Traumatic brain injury in children

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CHAPTER 5

FEEDBACK LEARNING AND BEHAVIOR PROBLEMS AFTER PEDIATRIC TRAUMATIC BRAIN INJURY

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ABSTRACT

BACKGROUND

Feedback learning is essential for behavioral development. This study investigated feedback learning in relation to behavior problems after pediatric traumatic brain injury (TBI).

METHODS

Children aged 6-13 years diagnosed with TBI (n = 112; 1.7 years post-injury) were compared to children with traumatic control (TC) injury (n = 52). TBI severity was defined as mild TBI without risk factors for complicated TBI (mild^{RF-} TBI, n = 24), mild TBI with ≥ 1 risk factor for complicated TBI (mild^{RF+} TBI, n = 51) and moderate/severe TBI (n = 37). The Probabilistic Learning Test was used to measure feedback learning, assessing the *effects of inconsistent feedback on learning* and *generalization of learning* from the learning context to novel contexts. The relation between feedback learning and behavioral functioning rated by parents and teachers was explored.

RESULTS

No evidence was found for an effect of TBI on learning from inconsistent feedback, while the moderate/severe TBI group showed impaired *generalization of learning* from the learning context to novel contexts (p = .03, d = -0.51). Furthermore, the mild^{RF+} TBI and moderate/severe TBI groups had higher parent and teacher ratings of internalizing problems (ps ≤ .04. ds ≥ 0.47) than the TC group, while the moderate/severe TBI group also had higher parent ratings of externalizing problems (p = .006, d = 0.58). Importantly, poorer *generalization of learning* predicted higher parent ratings of externalizing problems in children with TBI (β = -.21, p = .03) and had diagnostic utility for the identification of children with TBI and clinically significant externalizing behavior problems (area under the curve = .77, p = .001).

CONCLUSIONS

Moderate/severe pediatric TBI negatively impacts *generalization of learning*, which may contribute to post-injury externalizing problems.

INTRODUCTION

Worldwide an estimated 54-60 million individuals sustain traumatic brain injury (TBI) each year (Feigin et al., 2013). Children with moderate or severe TBI have persisting neurocognitive impairments (Babikian & Asarnow, 2009), which are thought to contribute to disabling behavior problems (Li & Liu, 2013). The ability to utilize feedback on current behavior to shape future behavior (i.e. feedback learning) is a neurocognitive function that is crucially involved in typical behavioral development (Rushworth & Behrens, 2008). Impaired feedback learning may affect the behavioral development of children with TBI, contributing to the increased risk of behavior problems as observed after moderate to severe pediatric TBI (Li & Liu, 2013; Schwartz et al., 2003).

A recent review of 50 studies confirms that children with mild, moderate and severe TBI have increased risks of persisting behavior problems. These behavior problems can both be internalizing (e.g. symptoms of depression and anxiety) and externalizing (e.g. aggression and symptoms of conduct disorder; Li & Liu 2013). Pre-injury factors including premorbid behavior problems, young age at injury, male gender and poor family functioning possibly contribute to the existence of behavior problems in children with TBI (Li & Liu, 2013), but complicated mild to severe TBI also triples a child's risk of developing post-injury psychiatric disorders associated with personality change and problems of anxiety, depression, inattention, hyperactivity and oppositional behavior (Brown & Chadwick, 1981; Max, Wilde, & Bigler, 2012). The reported behavior problems may not manifest until multiple years post-injury, suggesting that TBI affects a mechanism underlying behavioral development (Li & Liu, 2013). Importantly, behavior problems after pediatric TBI predict poor academic functioning (Yeates & Taylor, 2006), adverse social outcome (Rosema, Crowe, & Anderson, 2012) and delinquency (Timonen et al., 2002), highlighting the importance of understanding the development of behavior problems after pediatric TBI.

Typical behavioral development importantly relies on feedback learning (Rushworth & Behrens, 2008), which is mediated by a dopamine-driven fronto-striatal network that facilitates the use of positive and negative feedback on current behavior to optimize future behavior (Doya, 2008; Hämmerer & Eppinger, 2012). Feedback learning in daily life is complex, due to inconsistency in the feedback that children receive on their behavior (Doya, 2008) and dynamics in the context that children live in (Stokes & Baer, 1977). For example, feedback inconsistency may be introduced by differing criteria for feedback between caregivers (e.g. parents, guardians, teachers, etc.) and these criteria may additionally change over time. Furthermore, feedback on behavior is provided in a certain context (e.g. in class), but may also apply to other contexts (e.g. at home, at the playground, in the supermarket, etc.). Successful feedback learning in daily life thus requires the ability to learn from inconsistent feedback (Duijvenvoorde & Jansen, 2013) and requires generalization of learning from the learning context to novel contexts (Gershman, Niv, & Gershman, 2015; Tamminen, Davis, & Rastle, 2015).

