Predictors of Personality Change Due to Traumatic Brain Injury in Children and Adolescents Six to Twenty-Four Months After Injury

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Phenomenology and predictive factors of personality change due to traumatic brain injury (TBI) 6 to 24 months after injury was investigated in children, ages 5 to 14 years, enrolled from consecutive admissions and followed prospectively for 2 years. Injury and preinjury psychosocial variables were assessed. Personality change occurred in 13% of participants between 6 and 12 months after injury and 12% in the second year after injury. Severity of injury consistently predicted personality change, and preinjury adaptive function predicted personality change only in the second year postinjury. Lesions of the superior frontal gyrus were associated with personality change between 6 and 12 months following injury, after controlling for severity of injury and the presence of other brain lesions. Only lesions in the frontal lobe white matter were significantly related to personality change in the second year after injury. After childhood TBI, neural correlates of personality change evolve between 6 and 12 months and 12 to 24 months after injury. The data implicate the dorsal prefrontal cortex and frontal lobe white matter in the emergence of personality change involving the effortful or conscious regulation of affective states.

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Personality change due to traumatic brain injury (TBI) is the latest term given to a syndrome which has been recognized in one form or another for hun-

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dreds of years.[1] The current nomenclature established in DSM–IV[2] and was maintained in DSM–IV–TR.[3] The DSM[3] has postulated the existence of five major subtypes of personality change due to TBI that have remained relatively stable for almost 20 years: affective lability, aggression, disinhibited, apathetic, and paranoid. Other terms for the condition or its subtypes have included organic personality syndrome,[4] frontal lobe syndrome,[5] comportmental learning disabilities,[6] acquired sociopathy,[7] posttraumatic chronic behavior disorder,[8] and the regional prefrontal syndromes (e.g., dysexecutive, disinhibited, apathetic types).[1]

Despite the wide recognition of the classical clinical presentation of personality change due to TBI, there has been very little systematic research devoted to clinical predictors and correlates of this syndrome. Until recently, the authors have lacked a research instrument to diagnose the syndrome.[9] Even when single case or small case-series reports have provided information on this condition, the diagnosis has been seldom termed personality change due to TBI.[6,10–12] Prior to our investigations of personality change, there were only two reports of personality change due to traumatic brain injury-type behavior from unselected cohorts of children with TBI.[13,14] These reports together showed that between 16% and 38% of children with severe TBI developed the syndrome.

The authors reported that a persistent form of personality change occurred in 14/37 (38%) of children consecutively hospitalized with severe TBI an average of 2 years after injury.[15] An additional 8/37 (22%) of these children had a transient form of personality change due to TBI suggesting the need to investigate injury and psychosocial factors in personality change outcome. Persistent personality change in those children with severe TBI was significantly associated with severity of injury, adaptive and intellectual functioning deficits, and comorbid diagnosis of secondary attention deficit hyperactivity disorder, although it was not related to psychosocial adversity. Our data provided information about the form of personality change. The affective instability subtype was the most common form of personality change with the aggressive and disinhibited subtypes being the next most common forms. The apathetic and paranoid subtypes occurred infrequently.[16] These findings were based on merged data from a retrospective and prospective study that did not investigate preinjury psychosocial variables.

To expand knowledge of personality change beyond the studies described above, the authors conducted a large prospective study from which the authors report both shorter and longer term outcomes. During the first 6 months after injury, personality change occurred in 31/141 (22%) of children and was related to greater severity of injury although not to any demographic (age, gender, race, socioeconomic status) or preinjury psychosocial variables (family psychiatric history, family function, lifetime psychiatric disorder, adaptive function, psychosocial adversity).[17] Furthermore, lesion analysis based on research protocol MRI scans confirmed our hypothesis of a significant association between lesions of the superior frontal gyrus and personality change even when the presence of "any lesion" and also when severity of injury was controlled for in separate analyses. This was consistent with neuroscience evidence that the dorsal prefrontal region is implicated in states of affective dysregulation.[18]

The present study is concerned with longer-term outcome, from after the first 6 months after injury to 2 years postinjury. The authors hypothesized that 1) personality change would be significantly related to severity of injury and that lesions of the superior frontal gyrus would remain a significant predictor of personality change present between 6 and 12 months and between 12 and 24 months after injury; and 2) In view of the fact that a subgroup of children with personality change experience remission of their syndrome with the progression of time,[15] personality change at the assessments further from the time of injury would be significantly related to measures of preinjury psychosocial function (e.g., socioeconomic status [SES], family psychiatric history, family function, psychosocial adversity, or adaptive function).

