Predictors of Cognitive Function and Recovery 10 Years After Traumatic Brain Injury in Young Children

WHAT'S KNOWN ON THIS SUBJECT: Previous research has demonstrated that young children with traumatic brain injury are at elevated risk of poor outcomes, particularly following severe injuries. These deficits persist until at least 5 years postinsult. Factors predicting outcomes in this age group have not been established.

WHAT THIS STUDY ADDS: This study follows survivors of very early traumatic brain injury into adolescence. Results indicate that severe injury is associated with poorest outcome, but after 3 years, the gap between children with severe traumatic brain injury and peers stabilizes.

abstract

FREE

BACKGROUND AND OBJECTIVES: Childhood traumatic brain injury (TBI) has implications for functional outcomes, but few studies have documented long-term outcomes. The purpose of this study was to plot recovery of cognitive and functional skills after early childhood TBI to 10 years postinjury and to identify the contribution of injury, environment, preinjury characteristics, and acute functional recovery.

METHODS: Subjects were recruited consecutively to this prospective, longitudinal study, which used a between-factor design, with injury severity as the independent variable. Forty children with TBI aged 2 and 7 years were recruited on admission to a tertiary pediatric hospital, divided according to injury severity, and compared with 16 healthy controls acutely and 12 and 30 months and 10 years postinjury. Cognition, adaptive ability, executive function, and social/behavioral skills were examined.

RESULTS: Children with severe TBI had poorest outcomes, with deficits greatest for cognition. Recovery trajectories were similar across severity groups but with significant gains in verbal skills from 12 and 30 months to 12 months and 10 years. Predictors of outcome included preinjury ability (for adaptive function) and family function (social/behavioral skills).

CONCLUSIONS: Results confirm a high risk of persisting deficits after severe TBI in early childhood. Children with less severe TBI appear to recover to function normally. Contrary to speculation about "growing into deficits," after protracted recovery to 30 months, young children make age-appropriate progress at least to 10 years postinsult. Environmental factors were found to contribute to adaptive and social/behavioral recovery. *Pediatrics* 2012;129:e254–e261

AUTHORS: Vicki Anderson, PhD,[a,b,c] Celia Godfrey, DPsych,[a] Jeffrey V. Rosenfeld, MD, MS, FRACS,[d,e] and Cathy Catroppa, PhD[a,b,c]

[a]Department of Child Neuropsychology, Murdoch Childrens Research Institute, Melbourne, Australia; [b]Department of Psychology, Royal Children's Hospital, Melbourne, Australia; [c]Department of Psychological Sciences University of Melbourne, Melbourne, Australia; [d]Department of Medicine, Monash University, Melbourne, Australia; and [e]Neurosurgery Department, The Alfred Hospital, Melbourne, Australia

KEY WORDS

traumatic brain injury, young, children, recovery of function, intelligence

ABBREVIATIONS

ABAS-II—Adaptive Behavior Assessment System–II
BRIEF—Behavior Rating Inventory of Executive Function
FFQ—Family Function Questionnaire
FSIQ—full scale IQ
GCS—Glasgow Coma Score
PIQ—performance IQ
SES—socioeconomic status
SSRS—Social Skills Rating Scale
TBI—traumatic brain injury
VABS—Vineland Adaptive Behavior Scale
VC—verbal comprehension
VIQ—verbal IQ

www.pediatrics.org/cgi/doi/10.1542/peds.2011-0311

doi:10.1542/peds.2011-0311

Accepted for publication Oct 10, 2011

Address correspondence to Vicki Anderson, PhD, Department of Psychology, Royal Children's Hospital, Parkville, Victoria, 3052 Australia. E-mail: vicki.anderson@rch.org.au

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: *The authors have indicated they have no financial relationships relevant to this article to disclose.*

COMPANION PAPERS: Companions to this article can be found on pages e262 and e494 online at www.pediatrics.org/cgi/doi/10.1542/peds.2011-0438 and www.pediatrics.org/cgi/doi/10.1542/peds.2011-3403.

Childhood traumatic brain injury (TBI) is a frequent cause of disrupted development and more common than other conditions affecting the central nervous system (eg, childhood cancer). Between 219 and 345 in 100 000 children[1,2] experience TBI annually, and 1 in 30 newborns will suffer a TBI by age 16.[1] Because these figures represent cases presenting for medical attention, they likely underestimate the true incidence of childhood TBI.

Very young children are at particular risk, with those aged <3 years having double the risk of TBI of any other group through childhood.[2] Mortality rates are low, but 1 in 3 of survivors in this age group will sustain permanent impairment.[1] In this age range, where the brain is rapidly developing and neurobehavioral skills are immature, there is an elevated risk of disrupted development. Clinical reports and available research suggest residual problems in cognition, attention, executive function, and memory.[3,4] These problems will interfere with skill acquisition, causing adaptive deficits, academic failure, and social and behavioral dysfunction,[5,6] as well as personal and economic burden for the family and community.

We previously investigated survivors of early TBI to 5 years postinjury.[7] Our findings suggest a "double hazard" effect, with early, (< 7 years) severe injury associated with poor recovery and late (≥8 years), severe TBI or early, mild TBI characterized by better recovery.[7,8] Few studies, however, have prospectively followed survivors of early TBI into adolescence, and those available focus primarily on cognition. In addition, several factors have been identified that contribute to deficits after school-aged TBI (injury severity and age, premorbid child and family function),[9–13] but it is unclear whether these factors also explain outcomes for younger children.

