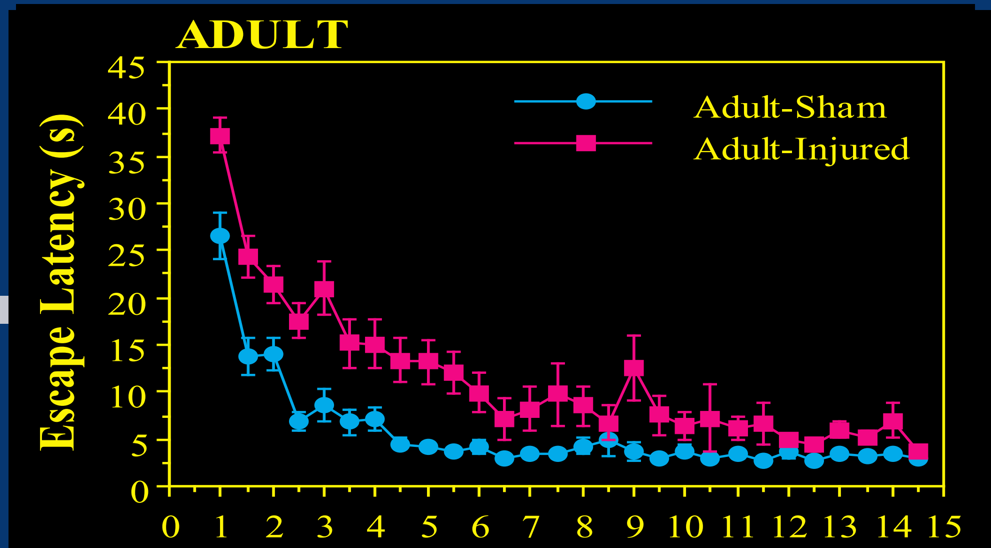
THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