METHOD

Participants

The participants consisted of 177 children and adolescents who were consecutively recruited during their initial hospitalization following a TBI at Children's Hospital and Health Center, San Diego, California, The Hospital for Sick Children in Toronto, Ontario, Canada, and one of three academic medical centers in Texas. Children and adolescents with mild to severe TBI were enrolled at all centers except San Diego, California, where recruitment was limited to moderate to severe TBI. Exclusion criteria included preexisting schizophre-

nia or autistic disorder, mental deficiency, and injury due to child abuse or penetrating missile injury. Children in San Diego, California, were excluded if they had attention-deficit/hyperactivity disorder prior to the injury. The parents/guardians of all children signed an informed consent and all children signed an assent to participate in accordance with the Institutional Review Boards at each site. Table 1 shows demographic, injury, and rehabilitation treatment indices for the participants. Data regarding the child's participation in rehabilitation treatment (inpatient or outpatient occupational therapy, physical therapy, sensory-integration therapy, speech and language therapy, and cognitive therapy) were systematically gathered. The authors summarized these data into a single variable indicating the presence or absence of any rehabilitation therapy at any time after injury. Racial classification of participants was as follows: Caucasians: 100 (56.5%); African American: 31 (17.5%); Hispanic: 32 (18.1%); Asian: 5 (2.8%); and Other: 9 (5.1%).

Measures

Psychiatric measures. The Neuropsychiatric Rating Schedule (NPRS)[9] is a semistructured interview designed to identify subtypes of personality change. Both parents and children served as informants in the interview that took place at baseline (soon after injury), and at 12, and 24 months after injury. The baseline assessment evaluated lifetime preinjury psychiatric history, the 6-month assessment rated the period from injury to 6 months, the 12-month assessment rated the period from 6 months to 12 months, and the 24-month assessment rated the period 12 months to 24 months. The NPRS interview defined the presence of the five major subtypes (labile, aggressive, disinhibited, apathetic, and paranoid) of personality change. The authors specifically waived the 1-year duration of symptomatology criterion to allow us to monitor the course of the disorder and to assess for lesion correlates for the behaviors of interest. The instrument has been shown to provide reliable and valid diagnoses of the common subtypes of personality change.[9] Interrater agreement for NPRS items is fair to excellent, test-retest reliability is fair to good and sensitivity to change has been demonstrated. Good convergent validity as well as discriminant validity has been demonstrated for personality change subtypes.[9]

Other DSM–IV psychiatric diagnoses[2] were derived by utilizing a semistructured interview, the Schedule for Affective Disorders and Schizophrenia for school-age children, present and lifetime version (K-SADS-PL).[19] The K-SADS-PL is an integrated parent–child interview, which generates diagnoses based on a clinician synthesizing data collected from parent and child separately, querying present and lifetime symptoms (at baseline)

TABLE 1. Demographic, Psychosocial, and Lesion Data of Traumatic Brain Injury Cohort (N = 177)

Demographic Variables		**N**
Age at injury mean (SD)	10.13 (2.77)	177
Gender: males (%)	125 (71%)	177
Socioeconomic Status mean (SD)	37.01 (12.90)	173
Psychosocial Variables		
Pre-injury Vineland Adaptive Behavior Composite Standard Score (mean; SD)	94.37 (15.43)	165
Pre-injury Psychosocial Adversity mean (SD)	0.82 (0.95)	165
Pre-injury Family Functioning mean (SD)	1.62 (0.47)	160
Family Psychiatric History mean (SD)	1.15 (1.07)	135
Pre-injury lifetime psychiatric disorder number (%)	56 (31.6%)	177
Injury Variables		
Lowest post-resuscitation GCS Score mean (SD)	10.85 (4.20)	177
Mechanism of Injury (N = 177)		N (%)
Hit by motor vehicle		49 (27.7)
Fall		41 (23.2)
Auto, truck, bus passenger		40 (22.6)
Sports or play		15 (8.5)
Recreational vehicle/Off-road vehicle		10 (5.6)
Bicycle		9 (5.1)
Motorcycle-moped		5 (2.8)
Hit by a falling object		5 (2.8)
Assaulted		1 (0.6)
Other		2 (1.1)
Rehabilitation Therapy		
Participated in any rehabilitation therapy		85 (48)

and symptoms present or past within the interval since the previous assessment (e.g., 12-month assessment covers symptomatology from 6 months to 12 months; and 24-month assessment covers symptomatology from 12 months to 24 months).

The interviewer generated best-estimate psychiatric diagnoses[20] after integrating the reports of the parent and the child from the NPRS and the K-SADS interviews and, when available, from the Survey Diagnostic Instrument[21] that the child's teacher completed.

Predictive Variables

Neurological assessments. The lowest postresuscitation score on the Glasgow Coma Scale (GCS)[22] which was recorded from clinical notes was the measure used to reflect severity of TBI. The GCS is the standard measure of severity of acute brain injury associated with closed head trauma. The scale measures eye opening, motor, and verbal responsiveness. Scores range from 3 (unresponsive) to 15 (normal).

MRI was conducted in most subjects 3 months after the injury. The protocol included a T1 volumetric spoiled gradient recalled echo (SPGR) and fluid attenuated-inversion recovery (FLAIR) sequences, acquired in coronal and sagittal planes according to a research protocol. Project neuroradiologists at each site coded lesion location. A total of 151 of the 177 enrolled children (85%) completed their follow up research MRI. Lesion data are available for 94% of children studied at 12 months (118/125) and 24 months (93/99) after injury. The distribution of lesions in children who completed the research MRI is shown on the left side of Table 2.