Relatively few studies have investigated the effects of pediatric TBI on feedback learning. Some studies used the Wisconsin Card Sorting Test to measure the ability to flexibly adapt behavior in response to consistent feedback based on changing rules. These studies showed that (more) severe TBI is associated with impaired task performance (Donders & Wildeboer, 2004; Kizilbash & Donders, 2010; Levin et al., 1997; Slomine et al., 2002), indicating impaired feedback-directed concept formation and set-shifting. Other studies used an adapted version of the Iowa Gambling Task to assess decision making in response to probabilistic feedback, defined by the magnitude of gains and losses in money or points. These studies showed risky decision making favoring short-term gains at the cost of larger long-term losses in children with moderate/severe TBI as compared to trauma controls (Schmidt, Hanten, & Li, 2012) and in children with raised vs. normal intracranial pressure after severe TBI (Slawik, Salmond, & Taylor-tavares, 2009). The latter study also used a probabilistic reversal learning task to show that children with raised intracranial pressure after severe TBI have impaired rule learning based on inconsistent feedback. An electrophysiological study in adults with severe TBI further provided evidence for impaired neural processing of changing contexts in which feedback is provided (Larson, 2007). To date, the role of feedback consistency and generalization of learning to novel contexts remain unexplored aspects of feedback learning along the full axis of TBI severity in children, and it is furthermore unclear how feedback learning deficits relates to daily life behavior problems in these children.

This study investigates feedback learning in relation to behavior problems after mild to severe pediatric TBI. Based on the existing literature, we expect that children with TBI will show impairments in the abilities to learn from increasingly inconsistent feedback and to generalize learning from the learning context to novel contexts. Based on the important role of feedback learning for typical behavioral development (Rushworth & Behrens, 2008), we also expect that impaired feedback learning relates to behavior problems after pediatric TBI. We included children with traumatic injury not involving the head in the trauma control group, accounting for the influence of pre-injury risk factors for trauma and psychological effects of hospitalization (Max, Koele, & Smith Jr., 1998). To our best knowledge, this is the first study to investigate the relation between feedback learning and behavioral functioning in children with TBI.

METHODS

PARTICIPANTS

SAMPLE

This study involved 112 children with TBI and 52 children with traumatic control (TC) injury not involving the head. All children were retrospectively recruited from a consecutive cohort of three university-affiliated level I trauma centers and several rehabilitation centers in the Netherlands. Inclusion criteria were: (1) age 6-13 years; (2) proficient in the Dutch language; (3) hospital admission with a clinical diagnosis of TBI for inclusion in the TBI group; (4) hospital admission for traumatic injuries below the clavicles for inclusion in the TC group (American College of Surgeons, 2004); and (5) more than two months post-injury. Exclusion criteria were: (1) previous TBI; (2) visual disorder interfering with neurocognitive testing; or (3) current condition affecting the central nervous system, other than TBI.

Of all 375 children admitted between October 2009-October 2013 that were eligible for inclusion (TBI vs. TC: n = 232 vs. n = 143), 54 were not traced (n = 39 vs. n = 15) and 137 declined participation (n = 68 vs. n = 69). The main reasons not to participate were: not interested (25% vs. 32%), no time (22% vs. 22%) or load on child (8% vs. 16%). Last, 18 children were excluded (TBI: n = 6 not proficient in Dutch, n = 5 age exceeding criterion, n = 1 motor retardation; TC: n = 3 not proficient in Dutch, n = 1 previous TBI, n = 1 brain tumor and n = 1 mental retardation). Parents of two children (TBI: $n = 1$; TC: $n = 1$) discontinued participation for unclear reasons. The remaining children with TBI (n = 112) and TC (n = 52) did not differ from their respective recruitment cohorts in terms of age or gender ($ps \geq .14$).

INJURY SEVERITY

Information on injury severity was extracted from medical files and included: (1) diagnosed injuries; (2) the lowest score on the Glasgow Coma Scale (GCS) on the day of admission; (3) admission duration; and (4) the presence of risk factors for complicated mild TBI according to the European Federation of Neurological Societies' guidelines on mild TBI (Vos & Battistin, 2002). These risk factors included: impaired consciousness (GCS = 14-13), focal neurological deficits, persistent vomiting (≥ 3 episodes), post-injury epileptic insults, progressive headache and abnormal head CT-scan. Injury severity was categorized into mild TBI (GCS = 15-13, loss of consciousness [LOC] duration ≤ 30 minutes, post-traumatic amnesia [PTA] duration ≤ 1 hour) without risk factors ($mild^{RF-}$ TBI, n = 24), mild TBI with at least one risk factor ($mild^{RF+}$ TBI, n = 52) and moderate/severe TBI (GCS = 12-3, LOC duration > 30 minutes, PTA duration > 1 hour; n = 37; Teasdale & Jennett 1976).

MEASURES

BACKGROUND INFORMATION

Data on gender, age, socio-economic status (SES) and clinical diagnoses of psychiatric or learning disorders were collected using a parental questionnaire. SES was defined as the average level of parental education ranging from 1 (no education) to 8 (postdoctoral education (Statistics Netherlands, 2006). Full-scale IQ (FSIQ) was estimated using a short form of the Wechsler Intelligence Scale for Children-III (including the subtests Vocabulary, Similarities, Block Design and Picture Arrangement), with excellent validity (r = .93) and reliability (r = .93) in estimating FSIQ (Kaufman, Kaufman & Baijgopal, 1996).