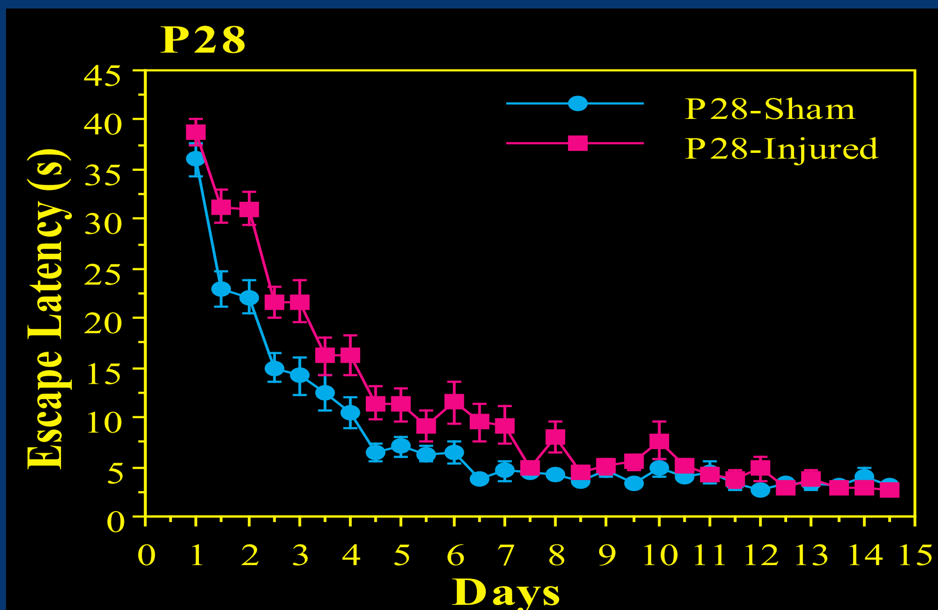
MWM acquisition in normal development

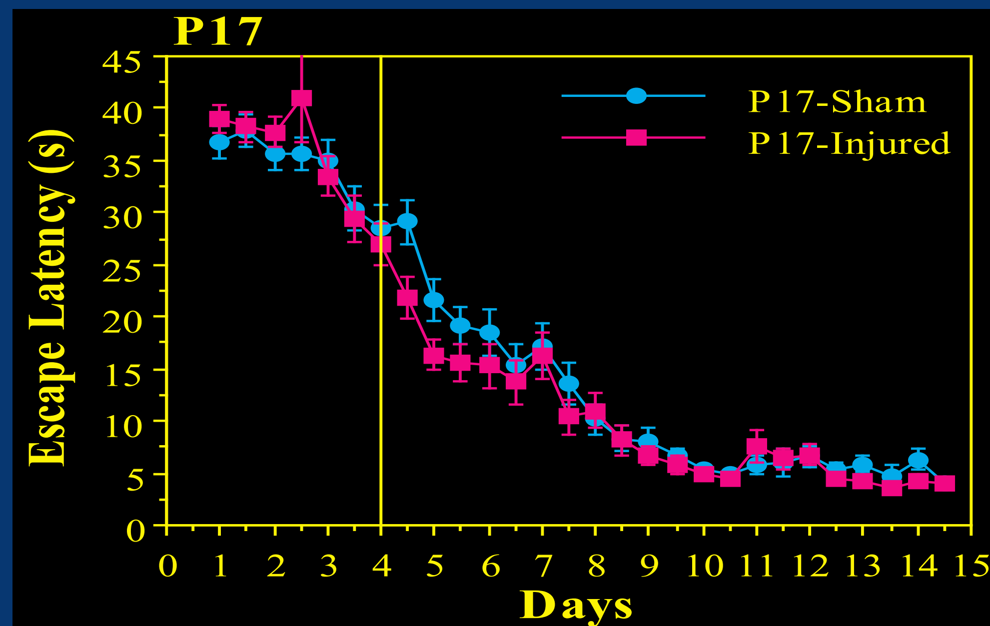


COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH



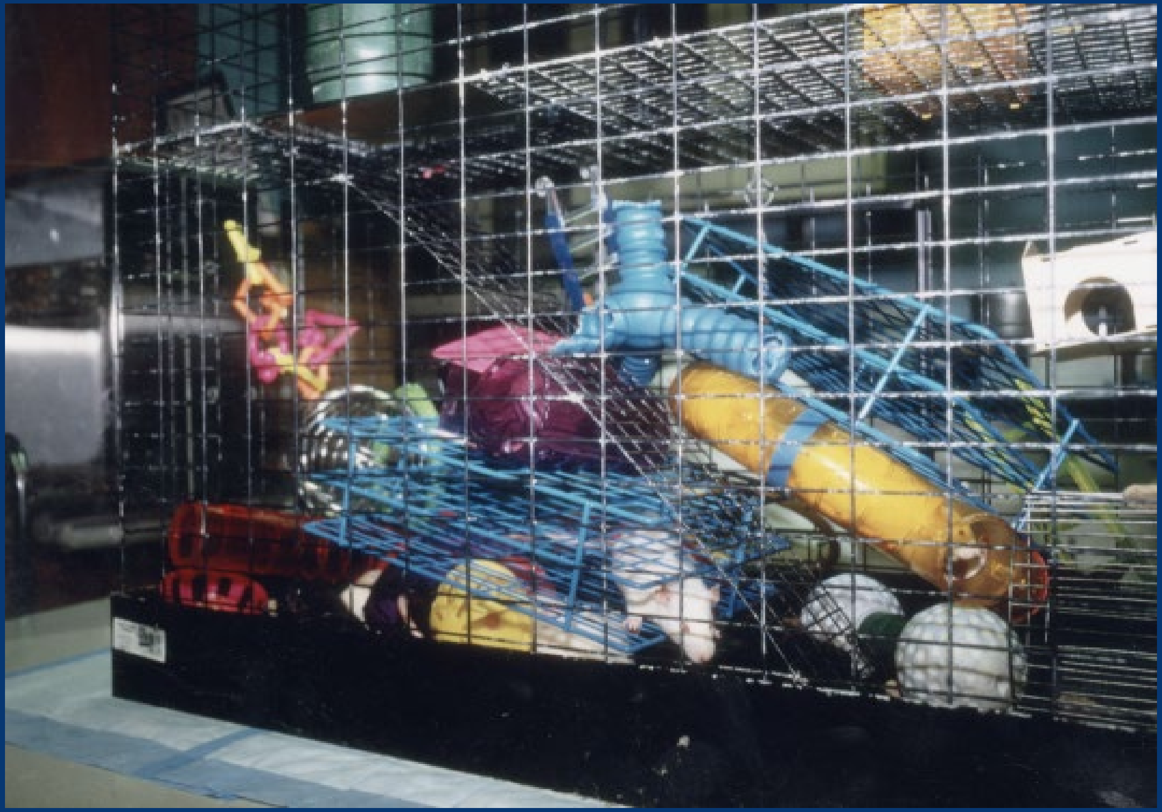




COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

Developmental plasticity & enriched environments



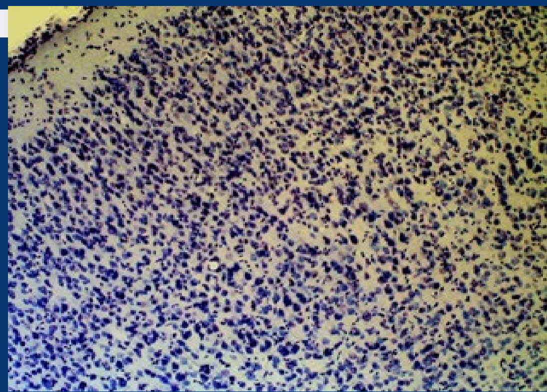
Enriched environment effects