Family psychiatric history. The Family History Research Diagnostic Criteria[23] interview was conducted by trained research assistants at each site. Criteria were modified to conform to DSM–IV criteria. At least one parent acted as the informant and was questioned about psychiatric disorders in each first-degree relative of the index child with TBI. Family ratings were then summarized for first degree relatives on a four-point scale[24] of increasing severity.

Family assessments. Global family functioning was assessed by using the Family Assessment Device general functioning scale based on the McMaster Model of Family Functioning.[25] The scale consists of 12 items in the format of a self-report questionnaire. The primary caretaker of each child responded to each item on a 4-point Likert scale. Scores range from 1 to 4 with lower scores represent healthier functioning.

Socioeconomic status. SES assessment was measured with the Four Factor Index.[26] Classification depends on scores derived from a formula involving both maternal and paternal occupational and educational levels. Scores range from 8 to 66 with higher scores indicating higher occupational and educational levels and higher SES.

Psychosocial adversity measure. The authors used a psychosocial adversity index that was similar to that used in a pioneering study of pediatric TBI.[13] Six areas were assessed. For each area with evidence of adversity a score of 1 was given and a score of 0 was given where there was no adversity. The areas are 1) child not living with biological or adoptive parents; 2) sibship of at least 4 children or a person:room ratio exceeding 1; 3) admission of the child into the care of the local authority because of family difficulties; 4) maternal "malaise inventory" score of 7 or more; 5) paternal criminality; and 6) father or mother with an unskilled or semiskilled job.

Adaptive functioning measure. Preinjury adaptive functioning was retrospectively assessed shortly after the injury using the Vineland Adaptive Behavior Scale interview.[27] This involved a semistructured interview of the primary caretaker conducted by a trained research assistant.

Enrollment. One hundred seventy-seven subjects who were enrolled in the study had a baseline psychiatric interview. Demographic details (age, gender, race, SES), injury indices (GCS scores, lesion distribution), and preinjury psychosocial variables (adaptive functioning, psychosocial adversity, family functioning scores, family psychiatric history ratings, preinjury lifetime psychiatric status) are provided in Table 1 and 2. Preinjury adaptive functioning indexed by the Vineland adaptive behavior composite was unrelated to the family psychiatric history rating but was significantly related to the presence versus absence of a preinjury lifetime psychiatric disorder (88.5 [SD = 15.1] [N = 55] versus 97.3 [SD = 14.8] [N = 110]; $t = 3.56$, $df = 163$, $p < 0.0005$).

Statistical Analyses

The association of each of the potentially predictive demographic (age at injury, gender, race, SES), preinjury

psychosocial (adaptive functioning, psychosocial adversity, preinjury lifetime psychiatric status, family psychiatric history ratings, family functioning scores), and severity of injury (GCS scores) variables of personality change was tested at both assessment points (12 and 24 months) by independent sample t tests or χ^2 analyses as appropriate. Variables that were associated at a significant ($p<0.05$) or trend level ($p<0.10$) were then entered in a logistic regression analysis to assess the independent contribution of each variable in accounting for the diagnosis of personality change.

A second series of analyses focused on lesion correlates of personality change at 12 months and also at 24 months after injury. The authors conducted univariate χ^2 analyses to assess the relationship between personality change and 8 to 9 gray matter lesioned regions, and 1 to 2 white matter lesioned regions depending on occasion (12 or 24 months). Only regions which were lesioned in 5 or more children who returned for their assessments were tested for this association. For each specific lesioned region that was significantly associated with personality change ($p<0.05$), the authors conducted a logistic regression analysis controlling for the "presence of any lesion" to determine whether there was an independent association with that specific lesioned region and personality change. All of the specific lesions that remained significantly associated with personality change in each of these regressions were placed together in another logistic regression analysis to determine their relative importance in accounting for personality change.

Finally the authors built upon the first two series of analyses to investigate the relative contribution of demographic, psychosocial, and severity of injury variables (first series of analyses) and specific lesion variables (second series of analyses) to predict the presence of personality change at each assessment. This was accomplished with a logistic regression analysis that included only the significant variable(s) from the regression in the first series of analyses and the significant variable(s) that emerged from last regression in the second series of analyses (lesioned regions with significant independent prediction of personality change).