This study examined a sample of children, 10 years post-TBI, which we have reported on previously.[4,7,14,15] Intellectual, adaptive, and executive abilities and social/behavioral skills were examined. To our knowledge, no previous study has prospectively followed young children with TBI for more than 5 years postinjury. We made 3 predictions: (1) more severe TBI would be associated with greatest impairment at 10 years postinjury, (2) preinjury abilities and environmental factors would contribute to 10-year outcomes, and (3) more severe TBI would be associated with slower recovery over the 10 years postinjury.

METHODS

Participants

The original TBI sample comprised 96 children, representing consecutive admissions to the neurosurgical ward at Royal Children's Hospital, Melbourne, Australia, between 1993 and 1997. Inclusion criteria were (1) injury age 2.0 to 7.0 years; (2) evidence of TBI, including a documented period of altered consciousness; (3) completion of study protocol; and (4) English speaking. Exclusion criteria were (1) nonaccidental TBI; (2) penetrating TBI; (3) previous TBI; and (4) preinjury neurologic, psychiatric, or developmental disorder.

For the 10-year TBI sample, children from the original sample (42%) were located and agreed to participate (time since injury: M = 10.54, SD = 1.57 years). Comparison of injury and sociodemographic characteristics (documented at study recruitment) of participating and nonparticipating groups identified no significant differences (see Table 1). Of note, high attrition rates are common in longitudinal research,[16,17] particularly in early TBI, in which families of young children are more mobile and difficult to locate with time.

Children with TBI were divided into groups: (1) mild TBI (n = 7): Glasgow Coma Score[18] (GCS; on admission) 13 to 15, no mass lesion or neurologic deficits; (2) moderate TBI (n = 20): GCS 9 to 12; and/or mass lesion, and/or neurologic impairment; (3) severe TBI (n = 13): GCS 3 to 8, and mass lesion and/or neurologic impairment.

The original control sample comprised 32 healthy control subjects identified via kindergartens and child-care centers. This group was followed at all time points. Inclusion criteria (3) and (4) and all exclusion criteria cited earlier applied to this group. Because cause of early TBI has been closely related to socioeconomic status (SES),[2] control subjects were chosen to match for these potential confounds.

The 10-year control sample included 16 children (50% of original sample). The remainder of the sample was unable to be located. Comparison of participating and nonparticipating groups, based on initial time point data, identified lower SES at recruitment for participants in 10-year follow-up, $F(1,34) = 5.77$, $P = .024$ (Table 1).

Materials

Injury and Demographic Information

During the acute stage, data were collected on each child's medical and developmental history, parent occupation, and family constellation. Medical records were reviewed daily and GCS, neurologic abnormalities (eg, epilepsy, hemiparesis), surgical interventions, and radiologic findings were recorded.

10-Year MRI Scans

Images were acquired with a 1.5-Tesla Avanto scanner (Siemens Medical Systems, Erlangen, Germany): T1-weighted sagittal spoiled gradient echo acquisition (repetition time = 1920, echo time = 3.93, number of excitations = 1) with 1.0mm contiguous slices and T2-weighted TSE axial acquisition of slices 4mm thick (repetition time = 4850, echo time = 103, number of

TABLE 1 Comparison of Injury and Demographic Characteristics (From Acute Assessment) of Participants and Nonparticipants

	TBI Sample		Control Subjects	
	Seen at 10 y	Not seen at 10 y	Seen at 10 y	Not seen at 10 y
n	40	56	16	16
Age at injury/first assessment (y), M (SD)	4.81 (1.92)	4.46 (2.07)	4.18 (1.65)	5.67 (1.57)
Male, *n* (%)	25 (62.50)	34 (60.71)	10 (62.50)	6 (37.50)
Intact families (at injury), *n* (%)	34 (85)	38 (69)	14 (87.50)	13 (81.30)
Family SES (at injury), M (SD)	4.21 (0.93)	4.32 (1.11)	3.15 (0.72)[a]	4.05 (0.45)
FSIQ acute, M (SD)	99.29 (18.93)	97.98 (18.59)	113.00 (15.43)	100.38 (14.18)
VABS preinjury, M (SD)	111.61 (19.02)	110.58 (18.44)	112.53 (15.28)	117.50 (17.88)
Acute GCS, M (SD)	9.65 (4.24)	9.11 (4.15)	—	—
Severity, *n* (%)				
Mild TBI	7 (17.50)	10 (17.90)	—	—
Moderate TBI	20 (50.00)	28 (50.00)	—	—
Severe	13 (32.50)	18 (32.10)	—	—

[a] The SES at recruitment was lower for participating control subjects at 10 y than for the nonparticipating group ($P < .05$).

excitations = 2). For quantitative analyses, cerebrospinal fluid, intracranial (gray matter + white matter + cerebrospinal fluid) and total brain volumes (gray + white matter) were computed by using the FSL software (Oxford Centre for Functional MRI of the Brain, Oxford, UK), as outlined in previous publications.[19]

Acute scans were visually inspected and coded by a pediatric neuroradiologist and neurosurgeon, blind to the injury status, using a standardized classification (frontal, extrafrontal, subcortical).[20] Where results differed (n = 2), raters discussed discrepancies and came to a consensus. These ratings were employed as sample descriptors.