- Increased cortical thickness
- Increased neuronal size
- Greater dendritic arborization
- Increased glia and capillaries
- More synapses
- Improved neurocognitive performance
- *More robust effects in young animals*

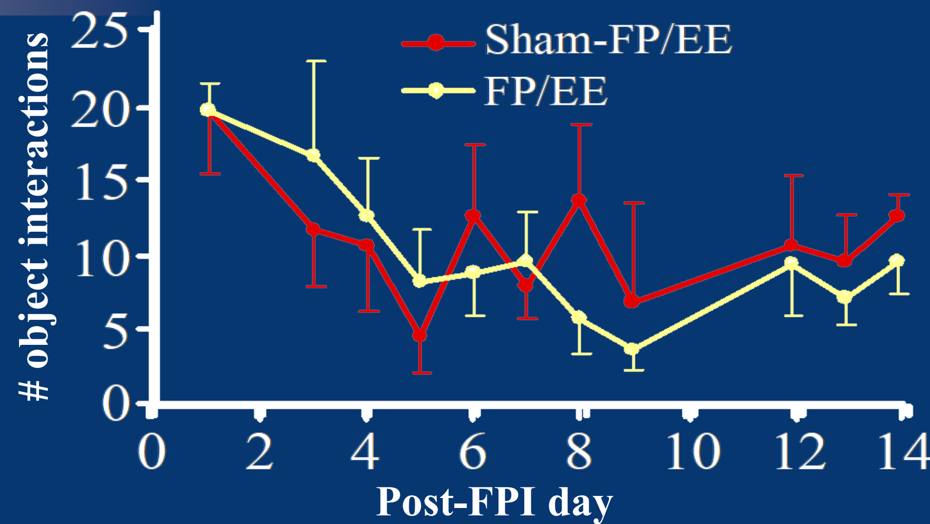
COLUMBUS Children's RESEARCH INSTITUTE

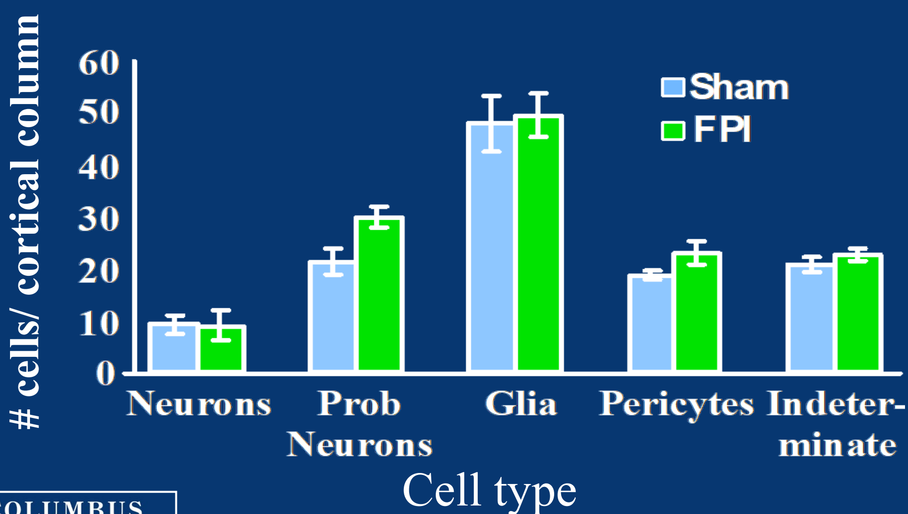
THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