RESULTS

Occurrence

The presence of personality change and its specific subtypes at both assessments is presented in Table 3. In addition the authors have included personality change

TABLE 2. Lesion Distribution in Entire Cohort (n = 151) and According to Presence of Personality Change During Follow Up Epochs

	Entire Cohort	12-Month Assessment			24-Month Assessment		
	n = 151	Personality Change (n = 15) N (%)	No Personality Change (n = 103) N (%)	sig	Personality Change (n = 11) N (%)	No Personality Change (n = 82) N (%)	sig
Any Lesion	108 (71.5)	12 (80%)	70 (68%)	ns	9 (82%)	58 (71%)	ns
Frontal Lobe							
Frontal Lobe White Matter	33 (21.9)	4 (27%)	17 (17%)	ns	6 (55%)	13 (16%)	0.008
Superior Frontal Gyrus	29 (19.2)	8 (53%)	14 (14%)	0.001	1 (9%)	14 (17%)	ns
Middle Frontal Gyrus	22 (14.6)	1 (7%)	18 (18%)	ns	2 (18%)	14 (17%)	ns
Inferior Frontal Gyrus	32 (21.2)	5 (33%)	18 (18%)	ns	3 (27%)	15 (18%)	ns
Cingulate Gyrus	1 (0.7)						
Orbital Gyrus	9 (6.0)	3 (20%)	3 (3%)	0.027	0 (0%)	5 (6%)	ns
Rectal Gyrus	19 (12.6)	4 (27%)	10 (10%)	ns	1 (9%)	11 (13%)	ns
Operculum	1 (0.7)						
Temporal Lobe	36 (23.8)	4 (27%)	26 (25%)	ns	3 (27%)	15 (18%)	ns
Parietal Lobe	33 (21.9)	2 (13%)	21 (20%)	ns	3 (27%)	17 (21%)	ns
Occipital Lobe	13 (8.6)	3 (20%)	5 (5%)	ns	1 (9%)	4 (5%)	ns
Basal Ganglia	10 (6.6)	1 (7%)	5 (5%)	ns			
Corpus Callosum: Anterior	3 (2.0)						
Mid	5 (3.3)						
Posterior	9 (6.0)	2 (13%)	3 (3%)	ns			
Thalamus	5 (3.3)						
Peduncles	1 (0.7)						
Midbrain	1 (0.7)						
Medulla	1 (0.7)						
Cerebellum Hemisphere	6 (4.0)						
Internal Capsule	4 (2.6)						
External Capsule	1 (0.7)						

that had been documented in the first 6 months after injury[17] to illustrate the course of personality change from the time of injury. The specific lesion distribution in each child with personality change at any point in the first 2 years after TBI is displayed in Table 4.

12-Month assessment. One child had a second TBI between the 6- and 12-month assessments that made her ineligible for these analyses. One hundred twenty-five of the remaining 176 children (71%) returned for the 12-month psychiatric assessment. Termination of the funding cycle accounted for 9 of the children who did not return, therefore effective participation was 125/167 (75%). The returning group was not significantly different from the children who did not return in age, gender, GCS score, lesion distribution, SES, psychosocial adversity, or preinjury Vineland adaptive behavior composite. More males than females did not return (42/125 males versus 9/51 females; Fisher's exact test = 0.024) and more African American children did not return compared with children of other races (there were 15 African Americans of a total of 51 children who did not return versus 16 African Americans of 125 children who did return; Fisher's exact test = 0.015). Personality change occurred in 16/125 (13%) children at some point between the 6-month and 12-month assessments. Personality change had already resolved in 6 of these 16 children by 12 months post injury. The most common presentation was the affective lability subtype (13 children, including 3 children with resolution of symptoms), followed by the aggressive subtype (7 children, including 5 children with resolution of symptoms), dis-

TABLE 3. Course of Personality Change by Subtype in Traumatic Brain Injury Cohort

Subject	6 Months (n = 31)	12 Months (n = 16)	24 Months (n = 12)
1	AIp	0	0
2	0	0	AG
3	AI/DISp	ND	ND
4	AI/AP	PAR/AI	ND
5	AI/AG/DIS	AI	ND
6	AIp	0	ND
7	ND	0	AI/DIS
8	AI/AG/AP	AIp/AGp/APp	AI/DIS
9	AI/DIS	0	AI/DIS
10	AI/DISp	0	ND
11	AI/AG	ND	AI/AG
12	AI/DISp/AP	AI/DIS	ND
13	AIp	AI/DIS	ND
14	0	AI	ND
15	AI/AG/DIS/AP	ND	ND
16	AIp/APp	ND	ND
17	AI/AG/DIS	ND	ND
18	AG	AGp	0
19	AI/AG	AIp/AGp	0
20	AI/AG	0	0
21	AI	ND	ND
22	AGp/DISp	0	0
23	AG	AI/AG	AI/AG
24	AI/AG	0	0
25	AI/AG	AGp	0
26	AI	0	0
27	AI	AI/DIS	AI/DISp
28	AI/AG/DIS	PAR/AI/AGp/DIS	PARp/0
29	AI/DIS	DISp	0
30	AI	AI	0
31	DIS	ND	ND
32	AI/AG	0	AI
33	ND	0	AI/AGp
34	0	0	AI
35	ND	AIp	AI
36	0	0	AI
37	AI/DIS/AP	AI/AG/DIS/AP	ND
38	AI	ND	ND

ND = no data; Subj = subject; 0 = no PC, AI = PC, affective instability subtype, AG = PC, aggression subtype, DIS = PC, disinhibited subtype, AP = PC, apathy subtype, PAR = PC, paranoid subtype, p = past/resolved

inhibited subtype (6 children, including 1 child with resolution of symptoms), apathetic subtype (2 children including 1 child with resolution of symptoms), and paranoid subtype (1 child with resolution of symptoms).