Environmental Factors

SES was coded at initial recruitment and at 10-year follow-up using Daniel's Scale of Occupational Prestige,[21] which rates parent occupation on a 7-point scale, with higher scores representing lower SES. Family function was measured using the Family Functioning Questionnaire (FFQ; P. Noller, PhD, unpublished data) acutely and at 10 years. Three factors were derived: Conflict, Intimacy, and Parenting Style, with higher scores reflecting more problems. The Intimacy factor was employed in statistical analyses because of its high correlation with both other factors.

Child Function—Preinjury

The Vineland Adaptive Behavior Scales (VABS),[23] completed by parents on recruitment, considers preinjury child function. Total Adaptive Behavior score (M = 100, SD = 15) was used in analyses.

Child Function—Acute

Choice of acute, 12-month, and 30-month IQ assessment measure was dependent on child's age: Bayley Scales of Infant Development[24]: children aged <30 months; Wechsler Preschool and Primary Scale of Intelligence—Revised[25]: children aged 30 months to 6.5 years; and Wechsler Intelligence Scale for Children—Third Edition[26]: children aged >6.5 years.

Child Function—10-Year Outcome Measures

The Wechsler Intelligence Scale for Children—Third Edition[26] and Wechsler Adult Intelligence Scale—Third Edition[27] were administered depending on participant age. Full scale IQ (FSIQ), verbal IQ (VIQ), performance IQ (PIQ), verbal comprehension (VC), perceptual organization, freedom from distractibility, and processing speed indices were recorded (M = 100, SD = 15).

The Adaptive Behavior Assessment System—Second Edition (ABAS-II)[28] was completed by parents or caregivers to measure adaptive function, providing 3 subscales: Conceptual, Practical and Social Composites, and a Total Composite score (M = 100, SD = 15).

The Behavior Rating Inventory of Executive Function (BRIEF)[29]: 2 index scores, Metacognition and Behavioral Regulation, and the General Executive Composite Score (M = 50, SD = 10) were calculated on the basis of parent ratings, with higher scores representing greater dysfunction, and scores ≥65 indicating abnormal elevation.

The Social Skills Rating System (SSRS)[30] was completed by parents and includes 4 domains: Cooperation, Assertion, Self-control, and Responsibility or empathy. A Composite Standard Score (M = 100, SD = 15) was derived.

Procedure

The study was approved by the Human Research Ethics Committee, Royal Children's Hospital. Children were enrolled on admission when parents completed a demographic questionnaire, the VABS, and the FFQ based on preinjury child and family function. Children were evaluated at 4 time points: time 1, acute (0–3 months postinjury); time 2, 12 months; time 3, 30 months; and Time 4, 10 years postinjury. Assessment occurred over two 1-hour sessions with a qualified child psychologist on an individual basis.

Statistical Analysis

Participating and nonparticipating groups were compared on demographic, preinjury, and psychosocial measures to identify any factors that might influence postinjury performance.

Missing data were identified for the 10-year follow-up sample. There were no missing data for acute or 10-year assessments. For data missing at 12 months (n = 5: 3 moderate, 1 severe, 1 mild)

and 30 months (n = 7, 2 moderate, 2 mild, 2 severe, 1 control), participants were allocated the mean score for their severity group at that time point.

To determine group differences at 10-year follow-up, multivariate analysis of variance was conducted on outcome measures. Partial η squared (η^2) values are reported, where appropriate, and interpreted as follows: small: 0.01; medium: 0.06; large: 0.14. Within the TBI group, Pearson correlations were calculated to explore relationships among predictor variables, and regression analyses were performed to investigate predictors of outcome. Variables in these analyses were injury factors (GCS, white matter volume), developmental stage (age at injury), preinjury abilities (VABS), and environmental parameters (SES, FFQ).

Repeated-measures analyses of variance were conducted to examine severity effects (mild, moderate, severe) and time since injury (for FSIQ: times 1–4; for VIQ and PIQ: times 2–4). Note that at time 1, some children completed the Bayley Scales of Infant Development, which provides a single mental development score, so only a global index of intellectual ability was available. When significant findings were identified from these analyses, post hoc analyses (Tukey) were conducted and reported.

RESULTS

Demographic and Injury Characteristics of Sample at 10 Years Post-TBI

There were no significant group differences for age at time 1 or time 4, preinjury VABS, or FFQ (Table 2). There was a group difference for SES: acute, F (3,54) = 3.52, P = .02, with control subjects having higher mean SES than TBI groups. There was also a significant difference between the severe TBI group and control subjects for FSIQ at time 1, F(3,55) = 3.36, P = .03, and at time 4, F(3,55) = 4.63, P = .01.

TBI groups differed for GCS, F(2,37) = 17.43, $P < .001$, acute CT/MRI findings, χ^2 (2,40) = 22.14, $P < .001$, neurologic signs, χ^2 (2,40) = 16.45, $P < .001$, surgical intervention, χ^2 (2,40) = 10.27, P = .006, and coma duration, χ^2 (2,40) = 32.52, P = .003. Most mild TBIs were due to falls, with motor accidents more common in severe TBI. Quantitative analysis of brain volumes showed no group differences; however, medium effect sizes were detected for total brain volume (η^2 = 0.06) and white matter (η^2 = 0.07), with lower volumes evident with severe TBI (Table 3).