Concussion in developing animals: Morphology and behavior



Occipital cortex 14 days post-FPI





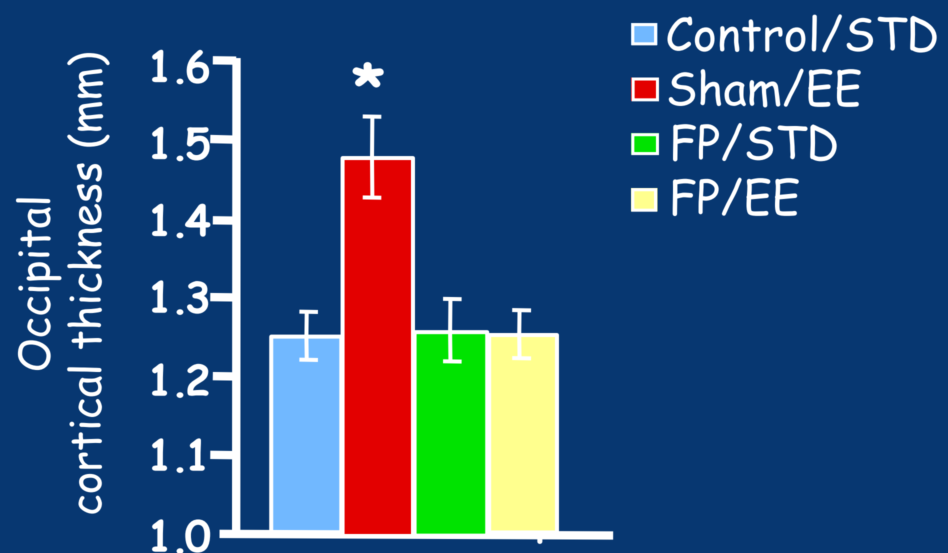
Rat *pups* show no significant morphological changes or behavioral differences after experimental brain concussion

COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

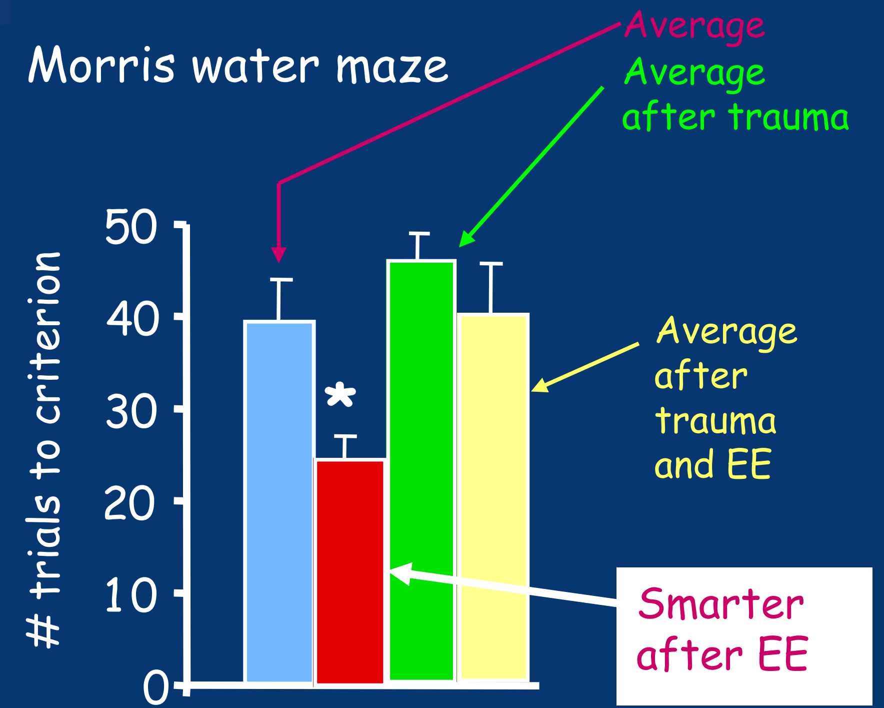
Early TBI and impaired plasticity

Cortical thickness



Occipital cortical thickness increases after housing in an enriched environment, but FAILS to do so after a moderate concussive injury

Morris water maze



Morris water maze performance improves after enrichment, but does not do so after developmental concussion

Fineman, Giza, et.al., J Neurotrauma, 2000

COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

Early TBI and altered dendritic arborization

Dendritic reconstruction

EE increases cortical dendritic branching, and developmental concussion impairs the normal dendritic response to rearing in EE.

Ip, Giza, et.al., J Neurotrauma, 2002

What about humans?

- Role of family and parenting in development
  - In school-age children with TBI, family environment moderates behavioral outcomes following severe TBI
  - In preschool children, parenting is a powerful influence on social development and psychosocial adjustment
- Might the family environment, and particularly parenting, influence recovery from TBI occurring during infancy and early childhood?

Ohio preschool TBI project

- Multi-site study in 3 to 6 year old children
- Prospective recruitment of children with moderate to severe TBI and comparison group of children with orthopedic injuries.
- Longitudinal follow-up of children and families at baseline, 6 months, 12 months, and 18 months post-injury