Personality change was significantly associated with the following other new onset disorders between 6 and 12 months after injury: 1) new-onset attention-deficit/hyperactivity disorder was present in 5/13 children with personality change versus 10/90 children with no personality change; Fisher's exact test = 0.021; 2) new-onset oppositional defiant disorder/conduct disorder/disruptive behavior disorder, not otherwise specified (ODD/CD/DBD) was present in 3/15 children with personality change versus 4/105 with no personality change; Fisher's exact test = 0.041; 3) new-onset depressive disorder (major depression/dysthymic disorder/depressive disorder, not otherwise specified) was present in 4/15 children with personality change versus 4/108 children with no personality change; Fisher's exact test = 0.008; and 4) new onset anxiety disorder (simple phobia, social phobia, panic disorder, obsessive-compulsive disorder, separation anxiety disorder, or posttraumatic stress disorder) was present in 5/16 children with personality change versus 8/109 with no personality change; Fisher's exact test = 0.013.

Children who presented with personality change be-

TABLE 4. Lesion Distribution Data for Children With Personality Change at Any Point Postinjury

Subject	0	FW	SF	MF	IF	OG	RG	OP	TL	PL	OL	BG	AC	MC	PCC	TH
1		X	X				X									
2	X															
3[1]		X										X				
4			X													
5			X						X							
6[2]					X				X			X		X	X	
7		X														
8		X			X				X					X		
9[3]		X							X	X	X					
10		X	X		X				X		X					
11		X														
12		X	X		X				X	X	X					
13	X															
14		X	X		X	X	X		X		X				X	
15[4]		X			X				X	X	X				X	
16		X	X		X				X	X	X					
17			X													
18						X	X									
19			X				X									
20										X						
21				X	X					X						
22[5]																
23	X															
24									X	X					X	
25[6]			X	X												
26												X				
27*																
28	X															
29			X		X							X				
30		X	X		X		X			X	X			X	X	
31[7]			X		X						X			X	X	X
32		X														
33				X	X		X	X	X	X		X				
34		X	X	X	X					X						
35[8]									X							
36													X			
37[9]						X										
38		X											X			

0 = no lesion, AC = anterior corpus callosum, BG = basal ganglia, FW = frontal lobe white matter, IF = inferior frontal gyrus, MC = mid corpus callosum, MF = middle frontal gyrus, OG = orbital gyrus, OL = occipital lobe, OP = operculum, PCC = posterior corpus callosum, PL = parietal lobe, RG = rectal gyrus, SF = superior frontal gyrus, TH = thalamus, TL = temporal lobe.

*no research MRI; [1]subject also displays lesions in the lateral ventricle, [2]subject also displays lesions in the internal capsule, [3]subject also displays lesions in the lateral ventricle and internal capsule, [4]subject also displays a cerebellar hemisphere lesion, [5]subject displays lesions in the subdural space, [6]subject also displays lesions in the external capsule, [7]subject also displays lesions in the midbrain, cerebellum hemisphere, cerebellum vermis, and subdural space, [8]subject also displays lesions in the epidural space, [9]subject also displays lesions in the epidural space.

tween 6 and 12 months postinjury were significantly more likely than those with no personality change to have participated in a form of rehabilitation therapy at some point after injury (12/16 versus 44/109; Fisher's exact test = 0.014). This was probably due to the recognition by clinicians of other specific deficits in these children.

Table 5 presents data on the variables tested as potential predictors of the development of personality change during the period 6 to 12 months after TBI. Compared to those who did not develop personality change, children who developed personality change had more severe injuries, as indexed by the lowest postresuscitation GCS score. There was a trend for children with greater psychosocial adversity scores to develop personality change. Personality change was not associated with age at injury, gender, SES, family psychiatric history, preinjury family function, preinjury adaptive function, or preinjury lifetime psychiatric disorder. A logistic regression analysis which included the variables associated with personality change at least at a trend level was significant (-2 log likelihood $\chi^2 = 8.83$, df = 2, $p<0.02$) and correctly classified 87% of children with personality change. However, only the lowest postresuscitation GCS score was significant (Wald $\chi^2 = 5.39$, df = 1, $p<0.03$) while psychosocial adversity was not in terms of unique contribution to this association.

Lesion correlates of personality change at 12 months. Personality change present between 6 and 12 months after injury was significantly associated with lesions within the superior frontal gyrus and the orbital gyrus (Table 2). These 2 associated areas were reanalyzed in the form of 2 separate logistic regression analyses controlling for the presence of "any" lesion. The regression with the superior frontal gyrus and the presence of "any" lesion was significant (-2 log likelihood $\chi^2 = 11.00$, df = 2, $p = 0.0041$) explaining 87% of cases correctly, and only the superior frontal gyrus (Wald $\chi^2 = 9.31$, df = 1, $p<0.003$) remained significant in accounting for personality change. The regression with orbital frontal gyrus and the presence of "any" lesion was not significant.