10-Year Outcomes

Group Differences

For IQ, severity effects, in the expected direction, were identified for FSIQ, VIQ, PIQ, VC, PO, and PS at 10 years. Tukey post hoc tests revealed differences

TABLE 2 Demographic Characteristics of the Sample

	Mild	Moderate	Severe	Control
n	7	20	13	16
Male, *n* (%)	3 (43)	13 (65)	9 (69)	10 (63)
Injury age, M (SD)	4.68 (1.60)	5.07 (2.04)	4.47 (1.94)	—
Age at acute assessment (y), M (SD)	4.81 (1.61)	5.22 (2.02)	4.67 (1.93)	4.27 (1.63)
Age at 10-y follow-up (y), M (SD)	14.39 (1.28)	15.45 (3.36)	15.27 (2.96)	14.53 (2.35)
SES: acute, M (SD)[a]	4.17 (0.96)	4.31 (0.54)	4.08 (1.05)	3.15 (0.72)
VABS: preinjury, M (SD)	116.60 (26.43)	117.83 (13.47)	102.55 (18.67)	112.53 (15.28)
FSIQ: acute, M (SD)[b]	98.00 (15.70)	103.10 (16.87)	90.77 (23.36)	111.81 (15.64)
FSIQ: 10 y, M (SD)[b]	98.86 (16.50)	102.40 (16.39)	91.85 (17.32)	112.94 (11.71)
FFQ: Intimacy preinjury, M (SD)	60.50 (21.04)	65.75 (4.98)	63.46 (8.01)	66.93 (3.63)
FFQ: Intimacy 10 y, M (SD)	59.43 (12.65)	59.12 (12.65)	63.42 (5.98)	61.40 (7.00)
FFQ: Conflict preinjury, M (SD)	23.67 (7.53)	22.75 (10.39)	30.75 (10.81)	23.07 (8.44)
FFQ: Conflict 10 y, M (SD)	27.86 (11.08)	27.41 (11.28)	29.50 (10.27)	24.53 (7.41)

[a] Significant difference between mild, moderate, severe groups versus control subjects: F(3,54) = 6.75, P = .001.
[b] Significant difference between severe versus control groups: FSIQ time 1: F(3,55) = 3.36, P = .026; FSIQ time 4: F(3,55) = 4.63, P = .006.

TABLE 3 Injury Characteristics of the 10-Year Sample

Injury characteristics	Mild	Moderate	Severe
n	7	20	13
GCS on admission, M (SD)[a]	13.57 (1.51)	10.85 (1.92)	5.69 (2.14)
Neurologic signs, *n* (%)[a]	—	9 (45.00)	12 (92.31)
Abnormal CT/MRI, *n* (%)[a]	—	15 (75.00)	13 (100)
Cause of injury			
Passenger, *n* (%)	—	1 (5.00)	3 (23.10)
Pedestrian, *n* (%)	—	2 (10.00)	4 (30.70)
Falls, *n* (%)	7 (100.00)	14 (70.00)	3 (23.10)
Other, *n* (%)	—	3 (15.00)	3 (23.10)
Pathology location: acute CT/MRI scan			
No pathology detected, *n* (%)	7 (100.00)	12 (60.00)	2 (15.38)
Frontal only, *n* (%)	—	2 (10.00)	5 (38.50)
Extrafrontal only, *n* (%)	—	5 (25.00)	2 (15.38)
Frontal + extrafrontal, *n* (%)	—	—	2 (15.38)
Subcortical, *n* (%)	—	1 (5.00)	1 (7.68)
Cortical + subcortical, *n* (%)	—	—	1 (7.68)
Surgical intervention, *n* (%)[a]	—	6 (30.00)	9 (69.23)
Coma <1 day, *n* (%)[a]	7 (100.00)	19 (95.00)	3 (23.10)
Brain area cm^3 (SD)			
Total brain volume	1236 (176)	1206 (118)	1144 (165)
Intracranial volume	1517 (154)	1493 (120)	1454 (171)
Cerebrospinal fluid	280 (45)	287 (63)	309 (40)
Gray matter	798 (125)	777 (92)	744 (99)
White matter	438 (57)	430 (45)	400 (71)

[a] Significant relationship between severity and injury characteristics, all Ps < .01.

between: severe TBI and control groups for all variables; moderate TBI and control subjects for FSIQ and VC; and mild TBI and control subjects for VC. There were no significant group differences on other variables (all *P*s > .1), although effect sizes were medium to large, with a trend for poorest performances for the severe TBI group (FFD Index: $\eta^2 = 0.12$; ABAS-II: $\eta^2 = 0.11$; BRIEF General Executive Composite: $\eta^2 = 0.09$; SSRS: $\eta^2 = 0.12$) (Table 4).

Predictors of 10-Year Outcomes

Significant, moderate correlations were detected between GCS and PIQ; white matter volume and injury age, FSIQ and PIQ, and for environmental factors: SES, FSIQ, and VIQ; FFQ and FSIQ; and PIQ and SSRS. Preinjury adaptive ability (VABS) was highly correlated with all IQ variables, and ABAS and acute FSIQ scores were robustly related to 10-year outcomes (Tables 5 and 6).

For FSIQ, the regression model was not significant, $F(6,15) = 1.32$, $P = .31$, explaining only 8.3% of variance, with no significant predictors. Similarly, no significant findings were identified for other IQ variables or BRIEF. In each case, the resultant models explained <10% of variance. For ABAS, preinjury VABS contributed to outcome, $\beta = 0.57$, $t = 2.52$, $P = .03$, suggesting that preinjury child function was predictive of 10-year adaptive abilities. SSRS was predicted by FFQ intimacy, $\beta = 0.51$, $t = 2.15$, $P = .05$, providing a link between family function and social/behavioral status.