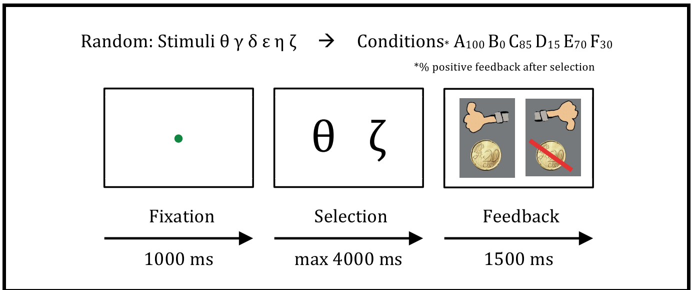
PROBABILISTIC LEARNING TEST (PLT)

We used a child-friendly version of the extensively validated Probabilistic Learning Test (Frank, Seeberger, & O'reilly, 2004) to measure feedback learning, which has successfully been used in typical developing children (van den Bos, Cohen, Kahnt, & Crone, 2012). In the training phase, children were presented two stimuli in each trial and were instructed to select the stimulus with the greatest probability of positive feedback (Figure 1). Three fixed pairs (AB, CD and EF) comprising six stimuli (A-F) were presented and children had to learn the associations between the stimuli and increasingly inconsistent positive and negative feedback. Feedback was consistent in the AB pair (A: 100% positive feedback; B: 100% negative feedback) and feedback was inconsistent in the CD pair (C: 85% positive and 15% negative feedback; D: 15% positive and 85% negative feedback) and the EF pair (E: 70% positive and 30% negative feedback; F: 30% positive and 70% negative feedback). Consequently, A, C and E are net positive stimuli and B, D and F are net negative stimuli, and it is increasingly difficult to learn that A is better than B, C is better than D and E is better than F. The training phase consisted of learning blocks of 60 trials with a maximum of 5 blocks, while children that reached above chance level performance in any given learning block (AB, CD and EF pair ≥ 70%, 65% and 60%, respectively) entered the test phase. No feedback is provided in the test phase, during which children have to select the best stimulus from all possible pair configurations of stimuli A-F (AB, AC, AD, AE, AF, BC, BD, BE, BF, CD, CE, CF, DE, DF and EF in 120 trials) based on feedback provided in the training phase.

The dependent variable was accuracy defined as the proportion correct responses (choosing stimuli A, C and E), excluding trials suspected of anticipatory responses (reaction time < 200 ms). *Learning rate* measured the rate of feedback learning, assessed by the accuracy in the last learning block in the training phase divided by the number of learning blocks completed. The *effects of feedback consistency on learning* were measured by the decrease in accuracy in response to increasing feedback inconsistency in the training phase (i.e. AB, CD and EF pairs). Last, *generalization of learning* measured the generalization of learning from the learning context (i.e. overall accuracy on AB, CD & EF pairs in the last learning block of the training phase) to novel contexts (i.e. overall accuracy on AC, AD, AE, AF, BC, BD, BE, BF, CE, CF, DE & DF pairs in the test phase). Descriptions of the PLT variables are also provided in Table 1.

BEHAVIORAL FUNCTIONING

Parent and teacher ratings of behavior were obtained using the Child Behavior Checklist and teacher equivalent, the Teacher Rating Form (Verhulst & van der Ende 2013). The broadband scales measuring internalizing (e.g. anxiety) and externalizing problems (e.g. aggression) were used, since these scales are known to have adequate validity and excellent reliability (Cronbach's α > .90; Verhulst & van der Ende 2013).



Training Pairs A_{100} B_0 C_{85} D_{15} E_{70} F_{30}

Test Pairs

	Net Positive Stimuli			Net Negative Stimuli		
	A_{100}	C_{85}	E_{70}	F_{30}	D_{15}	B_0
A_{100}		AC	AE	AF	AD	AB
C_{85}	Novel		CE	CF	CD	BC
E_{70}	Novel	Novel		EF	DE	BE
F_{30}	Novel	Novel	Training		DF	BF
D_{15}	Novel	Training	Novel	Novel		BD
B_0	Training	Novel	Novel	Novel	Novel	

Figure 1. The Probabilistic Learning Test (PLT)
Note. Stimuli are randomly assigned to condition A-F. In the training phase, children were presented two stimuli in each trial and were instructed to select the stimulus with the greatest probability of positive feedback. Three

fixed pairs (AB, CD and EF) comprising six stimuli (A-F) were presented and children had to learn the associations between the stimuli and increasingly inconsistent positive and negative feedback. No feedback is provided in the test phase, during which children have to select the best stimulus from all possible pair configurations of stimuli A-F (AB, AC, AD, AE, AF, BC, BD, BE, BF, CD, CE, CF, DE, DF and EF in 120 trials) based on feedback provided in the training phase. Color-coding refers to test phase pairs with new combinations of stimuli (i.e. novel context pairs).