Personality change at 12 months: combining demographic/psychosocial/injury severity predictors with specific lesion predictors. The final analysis conducted brought together the broader analysis of demographic, psychosocial, and injury severity as predictors of personality change with the narrower specific lesion-behavior analyses as predictors of personality change. Thus, the lowest postresuscitation GCS score and the superior frontal gyrus lesion variable were entered in a logistic regression analysis with personality change at the 12-month assessment as the dependent variable. The regression was significant (2 log likelihood $\chi^2 = 15.39$, df = 2, $p = 0.0005$) and correctly classified 87% of the cases. Both lowest postresuscitation GCS score (Wald $\chi^2 = 4.26$, df = 1, $p<0.04$) and presence of a superior frontal gyrus lesion (Wald $\chi^2 = 8.42$, df = 1, $p<0.004$) significantly and independently accounted for personality change.

24-Month assessment. Ninety-nine of the eligible 176 children (56%) returned for the 24-month psychiatric assessment. Termination of the funding cycle accounted for 41 children who did not return. Therefore effective participation was 99/135 (73%). The returning group was not significantly different from the children who did not return in age, gender, GCS score, lesion distribution, SES, psychosocial adversity, or preinjury Vineland adaptive behavior composite. However, significantly more African American children did not return compared with children of other races (there were 19 African Americans of a total of 77 children who did not return versus 12 African Americans of 99 children who

TABLE 5. Predictors of Personality Change Due to Traumatic Brain Injury 6 to 12 Months Postinjury

	Personality Change (n = 16)	No Personality Change (n = 109)	t	df	*sig*
Demographic Variables					
Age at injury mean (SD)	9.9 (2.5)	10.0 (2.8)	0.15	123	ns
Gender: males (%)	10 (63%)	73 (67%)		1	ns
Socioeconomic Status mean (SD)	32.7 (11.1)	37.8 (12.9) n = 106	1.51	121	ns
Psychosocial Variables					
Pre-injury lifetime psychiatric disorder number (%)	4 (25%)	29 (27%)		1	ns
Pre-injury Vineland ABC Standard Score (mean; SD)	95.6 (14.4) n = 14	95.2 (14.6) n = 104	−0.11	116	ns
Pre-injury Family Functioning mean (SD)	20.8 (6.6) n = 14	19.4 (5.8) n = 101	−0.82	113	ns
Family Psychiatric History mean (SD)	1.5 (1.1) n = 10	1.2 (1.1) n = 92	−0.96	100	ns
Pre-injury Psychosocial Adversity mean (SD)	1.3 (1.2) n = 15	0.8 (1.0) n = 106	−1.88	119	0.063
Injury Variables					
Lowest post-resuscitation GCS Score mean (SD)	8.6 (3.7)	11.3 (4.1)	2.47	123	0.015

did return; Fisher's exact test = 0.045). Personality change occurred in 12/99 (12%) children at some point between the 12-month and 24-month assessment and in no cases did all subtypes that were present in individual children with personality change completely resolve, although 2 children each had resolution of one of their personality change subtypes. Similar to the earlier assessments, the most common presentation was the affective lability subtype (11 children), followed by the aggressive subtype (4 children including 1 child with resolution of symptoms), disinhibited subtype (4 children including 1 child with resolution of symptoms). Neither the apathetic subtype nor the paranoid subtype was present in the 2nd year after TBI in this cohort.

Personality change was significantly associated with the following other new onset disorders between 12 and 24 months after injury: 1) new-onset attention-deficit/hyperactivity disorder was present in 6/10 children with personality change versus 11/72 children with no personality change; Fisher's exact test = 0.004; 2) new-onset ODD/CD/DBD was present in 6/10 children with personality change versus 4/85 with no personality change; Fisher's exact test = 0.000; 3) new-onset depressive disorder was present in 4/11 children with personality change versus 4/85 children with no personality change; Fisher's exact test = 0.005; and 4) new onset anxiety disorder was present in 3/12 children with personality change versus 2/87 with no personality change; Fisher's exact test = 0.012.

Personality change that presented in children between 12 and 24 months postinjury was not significantly associated with a history of participating in rehabilitation therapy after the injury.

Table 6 presents data on the variables tested as potential predictors of the development of personality change during the second year after TBI. Compared to those who did not develop personality change, children who developed personality change had more severe injury, as indexed by the lowest postresuscitation GCS score. In addition children with lower preinjury adaptive function (adaptive behavior composite) were more likely to manifest personality change. Personality change was not associated with age at injury, gender, family psychiatric history, psychosocial adversity, SES, preinjury family function, or preinjury lifetime psychiatric disorder. A logistic regression analysis which included the variables associated with personality change at least at a trend level was significant (-2 log likelihood χ^2 = 11.57, df = 2, $p<0.004$) and correctly classified 91% of children with personality change. Both the lowest postresuscitation GCS score (Wald χ^2 = 6.28, df = 1, $p<0.02$) and the Vineland adaptive behavior composite were significant (Wald χ^2 = 4.10, df = 1, $p<0.05$) in terms of unique contribution to this association. Because the Vineland adaptive behavior composite was significantly related to personality change, the authors conducted exploratory analyses to determine which more specific aspects of preinjury adaptive function (socialization, communication, or daily living skills) accounted for this finding. Results showed that the preinjury socialization domain was the only domain in which standard scores were significantly lower in children who did versus those who did not develop personality change (86.6 [SD = 16.1] versus 97.8 [SD = 14.1]; t = 2.43, df = 93, p = 0.017).