Recovery Trajectories

Analysis of change in FSIQ from acute to 10 years postinjury found that the only significant effect was for severity [severity: $F(3,52) = 5.29$, $P = .03$; $\eta^2 = 0.23$, time: $F(3,50) = 1.45$, $P = .94$, $\eta^2 = 0.08$] (Table 6). Post hoc analyses revealed differences between control subjects and mild TBI groups ($P = .04$), and control subjects and severe TBI groups ($P < .001$). There was no time by severity interaction, $F(9, 121.84) = 0.39$, $P = .78$, $\eta^2 = 0.02$.

For verbal skills, a main effect for severity was detected, $F(3,52) = 6.37$, $P = .001$, $\eta^2 = 0.27$, with difference between control subjects and all TBI groups (mild: $P = .01$; moderate: $P = .05$; severe: $P < .001$). A main effect was also evident for time, $F(2,51) = 5.66$, $P = .01$, $\eta^2 = 0.18$, with differences between times 2 and 4, $t(58) = -2.49$, $P = .02$ and times 3 and 4, $t(58) = -4.26$, $P < .001$. There was no significant time by severity interaction, $F(6, 102) = 0.66$, $P = .72$, $\eta^2 = 0.03$.

For nonverbal skills, a significant main effect was found for severity [severity: $F(3,52) = 4.29$, $P = .01$, $\eta^2 = 0.19$; time: $F(2,51) = 0.17$, $P = .85$, $\eta^2 = 0.01$], with differences detected between the control and severe TBI groups ($P = .001$). There was no significant interaction, $F(6102) = 0.80$, $P = .57$, $\eta^2 = 0.05$.

DISCUSSION

Consistent with previous literature,[3,7,14,30–34] our results confirmed the importance of injury severity for long-term outcome: young children with severe TBI recorded depressed intellectual abilities at 10 years, with medium to large effect sizes for adaptive, executive, and social abilities suggesting severity effects would be found in a larger sample for those domains as well. Few factors contributed to long-term outcome: preinjury adaptive function was associated with 10-year

TABLE 4 Intellectual, Adaptive, Executive, and Social/Behavioral Outcomes Across Groups at 10 y Post-TBI

	Mild, M (SD)	Moderate, M (SD)	Severe, M (SD)	Control, M (SD)	Significant Group Differences
Intelligence					
FSIQ[a]	98.86 (16.50)	102.40 (16.39)	91.85 (17.32)	112.94 (11.71)	$F(3,56) = 4.63$, $P = .01$, $\eta^2 = 0.21$
VIQ[a]	95.57 (13.48)	103.30 (14.58)	94.92 (16.11)	112.50 (13.10)	$F(3,56) = 4.30$, $P = .01$, $\eta^2 = 0.199$
PIQ[a]	102.86 (21.04)	103.50 (16.68)	89.77 (20.04)	111.56 (21.21)	$F(3,56) = 4.15$, $P = .01$, $\eta^2 = 0.19$
VC Index[a]	97.43 (12.88)	102.50 (16.33)	93.92 (15.15)	112.80 (13.79)	$F(3,56) = 4.04$, $P = .012$, $\eta^2 = 0.192$
PO index[a]	114.57 (20.82)	104.65 (15.78)	92.92 (18.31)	110.87 (13.49)	$F(3,56) = 2.82$, $P = .05$, $\eta^2 = 0.14$
FFD index	88.29 (19.04)	97.25 (19.45)	97.54 (15.65)	108.60 (17.17)	
PS Index[a]	99.29 (14.82)	101.35 (15.88)	88.62 (21.72)	114.80 (17.36)	$F(3,56) = 5.15$, $P = .01$, $\eta^2 = 0.23$
Adaptive behavior					
Conceptual	103.14 (14.98)	96.47 (19.94)	89.00 (14.50)	103.81 (12.49)	
Practical	98.57 (12.88)	92.84 (21.95)	85.82 (22.24)	95.75 (13.44)	
Social	104.71 (11.62)	95.95 (16.60)	89.45 (17.54)	101.25 (12.09)	
Total composite	102.86 (15.26)	94.89 (20.00)	86.00 (19.38)	100.63 (13.32)	
Executive function					
BR Index	57.71 (17.95)	53.58 (15.53)	59.08 (11.74)	48.21 (9.42)	
MC Index	59.57 (12.21)	54.32 (13.74)	58.46 (10.58)	49.71 (11.41)	
GEC	59.29 (14.51)	54.21 (15.10)	59.54 (11.16)	49.07 (10.35)	
Social/behavioral					
Problem behavior	104.57 (19.65)	99.33 (13.05)	105.00 (13.92)	92.79 (8.75)	

BR, behavioral regulation; FFD, freedom from distractibility; GEC, global executive composite; MC, metacognitive; PO, perceptual organization; PS, processing speed.
[a] Significant difference found between groups.