PROCEDURE

The families of eligible children were sent an information letter and contacted by telephone two weeks later. After written informed consent was provided by parents and children aged >11 years, trained examiners administered the PLT while parents filled out questionnaires in a waiting room. Thereafter, teachers were contacted to fill out questionnaires. During the PLT, children were seated in front of a 15-inch laptop with a 50-centimeter viewing distance to minimize eye movements. Standardized instructions and practice trials were used to familiarize children with the task. Task duration ranged between 15-25 minutes. This study was approved by the medical ethical committee of the VU University Medical Centre (NL37226.029.11).

STATISTICAL ANALYSIS

All analyses were performed using SPSS version 22.0 (SPSS inc., 2013). Missing values (1-5%) were replaced using multiple imputing (Sterne et al., 2009). All dependent variables were screened for outliers ($P < .001$), which were rescaled using Winsorizing (Tabachnick & Fidell, 2012). To investigate group comparability, all TBI severity groups (TC, mild^{RF-} TBI, mild^{RF+} TBI and moderate/severe TBI) were compared on demographics, injury-related variables, prevalence of clinical diagnoses and FSIQ using ANOVA and chi-square tests, where appropriate.

With regard to PLT performance, we assessed successful feedback learning at the group level by testing the accuracy in all dependent variables against chance level performance using one-sample t-tests in the whole sample ($H_0 = 0.5$). The effect of TBI on *learning rate* (defined by the overall accuracy in the last learning block of the training phase divided by the number of learning blocks completed) was assessed with ANOVA, using TBI severity as between-subject factor (TC, mild^{RF-} TBI, mild^{RF+} TBI & moderate/severe TBI). We identified children that did not satisfy the training phase criteria to enter the test phase after the maximum of five learning blocks (i.e. chance level performers) and assessed their distribution across TBI severity groups (TC, mild^{RF-} TBI, mild^{RF+} TBI & moderate/severe TBI) using chi-square testing. Chance level performers were precluded from analyses involving the test phase, to prevent chance level performances of contaminating analyses on *generalization of learning* to novel contexts in the test phase.

Two repeated measures ANOVAs were performed on accuracy with group as between-subject factor and the following within-subject factors: (1) *effects of feedback consistency* (feedback consistency with 3 levels: AB, CD & EF pairs across blocks in the training phase); and (2) *generalization of learning* (PLT phase with 2 levels: last learning block of the training phase vs. test phase). In these analyses, the main effect of within-subject factors assessed the validity of PLT manipulations, while the interactions between TBI severity and within-subject factors assessed the selective impact of TBI on (1) *effects of feedback consistency on learning* and (2) *generalization of learning.* The impact of TBI on ratings of internalizing problems and externalizing problems was assessed using ANOVA. The main effect of TBI severity (TC, mild^{RF-} TBI, mild^{RF+} TBI & moderate/severe TBI) was assessed by linear contrasts in all described factorial analyses, of which significant effects were followed-up by LSD post-hoc testing. In repeated measure analyses with significant interaction effects, the main effect of TBI severity was assessed for each level of the within-subject variable separately.

Last, we investigated the relation between feedback learning and behavior problems in children with TBI. PLT variables for which group differences were obtained were inserted as predictors of parent and teacher ratings of behavior problems for which group differences were obtained, in separate multiple linear regression models while correcting for the demographic variables age, gender and SES. To avoid suppressor effects, we used backward selection to select the most efficient prediction model (entry criterion: $F > .05$, removal criterion: $F < .10$; Field, 2009). We used Receiver-Operating Characteristic (ROC) analysis to investigate the diagnostic utility of significant predictors for the identification of children with TBI and clinically significant behavior problems (score on relevant scale > M + 2SD of the TC group) amongst all other children. All statistical testing was two-sided at $\alpha = .05$.

Table 1. Overview of variables derived from the Feedback Learning Test

Variable	Description
Learning Rate	The rate of feedback learning, defined as accuracy in the last learning block of the training phase divided by the number of learning blocks completed to satisfy training phase criteria or entering the test phase (higher values reflect faster *learning rate*).
Effects of Feedback Consistency on Learning	The impact of increasing feedback inconsistency on feedback learning, defined as the decrease in accuracy on the AB, CD and EF pairs (associated with an increase in inconsistency of feedback) in the training phase (lower decrement reflects a smaller effect of feedback consistency on feedback learning).
Generalization of Learning	The transfer of learning from the learning context to novel contexts, defined by the decrease in accuracy from the last learning block of the training phase to the test phase (lower decrement reflects better *generalization of learning*).