Lesion correlates of personality change at 24 months. Personality change present between 12 and 24 months after injury was significantly associated with lesions within the frontal white matter (Table 2). This associated area was reanalyzed in a separate logistic regression analysis controlling for the presence of "any" lesion. The regression was significant (-2 log likelihood χ^2 = 7.36, df = 2, p = 0.0252) explaining 88% of cases correctly, and

TABLE 6. Predictors of Personality Change Due to Traumatic Brain Injury in the 12 to 24 Months Postinjury

	Personality Change (n = 12)	No Personality Change (n = 87)	t	df	*sig*
Demographic Variables					
Age at injury mean (SD)	10.1 (2.8)	9.9 (2.8)	−0.17	97	ns
Gender: males (%)	8 (67%)	57 (64%)		1	ns
Socioeconomic Status mean (SD)	30.9 (11.3) n = 11	36.9 (12.7)	1.51	96	ns
Psychosocial Variables					
Pre-injury lifetime psychiatric disorder number (%)	3 (25%)	27 (31%)		1	ns
Pre-injury Vineland ABC Standard Score (mean; SD)	86.8 (15.4) n = 11	97.0 (15.1) n = 84	2.09	93	0.039
Pre-injury Family Functioning mean (SD)	21.7 (4.4) n = 10	19.4 (6.0) n = 83	−1.15	91	ns
Family Psychiatric History mean (SD)	0.6 (0.7) n = 8	1.3 (1.1) n = 81	1.57	87	ns
Pre-injury Psychosocial Adversity mean (SD)	1.1 (0.5) n = 11	0.9 (1.1) n = 84	−0.70	93	ns
Injury Variables					
Lowest postresuscitation GCS Score mean (SD)	8.8 (4.7)	11.5 (3.9)	2.22	97	0.029

only the frontal white matter (Wald $\chi^2 = 6.25$, df = 1, $p<0.02$) remained significant in accounting for personality change.

DISCUSSION

Personality change is a relatively common complication of head trauma in children. The new pieces of information in this article are that the occurrence of personality change evolves over time after childhood TBI; that injury severity and the presence of dorsal frontal damage increase the occurrence of personality change, and that preinjury adaptive function is a predictor of long-term personality change.

The occurrence of personality change declined from the first 6 months after injury from 22% to a relatively stable rate of 12–13% from 6–12 to 12–24 months post injury. As in our previous study[15,16] and the 6 month follow up from this same cohort,[17] affective instability remained the most common subtype of the disorder, followed by the aggressive subtype and the disinhibited subtype. The apathetic and paranoid subtypes were rare and tended to resolve for unclear reasons. Personality change is significantly comorbid with several categories of new-onset psychiatric disorders including externalizing disorders (i.e., disruptive behavior disorders) and internalizing disorders (i.e., mood or anxiety disorders). This pattern of multiple comorbid diagnoses typically reflects increasingly severe psychopathology in psychiatric studies of children.[28]

Severity of injury was a consistent predictor of personality change during both follow up intervals. This effect is consistent with previous findings[15] and supports the validity of the diagnosis which is one of the few DSM–IV diagnoses which by definition is linked to a specific cause.

Not only was injury severity a predictor of personality change, but a more specific characterization of the pattern of the injury added to the predictive utility of injury indices. Indeed, the authors found, as hypothesized, that lesions within the superior frontal gyrus predicted personality change between 6 and 12 months post injury. Furthermore, this specific lesion predictor contributed independently with regard to severity of injury to the prediction of personality change which result is similar to our earlier finding for personality change presenting between injury and 6 months post injury.[17]

The finding that frontal lesions are involved in the generation of personality change is consistent with models of affective regulation developed to explain the pathophysiology of depression.[29,30] In these models, the dorsal frontal system, which includes dorsolateral prefrontal cortex, dorsomedial prefrontal cortex, dorsal anterior cingulate gyrus, and hippocampus, is important for effortful regulation of affective states resulting from the activity of the ventral system. The ventral neural system, which includes amygdala, insula, ventrolateral prefrontal cortex, orbitofrontal cortex, ventral anterior cingulate gyrus, thalamus, ventral striatum, and brainstem nuclei, is necessary for the identification of the emotional significance of environmental stimuli, and the production of affective states. The ventral system is also important for regulation and mediation of autonomic responses to emotional stimuli and contexts accompanying the production of affective states. In personality change associated with superior frontal gyrus injury, the complex interconnectivity between the dorsal and ventral systems is likely disrupted such that affective states produced by the ventral system cannot be sufficiently regulated by the dorsal neural network.