TABLE 5 Pearson Correlations for Outcome Variables and Predictor Variables for the TBI Group

		FSIQ: Time 4	VIQ: Time 4	PIQ: Time 4	BRIEF: Time 4	ABAS: Time 4	SSRS: Time 4
GCS on admission	Pearson	0.306	0.206	0.392	−0.175	0.287	−0.303
	Sig. (2-tailed)	0.055	0.203	0.012	0.286	0.085	0.068
White matter	Pearson	0.343	0.291	0.365	0.021	0.026	−0.035
	Sig. (2-tailed)	0.047	0.095	0.034	0.909	0.889	0.851
Injury age	Pearson	0.052	0.043	0.148	−0.079	0.082	−0.015
	Sig. (2-tailed)	0.749	0.791	0.362	0.633	0.628	0.928
SES: time 1	Pearson	−0.277	−0.333	−0.166	0.186	−0.185	0.146
	Sig. (2-tailed)	0.035	0.011	0.212	0.171	0.176	0.291
FFQ: time 1	Pearson	0.321	0.238	0.350	−0.077	0.063	−0.354
	Sig. (2-tailed)	0.030	0.112	0.017	0.621	0.688	0.020
VABS: time 1	Pearson	0.403	0.431	0.292	−0.150	0.454	−0.255
	Sig. (2-tailed)	0.006	0.003	0.049	0.332	0.002	0.103
FSIQ: time 4	Pearson		0.897	0.907	−0.340	0.509	−0.437
	Sig. (2-tailed)		0.000	0.000	0.010	0.000	0.001
VIQ: time 4	Pearson			0.666	−0.313	0.457	−0.361
	Sig. (2-tailed)			0.000	0.018	0.000	0.007
PIQ: time 4	Pearson				−0.247	0.418	−0.394
	Sig. (2-tailed)				0.064	0.001	0.003
BRIEF: time 4	Pearson					−0.557	0.727
	Sig. (2-tailed)					0.000	0.000
ABAS: time 4	Pearson						−0.494
	Sig. (2-tailed)						0.000

GCS, Glasgow Coma Score.

TABLE 6 Recovery of Intellectual Abilities from Time 1 to Time 4 (Acute to 10 y Post-TB)

	Mild (n = 7)	Moderate (n = 20)	Severe (n = 13)	Control (n = 16)
FSIQ				
Time 1	98.00 (15.70)	103.10 (16.87)	90.77 (23.36)	111.81 (15.64)
Time 2	96.14 (12.25)	103.15 (13.36)	92.31 (15.36)	109.69 (14.26)
Time 3	96.43 (12.11)	100.70 (12.33)	90.85 (15.60)	108.00 (10.11)
Time 4	98.86 (16.50)	102.40 (16.39)	91.85 (17.32)	112.94 (11.71)
VIQ				
Time 2	95.00 (8.33)	101.10 (13.25)	84.00 (28.18)	106.50 (10.59)
Time 3	92.29 (9.83)	98.15 (12.48)	91.00 (12.25)	107.06 (12.25)
Time 4	95.57 (13.48)	103.30 (14.58)	94.92 (16.11)	112.50 (13.10)
PIQ				
Time 2	97.71 (16.88)	104.85 (13.13)	93.69 (18.42)	110.94 (16.67)
Time 3	102.43 (16.68)	103.25 (11.99)	91.08 (17.65)	107.81 (10.48)
Time 4	102.86 (21.04)	103.50 (15.68)	89.77 (20.04)	111.56 (12.21)

adaptive skills, and family function was related to children's social/behavioral skills. A number of robust relationships were found between predictor variables and outcomes, most particularly between preinjury adaptive ability and acute IQ and functional outcomes. Weak but significant correlations were present between nonverbal abilities and injury severity; white matter volume and family function; verbal abilities and SES; and social/behavioral status and family function. Although younger injury age was linked to lower white matter volume, it was unrelated to functional outcomes.

At 10 years, the persisting impact of early TBI remained evident for IQ, with group differences identified on all scores, with the exception of FFD. Children with severe TBI recorded lowest results, with mean IQ scores falling at the lower end of Average or in the Low Average range. Compared with control subjects, mean IQ scores for the severe TBI group were lower by 18 to 26 points (1–2 SD). These findings are in contrast to those reported for adults and school-age children, where IQ is often intact postinjury.[35] For adaptive, executive, and social/behavioral domains, results failed to reach statistical significance, but medium to large effect sizes suggest that, with a larger sample, severity differences would become apparent, and visual inspection indicates the expected dose-response relationship, with more severe injury associated with poorer function.

Predictors of functional outcomes were surprisingly few, with no injury or developmental variable contributing to 10-year scores. Preinjury adaptive function was predictive of 10-year adaptive abilities. Social/behavioral outcomes were predicted by family function, in keeping with previous reports from school-age samples and evaluation more proximal to time of injury.[10,12,15] Apparently, although injury factors, such as severity and brain pathology, are relevant to early outcome, they become less important with time since injury.

Examination of IQ recovery trajectories from acute to 10 years postinjury confirms previous findings that early

injury has long-lasting effects, with no evidence for enhanced recovery or underlying plasticity or cerebral reorganization.[7,8,29,32] Children with severe TBI demonstrated lowest mean scores at all time points on all IQ measures, suggesting that serious TBI in early childhood results in global and persisting intellectual deficits. In addition, the dose-response relationship present early postinjury (more severe injury–poorer function) is maintained over time; however, there was no evidence of severity-related differences in recovery rate.