RESULTS

BACKGROUND INFORMATION

Group characteristics concerning demographics, injury-related information, clinical diagnoses and FSIQ are displayed in Table 2. There were no differences between any of the groups on demographics (*p*s ≥ .21), except for lower SES in all TBI groups as compared to the TC group (*p*s < .05). The moderate/severe TBI group had longer hospital admission, lower GCS score and more neurosurgery than all other groups (*p*s ≤ .001). By definition, no cranial fractures or intracranial pathology were present in the mild^{RF-} TBI group, while the mild^{RF+} TBI and moderate/severe TBI groups had progressively increased prevalence of cranial fractures and intracranial pathology (*p*s ≤ .01). Differences in the prevalence of psychiatric conditions only reached significance between the mild^{RF+} TBI group and TC group (*p* = .05). There was found a main effect of TBI severity on FSIQ, reflecting that more severe TBI was associated with lower FSIQ. Post-hoc analysis only revealed lower FSIQ in the mild^{RF+} TBI and moderate/severe TBI groups as compared to the TC group (*p* = .01, *d* = -0.53 and *p* = .02, *d* = -0.55, respectively).

Table 2. Descriptives of demographics and injury-related information, diagnoses and fsiq

	Group				Contrasts[a]
	TC	Mild RF- TBI	Mild RF+ TBI	Moderate/Severe TBI	
n	52	24	51	37	
Demographics					
Males, *n* (%)	27 (52)	11 (46)	31 (61)	21 (57)	NS
Age at testing in y, M (SD)	9.3 (2.1)	8.7 (2.1)	8.8 (2.0)	8.8 (2.0)	NS
SES, M (SD)	5.9 (1.2)	5.3 (1.2)	5.4 (1.2)	5.3 (1.4)	1, 2, 3 < TC
Injury-related information					
Age at injury in y, M (SD)	7.7 (2.2)	7.1 (2.4)	7.1 (2.2)	6.9 (2.5)	NS
Lowest GCS, M (SD)	-	15.0 (0.0)	14.6 (0.7)	8.3 (2.8)	1, 2 > 3
Hospital admission in *d*	2.4 (1.8)	1.9 (0.3)	3.3 (2.8)	18.0 (29.4)	3 > TC, 1, 2
Time post-injury in y, M (SD)	1.6 (0.8)	1.7 (1.0)	1.7 (1.0)	1.8 (1.2)	NS
Range	0.4-3.5	0.5-3.8	0.3-4.4	0.4-5.4	
Extracranial fracture, *n* (%)	39 (75)	1 (4)	8 (16)	8 (22)	1, 2, 3 < TC
>1 Extracranial fractures, *n* (%)	4 (8)	0 (0)	3 (6)	4 (11)	NS
Cranial fracture, *n* (%)	-	0 (0)	17 (33)	23 (62)	3 > 2 > 1
Intracranial pathology, *n* (%)	-	0 (0)	16 (31)	25 (68)	3 > 2 > 1
Orthopedic surgery, *n* (%)	42 (81)	1 (4)	7 (14)	1 (3)	1, 2, 3 < TC
Neurosurgery, *n* (%)	-	0	0	32	3 > 2, 1
Clinical Diagnoses					
Psychiatric disorder, *n* (%)	1 (2)	1 (4)	6 (12)	2 (5)	2 > TC
Premorbid ADHD, *n* (%)	0 (0)	0 (0)	3 (6)	1 (3)	NS
Learning disorder, *n* (%)	3 (6)	2 (8)	4 (8)	3 (8)	NS
Intelligence					
FSIQ	105.5 (14.0)	102.0 (16.3)	97.8 (15.1)	97.6 (15.4)	2, 3 < TC

Note. ADHD = attention deficit hyperactivity disorder; FSIQ = full-scale intelligence quotient; d = days; GCS = Glasgow Coma Scale; NS = not significant; RF = risk factor; SD = standard deviation; SES = socio-economic status; TBI = traumatic brain injury; y = years.

[a]1 = mild RF- TBI; 2 = mild RF+ TBI; 3 = moderate/severe TBI, TC = trauma control.

FEEDBACK LEARNING

PLT performance is displayed in Table 3. Accuracy was above chance level for all PLT variables ($\geq .57$, *p*s $< .001$), indicating successful feedback learning in the training phase and successful *generalization of learning* to new contexts in the test phase –at the group level.

LEARNING RATE

The main effect of TBI severity on *learning rate* (i.e. accuracy in the last training block divided by the number of learning blocks completed in the training phase) was not significant, indicating that TBI does not affect the rate of feedback learning. At the individual level, 21 chance level performers were identified (i.e. children that did not reach the training phase criteria). Chance level performers were not more likely to be part of the mild^{RF-} TBI group (*n* = 0), mild^{RF+} TBI group (*n* = 4) or moderate/severe TBI group (*n* = 10) than the TC group (*n* = 7; *p*s $\geq .11$). After precluding chance level performers from subsequent analyses of PLT performance, the resulting sample did not differ from the original sample on demographics, injury-related information or FSIQ (*p*s $\geq .52$).

EFFECTS OF FEEDBACK CONSISTENCY ON LEARNING

The PLT manipulation measuring the influence of feedback consistency on feedback learning was assessed by the main effect of feedback consistency in the training phase (i.e. increasing inconsistency in AB, CD & EF pairs) on accuracy. As expected, this main effect of feedback consistency was significant, validating that more inconsistent feedback affects learning. The impact of TBI on the *effects of feedback consistency on learning* was assessed by the interaction between TBI severity and feedback consistency on accuracy, which was not significant. Likewise, there was no main effect of TBI severity on overall accuracy in the training phase. These findings indicate that TBI did not affect feedback learning from inconsistent feedback.