The finding that preinjury adaptive function predicted personality change at the 2-year assessment is new and suggests that even in this disorder, the behavioral manifestations of which are classically associated with the direct effect of brain damage, preinjury personal characteristics of the child may influence outcome. The design of our previous study (based on a combined sample of children prospectively and retrospectively recruited) precluded the investigation of preinjury psychosocial variables as potential predictors of personality change but as in the present study showed that severity of injury remained a significant predictor of personality change approximately 2 years after TBI. A possible explanation for this finding is that with the process of recovery, preinjury brain reserve[31] or previously learned socialization and broader adaptive behavior skills reemerge more readily, albeit belatedly, to result in improved modulation of affect, aggression, and disinhibited behavior. Another possible explanation is that measures of preinjury adaptation may be markers of the ability to relearn inhibitory control and modulate affect. Preinjury psychosocial variables commonly influence early and later behavioral outcome,[13,32,33] therefore the delayed emergence of significance for preinjury adaptive function (in this instance) may serve to emphasize

the close relationship of personality change to injury variables early in the follow up.

Another change in the pattern of predictors of personality change with the extended follow up was the emerging relationship with frontal white matter lesions and the loss of the relationship with superior frontal gyrus lesions. Closer review of the data shows that a number of children with personality change and superior frontal gyrus lesions experienced resolution of their personality change in the second year of follow up. However, there were also a number of children with personality change and superior frontal gyrus lesions whose data were missing at extended follow up. It is not possible to know how this may have affected the findings. The authors have shown that there was no association between superior frontal gyrus lesions and lack of follow up in the second year. Where possible, related neural structures might have subsumed the function of affective regulation, a process that was limited by severity of injury and diffuse axonal injury particularly in the frontal lobe. Frontal white matter is important in many cortical networks, and diffuse injury results in a less efficient and relatively less connected complex of neural systems.[34] More broadly, the data underscore the relevance of white matter damage to many adverse outcomes in childhood disorders of brain and behavior.

Our data on childhood TBI are both similar to and different from findings of a comparable study of adult TBI[35] in which aggression in adults was associated with preinjury personal psychiatric and behavioral history in terms of a higher rate of alcohol abuse, drug abuse, mood disorder, and legal interventions for aggressive behavior. However, preinjury personal history was evident as a predictive factor at the earliest points in follow-up in adults, in contrast to the delayed emergence of this factor (preinjury adaptive function but not preinjury psychiatric disorder indices) in children. Unlike the data in children, aggression in adults was not associated with severity of injury. The difference may be partly explained by the fact that the aggression ratings in the adults were postinjury scores and did not capture change from before injury, whereas personality change was diagnosed in the children only if the syndrome was a change from before injury.

The findings of this study must be considered within its limitations. Interrater reliability assessments for the diagnosis of personality change were not directly tested based on videotaped interviews. However, the child psychiatrists or psychologists at each site closely supervised the assessments; and, further, fidelity in diagnosis was maintained across sites by frequent telephone conferences and transmission of written summaries of psychiatric assessments that were critiqued by the first author and other interviewers, resulting in a consensus diagnosis. The image analysis did not employ volumetric measurements that might have more clearly delineated lesion correlates of personality change. However, the images themselves were of research quality required for such volumetric assessments that allowed project neuroradiologists to document even very small lesions. As in many long-term follow-up studies, attrition was notable yet remained stable between 25% and 27% at the 12-month and 24-month follow up assessment. Overall there were few demographic (e.g., African American children), psychosocial, or injury variables upon which the children who did not return differed from those who returned. While our hypotheses did not call for an orthopedic injury comparison group, such a group could control for new onset emotional lability in children predisposed to and exposed to injuries.

The study had a number of notable strengths. This is the largest prospective child TBI psychiatric interview study of a consecutively admitted nonreferred population. The breadth and depth of assessments were extensive and included interview assessments of psychopathology, adaptive function, and family psychiatric history, in addition to rating scales encompassing injury and other psychosocial risk factors for new onset psychiatric disorder. Furthermore, lesion analysis was based on readings by expert neuroradiologists. Importantly, relationships were not simply described but were explored in regression models.

CONCLUSIONS AND CLINICAL IMPLICATIONS

Personality change is a relatively common and critically important syndrome that complicates pediatric TBI. This article extends our previous findings on the predictors of personality change beyond the first 6 months after injury to 2 years postinjury. There is a consistent relationship of personality change to severity of injury. Specific lesion correlates of personality change include superior frontal gyrus lesions in the first postinjury year and this is compatible with models of affective regulation. Personality change in the second postinjury year is related to severity of injury, diffuse frontal lobe white matter lesions and presumed resultant disrupted neu-

ronal connectivity, in addition to preinjury adaptive function. Controlled pharmacological and psychosocial treatment trials are lacking and are needed to positively influence the course of this syndrome.

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