These results question traditional views of enhanced recovery for the immature brain.[31] Rather, they support animal data showing poorer recovery from diffuse insult in young animals.[31] Equally, these findings are inconsistent with the argument that young children "grow into deficits" through childhood.[32,33] Instead, results suggest an initial, protracted period of disrupted development postinjury in young children, while the brain copes with the impact of injury and begins to recover. After this initial recovery, there may be an opportunity for relatively normal developmental progression, at least from 30 months postinsult (as evidenced by stable age-standardized IQ scores). Although this does not suggest that children "catch up" to peers, it does imply that the gap does not widen during this period.

This study is the first to prospectively follow a substantive sample of very young children over an extended period; however, such longitudinal designs are prone to attrition.[16,17] In this study, the particularly small sample size for the mild TBI group needs to be taken into account when interpreting study findings. To account for the small sample at 10-year follow-up, we have considered effect size as well as traditional *P* values when interpreting our results. However, future studies, recruiting much larger samples, including adequate numbers of children with mild TBI, will be important to increase knowledge. We believe that collection of acute injury and demographic data ensured that we were able to identify sample bias issues, and the single significant bias in our 10-year sample (lower SES in participating versus nonparticipating control subjects) would likely lead to a more conservative interpretation of TBI effects. Inspection of sample characteristics also identified some nonsignificant group differences, which must be considered when interpreting findings. First, the IQ of the 10-year control group was high (112.94). This may be due to a selective participation of high-functioning participants; however, given that this group had similar preinjury IQ levels to TBI groups, it is possible that this higher score represents a practice effect, associated with serial assessments.

Age at injury for the sample ranged from 2 to 7 years. Research from the developmental neurosciences describes rapid brain maturation across this age range,[36,37] paralleling cognitive development,[33] suggesting that age at injury effects may vary across our sample. Although analyses detected no significant impact of injury age on outcome, if these effects are nonlinear, they may be difficult to identify. An additional problem faced by longitudinal child studies, in which age at assessment varies markedly, is the lack of measures covering the age span of interest. To maximize the reliability of our findings, we focused on IQ measures, which have robust psychometric properties but limit our ability to consider recovery trajectories across other functional domains. We were, however, able to assess these domains at 10-year follow-up.

CONCLUSIONS

This study confirms the high risk of persisting functional deficits associated with severe early brain insult but demonstrates an "injury threshold" beneath which children may escape serious sequelae. In contrast to the "severity"-specific recovery observed in acute and subacute periods, findings illustrate that recovery trajectories plateau from 5 to 10 years for all groups, regardless of injury severity. This result is important because it questions previous speculation that children with severe brain insults "grow into deficits" with time since injury. Rather, it appears that, after a protracted recovery period, these children gradually stabilize and begin to make some developmental gains, suggesting that even many years postinsult, intervention may be effective. Finally, we demonstrated that environmental and child factors contributed to recovery at 10 years postinsult. In particular, preinjury function predicted 10-year adaptive abilities, whereas family intimacy was linked to social and behavioral function.

ACKNOWLEDGMENTS

This research was supported by a grant from the Australian National Health and Medical Research Council (Anderson, Catroppa & Rosenfeld) and by the Victorian Government Operational Infrastructure Support Program

REFERENCES

1. Kraus JF. Epidemiological features of brain injury in children. In: Broman SH, Michel ME, eds. *Traumatic Head Injury in Children.* New York, NY: Oxford University Press; 1995:117–146
2. Crowe L, Babl F, Anderson V, Catroppa C. The epidemiology of paediatric head injuries: data

from a referral centre in Victoria, Australia. *J Paediatr Child Health*. 2009;45(6):346–350