GENERALIZATION OF LEARNING

Generalization of learning from the learning context to novel contexts was assessed by the main effect of PLT phase (i.e. last learning block of the training phase vs. test phase) on accuracy. According expectations, the main effect of PLT phase was significant, reflecting a decrease in accuracy from the training phase to the test phase. This finding validates that *generalization of learning* occurs at the cost of accuracy. The effect of TBI on *generalization of learning* was assessed by the interaction between TBI severity and PLT phase on accuracy, which was significant. This finding indicates that TBI severity moderates *generalization of learning*. Follow-up comparisons revealed a linear effect of TBI severity on accuracy in the test phase, reflecting that more severe TBI related to poorer test phase performance. Post-hoc group comparisons (Figure 2) revealed poorer performance in the moderate/severe TBI group than the TC group ($p = .03$, $d = -0.51$), and the mild^{RF-} group ($p = .03$, $d = -0.65$). No effect of TBI severity on accuracy in the last learning block of the training phase was found. Together, these findings indicate that moderate/severe TBI selectively impairs *generalization of learning* to novel contexts.

Table 3. Descriptive and inferential statistics of plt performance

PLT Performance	Group				Main and Interaction Effects					
	TC	Mild RF- TBI	Mild RF+ TBI	Moderate/ Severe TBI	PLT Manipulation		Group x PLT		Group	
					F	*p*	F	*p*	*F*	*p*
n	52	24	51	37						
Training Phase										
Learning rate	0.57 (0.27)	0.63 (0.26)	0.54 (0.27)	0.52 (0.31)	-	-	-	-	1.7[a]	.19
Chance level performers, *n*	7	0	4	10	-	-	-	-	-	-
Effects of Feedback Variability					47.6[b]	**< .001**	1.4[c]	.22	0.0[a]	.98
Overall AB Pair	0.88 (0.09)	0.88 (0.09)	0.84 (0.10)	0.86 (0.09)						
Overall CD Pair	0.81 (0.13)	0.85 (0.12)	0.84 (0.12)	0.84 (0.11)						
Overall EF Pair	0.73 (0.16)	0.68 (0.10)	0.70 (0.16)	0.74 (0.16)						
Test Phase										
Generalization of learning					204.7[d]	**< .001**	2.7[e]	**.05**	-	-
Last Training Block	0.87 (.07)	0.85 (0.06)	0.86 (0.07)	0.87 (0.08)					0.1[f]	.82
Test Phase	0.74 (0.12)	0.74 (0.07)	0.71 (0.11)	0.68 (0.12)					6.8[f]	**.01**

Note. Data reflect mean (standard deviation), unless otherwise indicated. PLT = Probabilistic Learning Test; RF = risk factor; TBI = traumatic brain injury; TC = trauma control.
[a]Degrees of freedom: 1,163. [b]Degrees of freedom: 1,160. [c]Degrees of freedom: 3,160. [d]Degrees of freedom: 1,139. [e]Degrees of freedom: 3,139. [f]Degrees of freedom: 1,142.

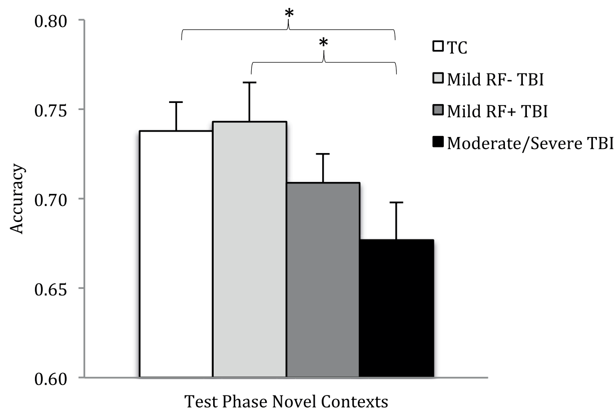


Figure 2. PLT performance of TBI severity groups in novel contexts during the test phase
Note. Figure shows overall mean accuracy (standard error) of TBI severity groups on test pairs with novel combinations of stimuli from the training phase, requiring *generalization of learning* from the learning context to novel contexts. PLT = Probabilistic Learning Test; RF = risk factor; TBI = traumatic brain injury; TC = trauma control.
*$p < .05$. **$p < .01$.