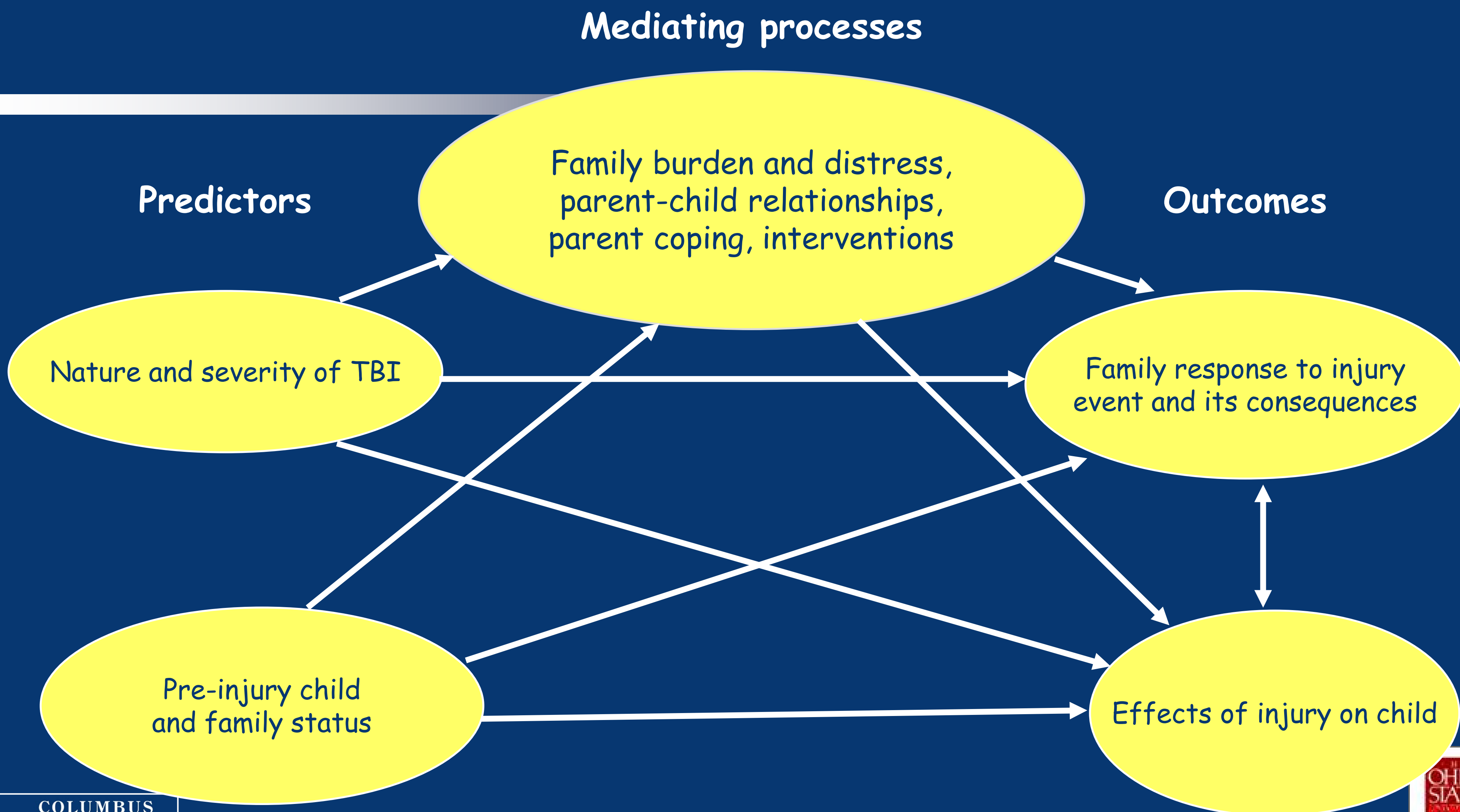
Ohio preschool TBI project

- Study began in fall 2002
- Multiple sites
  - Children's Hospital, Cincinnati, OH
  - Rainbow Babies and Children's Hospital, Cleveland, OH
  - Children's Hospital, Columbus, OH
- Investigators
  - S. Wade (PI), H. G. Taylor (Cleveland PI), K. O. Yeates (Columbus PI)

Study hypotheses

- Moderate to severe TBI adversely affects families more than OI (i.e., traumatic injuries not involving the brain)
- Pre- and post-injury parent and family characteristics predict children's outcomes after TBI
  - Even after controlling for children's pre-injury status and injury severity

Causal model



Study groups and selection criteria

- All children
  - Hospitalized for trauma
  - 3-6 years age at injury
  - No history of abuse or prior neurological disorder
  - English-speaking household
- Severe TBI
  - Blunt trauma, GCS < 9
- Moderate TBI
  - Blunt trauma, GCS 9-12, or GCS >12 with persistent LOC or neuroimaging abnormality
- Orthopedic injury (OI)
  - Fracture without evidence of CNS insult

COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

Child measures

- Cognitive and neuropsychological skills
  - Social information processing
- Academic achievement
- Early school performance
- Social competence
- Adaptive behavior
- Behavioral adjustment