3. Anderson V, Catroppa C, Morse S, Haritou F, Rosenfeld JV. Intellectual outcome from preschool traumatic brain injury: a 5-year prospective, longitudinal study. *Pediatrics*. 2009;124(6). Available at: www.pediatrics.org/cgi/content/full/124/6/e1064
4. Jaffe KM, Fay GC, Polissar NL, et al. Severity of pediatric traumatic brain injury and neurobehavioral recovery at one year—a cohort study. *Arch Phys Med Rehabil*. 1993;74(6):587–595
5. Benz B, Ritz A, Kiesow S. Influence of age-related factors on long-term outcome after traumatic brain injury (TBI) in children: a review of recent literature and some preliminary findings. *Restor Neurol Neurosci*. 1999;14(2–3):135–141
6. McKinlay A, Dalrymple-Alford JC, Horwood LJ, Fergusson DM. Long term psychosocial outcomes after mild head injury in early childhood. *J Neurol Neurosurg Psychiatry*. 2002;73(3):281–288
7. Anderson V, Catroppa C, Morse S, Haritou F, Rosenfeld J. Functional plasticity or vulnerability after early brain injury? *Pediatrics*. 2005;116(6):1374–1382
8. Anderson V, Moore C. Age at injury as a predictor of outcome following pediatric head injury. *Child Neuropsychol*. 1995;1(3):187–202
9. Anderson VA, Catroppa C, Dudgeon P, Morse SA, Haritou F, Rosenfeld JV. Understanding predictors of functional recovery and outcome 30 months following early childhood head injury. *Neuropsychology*. 2006;20(1):42–57
10. Catroppa C, Anderson V, Morse S, Haritou F, Rosenfeld J. Outcome and predictors of functional recovery 5 years following pediatric traumatic brain injury (TBI). *J Pediatr Psychol*. 2008;33(7):707–718
11. Taylor HG, Yeates KO, Wade SL, Drotar D, Stancin T, Montpetite M. Long-term educational interventions after traumatic brain injury in children. *Rehabil Psychol*. 2003;48(4):227–236
12. Yeates KO, Taylor HG, Walz NC, Stancin T, Wade SL. The family environment as a moderator of psychosocial outcomes following traumatic brain injury in young children. *Neuropsychology*. 2010;24(3):345–356
13. Yeates KO, Swift E, Taylor HG, et al. Short- and long-term social outcomes following pediatric traumatic brain injury. *J Int Neuropsychol Soc*. 2004;10(3):412–426
14. Anderson VA, Morse SA, Klug G, et al. Predicting recovery from head injury in young children: a prospective analysis. *J Int Neuropsychol Soc*. 1997;3(6):568–580
15. Anderson VA, Morse SA, Catroppa C, Haritou F, Rosenfeld JV. Thirty month outcome from early childhood head injury: a prospective analysis of neurobehavioural recovery. *Brain*. 2004;127(pt 12):2608–2620
16. Ewing-Cobbs L, Barnes M, Fletcher JM, Levin HS, Swank PR, Song J. Modeling of longitudinal academic achievement scores after pediatric traumatic brain injury. *Dev Neuropsychol*. 2004;25(1–2):107–133
17. Yeates KO, Armstrong K, Janusz J, et al. Long-term attention problems in children with traumatic brain injury. *J Am Acad Child Adolesc Psychiatry*. 2005;44(6):574–584
18. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. *Lancet*. 1974;2(7872):81–84
19. Maller JJ, Daskalakis ZJ, Fitzgerald PB. Hippocampal volumetrics in depression: the importance of the posterior tail. *Hippocampus*. 2007;17(11):1023–1027
20. Anderson V, Spencer-Smith M, Leventer R, et al. Childhood brain insult: can age at insult help us predict outcome? *Brain*. 2009;132(pt 1):45–56
21. Daniel A. *Power, Privilege and Prestige: Occupations in Australia*. Melbourne, Australia: Longman-Chesire; 1983
22. Noller P. ICPS Family Functioning Scales. Unpublished manuscript. University of Queensland; 1988.
23. Sparrow S, Balla DA, Cicchetti DV. *Vineland Adaptive Behavior Scales: Interview Edition. Survey Form Manual*. Circle Pines, MN: American Guidance Services; 1984
24. Bayley N. *Bayley Scales of Infant Development: Birth to Two Years*. San Antonio, TX: The Psychological Corporation; 1969
25. Wechsler D. *Manual for the Preschool and Primary Intelligence Scale—Revised*. New York, NY: Psychological Corporation; 1989
26. Wechsler D. *Manual for the Wechsler Scale of Children's Intelligence—III*. New York, NY: Psychological Corporation; 1991
27. Wechsler D. *Manual for the Wechsler Adult Intelligence Scale—III*. New York, NY: Psychological Corporation; 1997
28. Harrison P, Oakland T. *Adaptive Behavior Assessment System*, 2nd ed. New York, NY: Elsevier; 2008
29. Gioia GA, Isquith PK, Guy SC, Kenworthy L. *Behavior Rating Inventory of Executive Function*. Odessa, FL: Psychological Assessment Resources; 2000
30. Taylor HG, Yeates KO, Wade SL, Drotar D, Stancin T, Minich N. A prospective study of short- and long-term outcomes after traumatic brain injury in children: behavior and achievement. *Neuropsychology*. 2002;16(1):15–27
31. Bittigau P, Sifringer M, Pohl D, et al. Apoptotic neurodegeneration following trauma is markedly enhanced in the immature brain. *Ann Neurol*. 1999;45(6):724–735
32. Giza CC, Prins ML. Is being plastic fantastic? Mechanisms of altered plasticity after developmental traumatic brain injury. *Dev Neurosci*. 2006;28(4–5):364–379
33. Dennis M. Language and the young damaged brain. In: Boll T, Bryant BK, eds. *Clinical Neuropsychology and Brain Function: Research, Measurement and Practice*. Washington, DC: American Psychological Association; 1989:85–124
34. Ewing-Cobbs L, Miner ME, Fletcher JM, Levin HS. Intellectual, motor, and language sequelae following closed head injury in infants and preschoolers. *J Pediatr Psychol*. 1989;14(4):531–547
35. Walsh K. *Neuropsychology: A Clinical Approach*. 3rd ed. Edinburgh, Scotland: Churchill; 1985
36. Gogtay N, Giedd JN, Lusk L, et al. Dynamic mapping of human cortical development during childhood through early adulthood. *Proc Natl Acad Sci U S A*. 2004;101(21):8174–8179
37. Giedd JN, Blumenthal J, Jeffries NO, et al. Brain development during childhood and adolescence: a longitudinal MRI study. *Nat Neurosci*. 1999;2(10):861–863

Predictors of Cognitive Function and Recovery 10 Years After Traumatic Brain Injury in Young Children

Vicki Anderson, Celia Godfrey, Jeffrey V. Rosenfeld and Cathy Catroppa

Pediatrics 2012;129;e254
DOI: 10.1542/peds.2011-0311 originally published online January 23, 2012;

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Predictors of Cognitive Function and Recovery 10 Years After Traumatic Brain Injury in Young Children

Vicki Anderson, Celia Godfrey, Jeffrey V. Rosenfeld and Cathy Catroppa

Pediatrics 2012;129;e254
DOI: 10.1542/peds.2011-0311 originally published online January 23, 2012;