BEHAVIORAL FUNCTIONING

Analyses on behavioral functioning (Table 4) revealed significant linear main effects of TBI severity on parent ratings of internalizing and externalizing problems, and teacher ratings of internalizing problems, indicating that more severe TBI was associated with more behavior problems. Post-hoc group comparisons revealed no differences between the mild^{RF-} TBI group and TC group regarding behavior ratings (*p*s ≥ .13, *d*s: 0.37-0.46), except for higher teacher ratings of internalizing problems in the mild^{RF-} TBI group ($p = .02$, $d = 0.69$). Compared to the TC group, the mild^{RF+} TBI and moderate/severe TBI groups had higher parent ratings of internalizing problems ($p = .04$, $d = 0.47$ and $p < .001$, $d = 0.75$) and higher teacher ratings of internalizing problems ($p = .008$, $d = 0.58$ and $p = .01$, $d = 0.58$). In addition, the moderate/severe TBI group had higher parent ratings of externalizing problems than the TC group ($p = .006$, $d = 0.60$), while this difference did not reach conventional levels of significance between the mild^{RF+} TBI and TC groups ($p = .08$, $d = 0.42$).

Table 4. Parent and teacher ratings of behavioral functioning

	Group				TBI severity		
	TC	Mild RF- TBI	Mild RF+ TBI	Moderate/Severe TBI	*F*(1,163)	*p*	Contrasts[a]
n	52	24	51	37			
Parent ratings							
Internalizing problems,	5.2 (5.0)	7.7 (6.1)	7.9 (6.1)	10.2 (8.5)	11.2	**.001**	2, 3 > TC
Externalizing problems	4.9 (4.1)	6.5 (5.1)	7.1 (6.3)	8.7 (9.2)	7.5	**.007**	3 > TC
Teacher ratings							
Internalizing problems	2.6 (3.6)	5.3 (4.8)	5.0 (4.8)	5.2 (5.2)	5.5	**.02**	2, 3 > TC
Externalizing problems	4.4 (6.6)	4.6 (6.3)	5.8 (6.8)	3.4 (5.5)	0.2	.65	-

Note. Data reflect mean (standard deviation), unless otherwise indicated. RF = risk factor; TBI = traumatic brain injury; TC= trauma control.
[a]1 = mild RF- TBI; 2 = mild RF+ TBI; 3 = moderate/severe TBI, TC = trauma control.

FEEDBACK LEARNING AND BEHAVIOR PROBLEMS AFTER PEDIATRIC TBI

We investigated the predictive value of *generalization of learning* (i.e. accuracy for novel pairs in the test phase) for ratings of behavior (parent and teacher ratings of internalizing problems and parent ratings of externalizing problems) in the TBI group. Poorer *generalization of learning* significantly predicted higher parent ratings of externalizing problems ($\beta = -.21$, $p = .03$), while SES ($\beta = -.29$, $p = .003$) was also captured in the prediction model ($R^2 = .15$, $p < .001$). This finding indicates that poorer *generalization of learning* from the learning context to novel contexts after pediatric TBI relates to more externalizing problems as observed by parents. Prediction models for parent and teacher ratings of internalizing problems and teacher ratings of externalizing problems did not include PLT variables. Last, ROC analysis revealed that *generalization of learning* has diagnostic utility for the identification of children with TBI and clinically significant parent rated externalizing behavior problems (mild^{RF-} TBI: n = 1 [4%]; mild^{RF+}: n = 7 [15%]; moderate/severe: n = 6 [22%]) amongst all other children (area under the curve= .77, p = .001), with a sensitivity of 86% and a specificity of 72%.

ANALYSIS OF CONFOUNDERS

SES was lower in all TBI groups relative to the TC group, while lower SES also related to higher behavior ratings (ps < .05). To investigate the influence of SES on the reported effects of mild^{RF+} and moderate/severe TBI on behavior ratings, we matched the TC group 1:2 to the collapsed mild^{RF+} TBI and moderate/severe TBI group on SES (±2; age, gender and SES: ps ≥ .16), and reran the relevant analyses, replicating the reported differences (data available with first author).

DISCUSSION

This study investigated feedback learning in children with mild to severe TBI in relation to post-injury behavior problems. The results show that moderate/severe TBI affects *generalization of learning*, reflecting impaired transfer of learning from the learning context to novel contexts. *Generalization of learning* further predicted higher parent ratings of externalizing problems in children with TBI, suggesting that impaired *generalization of learning* may contribute to behavior problems after pediatric TBI. *Generalization of learning* further showed diagnostic utility to identify children with TBI and clinically significant externalizing behavior problems.

Based on the existing pediatric and adult literature, we expected detrimental effects of pediatric TBI on feedback learning. Partly contrasting our expectations, we found no evidence indicating that pediatric TBI affects learning from increasingly inconsistent feedback. This finding also contradicts a previous report of impaired performance on a probabilistic reversal learning task in children with raised-intracranial pressure after severe TBI (Slawik et al., 2009), possibly implicating that only very severe forms of pediatric TBI affect learning from inconsistent feedback. As expected, we found that children with moderate/severe TBI had impaired *generalization of learning*. This finding adds to the existing literature describing that children with severe TBI have impaired feedback-directed concept formation and set-shifting (Levin et al., 1997) and that children with moderate/severe TBI have impaired decision making based on feedback in terms of gains and losses in money or points (Schmidt et al., 2012). This study is the first to show that children with moderate/severe TBI have impaired ability to use feedback on behavior in a certain context to direct behavior in a novel context, which is in line with electrophysiological evidence of impaired neural processing of changing feedback contexts in adults with severe TBI (Larson, 2007).