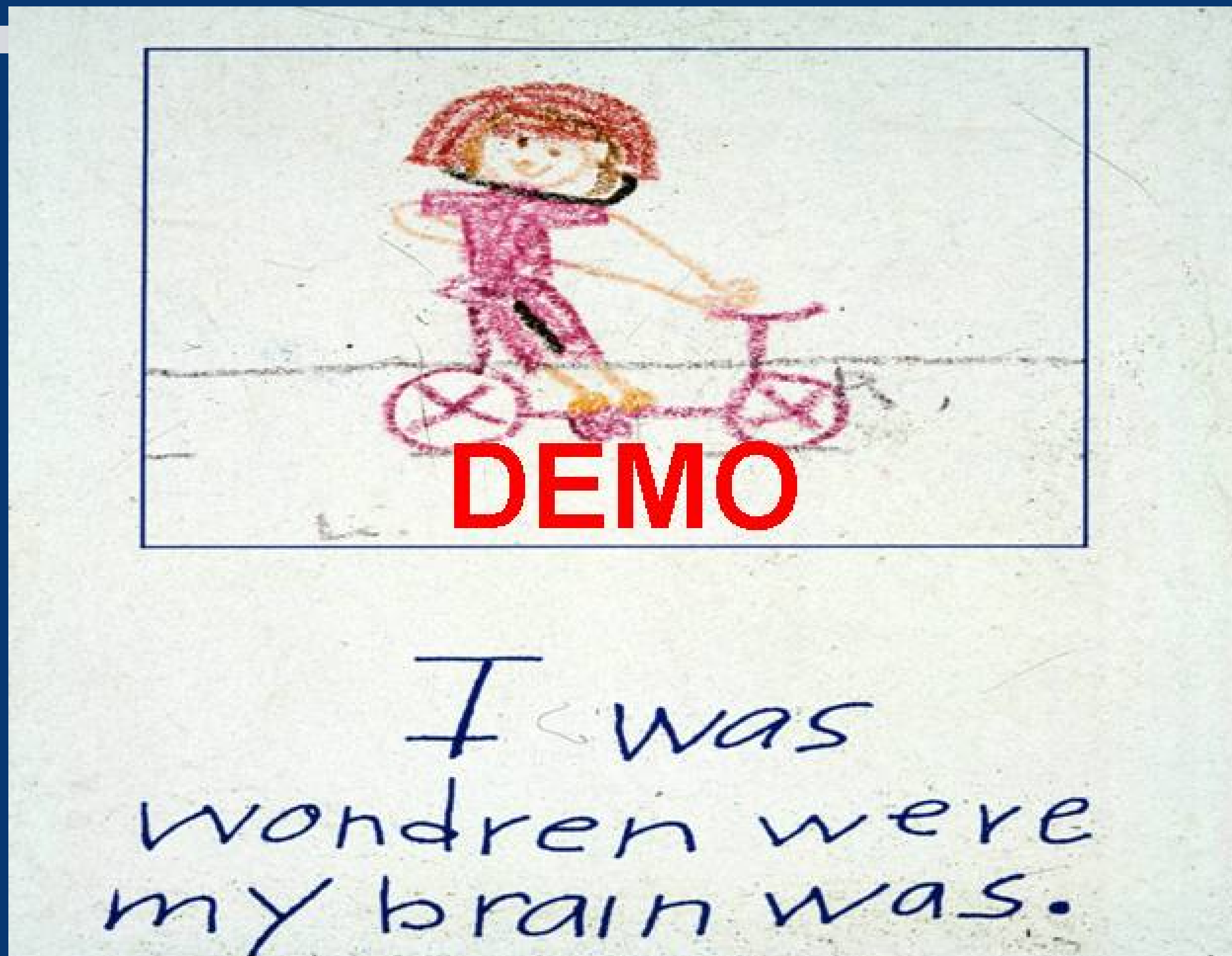
Family and parent measures

- Parent psychological distress
- Perceived family burden
- Other stressors and resources
- Parent-child interactions
    - Warmth and mutuality
- General family functioning

Future research needs

- Prospective, longitudinal designs
- Efforts to avoid selective attrition
- Neuroimaging to assess severity
- Better outcome measures
  - Social cognition
  - Emotional regulation
- Environmental moderators
  - Parenting and parent-child interactions

So what?



COLUMBUS Children's RESEARCH INSTITUTE

OHIO STATE COLLEGE OF MEDICINE AND PUBLIC HEALTH

Implications for evaluation

- Neurobehavioral functioning after early TBI is multi-determined
  - Conventional measures of injury severity do not tell the whole story
    - Advances in neuroimaging will help
  - Evaluating expected status is difficult
    - Multiple methods and measures
  - Evaluating environmental context is important
    - Standard measures are available

COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH

Implications for evaluation

- Neurological and ecological validity of neuropsychological testing is constrained by focus on cognition
  - Poorest outcomes are psychosocial in nature
- Neuropsychological testing does not tap important aspects of functioning
  - Mental state understanding ("theory of mind")
  - Emotion regulation
  - Emotive communication

Implications for management

- Multi-factorial model implies need for multiple levels of intervention
  - Pharmacotherapy
  - Cognitive rehabilitation
  - Educational intervention
  - Behavioral health services
  - Family support

Implications for management

- Future prospects?
  - Genetic therapy
  - Metabolic therapy
  - Peer relationships intervention
  - On-line family intervention

An ounce of prevention....

COLUMBUS Children's RESEARCH INSTITUTE

THE OHIO STATE UNIVERSITY COLLEGE OF MEDICINE AND PUBLIC HEALTH