Analyses of daily life behavior problems revealed that children with mild^{RF+} TBI or moderate/severe TBI had more internalizing problems as observed by parents as well as teachers. Children with moderate/severe TBI additionally had more externalizing problems as observed by parents. These findings are in line with a recent review (Li & Liu, 2013), although it is somewhat surprising that no effects of TBI on teacher ratings of externalizing problems were observed. Possibly, externalizing problems of children with TBI specifically manifest at home, which may represent a relatively unstructured environment as compared to school. Interestingly, our results indicate that increased parent ratings of externalizing problems in children with TBI were predicted by impaired *generalization of learning*, suggesting that impaired ability to generalize feedback to novel contexts may contribute to the development of conflict-prone behavior (i.e. externalizing problems) after TBI. This idea is supported by the suggested involvement of fronto-striatal networks in both feedback learning (Hämmerer & Eppinger, 2012; Maia & Frank, 2011) and the emergence of disturbing behavior after pediatric TBI (Li & Liu, 2013; Max et al., 2012). ROC analyses further revealed that *generalization of learning* has good sensitivity (86%) and reasonable specificity (72%) to identify children with TBI and clinically significant externalizing behavior problems. This finding suggests that early assessment of feedback learning after TBI may identify children at risk of developing behavior problems later in life, although this hypothesis awaits confirmation in a longitudinal investigation.

The findings from our study suggest that *generalization of learning* is more vulnerable to the effects of TBI than learning from inconsistent feedback, implicating that differential neural (sub)networks underlie these aspects of feedback learning. This idea is supported by a review suggesting that feedback learning is facilitated by dynamic interplay between feedback information processing in a ventral fronto-striatal network (i.e. the reward loop) and executive processes that translate feedback history into behavior in a dorsal fronto-striatal network (i.e. the executive control loop; Hämmerer & Eppinger, 2012). The literature further suggests that learning from inconsistent feedback is mediated by the reward loop (van den Bos et al., 2012), while processing of feedback context has been associated with brain areas in the executive control loop (Gläscher, Daw, Dayan, & O'Doherty, 2010). We speculate that the observed vulnerability of *generalization of learning* to the effects of moderate/severe TBI may arise from the relatively late maturation of prefrontal brain areas involved in executive control loop (i.e. in adulthood; Gogtay et al., 2004) as compared to the reward loop (i.e. in late childhood; van den Bos et al., 2012). The absence of effects of mild TBI on feedback learning in this study, relative to the observed effects of moderate/severe TBI, may be explained by the outcome of two meta-analyses of diffusion tensor imaging studies indicating that frontal white matter damage is not implicated in the neuropathology of mild TBI (Aoki, Inokuchi, Gunshin, Yahagi, & Suwa, 2012), but is implicated in more severe TBI (Roberts, Mathias, & Rose, 2014).

This study has some weaknesses. We used a highly standardized computer environment to model feedback learning, which allowed us to isolate the effects of feedback consistency and context on learning, but may not directly translate to feedback learning in daily life. However, we did show that *generalization of learning* was related to daily life behavior problems as observed by parents. Further, the small sample size of the mild^{RF-}TBI group limited statistical power in comparisons involving this group. Strengths of this study include the recruitment from a multicenter consecutive cohort (increasing the generalizability of the results) and the use of a trauma control group (controlling for the effects of pre-injury trauma risk factors and psychological effects of hospitalization).

To our best knowledge, this study is the first to report evidence suggesting that impaired *generalization of learning* may underlie the increased prevalence of externalizing behavior problems after pediatric TBI. This finding is important given that externalizing behavior problems in childhood predict poor academic attainment (Breslau et al., 2009), poor social functioning (Bongers & Koot, 2008) and delinquency (Broidy et al., 2003) later in life. Early assessment of feedback learning may have potential to identify children that could benefit from rehabilitation interventions to prevent the emergence of externalizing behavior problems after TBI.

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SUPPORTING INFORMATION

MISSING DATA ANALYSIS

There were missing data for parent and teacher ratings of behavior problems (see Table S1). No group differences were observed in the prevalence of missing data and therefore missing data were imputed using multiple imputation. Missing data imputations were generated in five cycles on draws of 50 participants using draws of two predictors from the following variables that were entered in the imputation model: age, gender, SES and TBI severity group. The means of imputed values were used in the statistical analyses.

Table S1. Missing data analysis

	Group		Contrast		TBI severity Group			Contrast	
	TBI	TC	x^2	*p*	Mild RF-	Mild RF+	Moderate/ Severe	x^2	*p*
N	112	52			24	51	37		
Missing data									
Parent ratings, *n* (%)	2 (2%)	1 (2%)	0.0	.95	0 (0%)	2 (4%)	0 (0%)	2.4	.50
Teacher ratings, *n* (%)	6 (5%)	3 (6%)	0.0	.91	1 (4%)	3 (65)	2 (5%)	1.0	.81

Note. RF = risk factor; TBI = traumatic brain injury; TC = trauma control.

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