Paper III

Self-reported executive, emotional and behavioural function 2-5 years after moderate and severe traumatic brain injury – a prospective follow-up study

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Objective: To assess self-reported executive, emotional, and behavioural problems 2-5 years after moderate and severe traumatic brain injury (TBI), and examine predictors and associates for self-reported function. **Method:** Self-reported executive function, emotional, and behavioural problems in moderate and severe TBI (N=67) were assessed with Behavioral Rating Inventory of Executive Function – Adult version (BRIEF-A), and Achenbach System of Empirically Based Assessment (ASEBA); Adult Self Report (ASR). **Results:** Persons with TBI reported significantly more problems related to attention, emotional regulation, and symptoms of depression, anxiety, and aggressive behaviour >2 years post-injury compared to healthy individuals. Younger age at injury predicted endorsement of greater problems with aggressive and rule-breaking behaviour, fewer years of education predicted greater problems with self-reported executive function, and presence of traumatic axonal injury (TAI) in early MRI predicted later internalizing problems. Symptoms of depression one year post-injury predicted later self-reported executive, emotional and behavioural problems. No association between performance-based measures of cognitive function in the sub-acute phase and later self-reported measures were observed. **Conclusion:** Executive, emotional and behavioural problems were commonly reported 2-5 years after TBI. Systematic identification of TAI and symptoms of depression should be implemented in the clinic as it gives important warning of future problems.

Survivors of moderate and severe traumatic brain injury (TBI) often experience long-lasting cognitive, emotional, and behavioural problems after the initial injury.[1-5] A few prospective studies of long-term cognitive outcome assessed with performance based neuropsychological tests beyond 2 years post-injury have demonstrated chronic impairments in the majority of persons with TBI regarding executive function, processing speed, memory, and attention.[6-8] In particular, executive dysfunction has been demonstrated to have a profound impact on the ability to resume education, employment, and independent living.[9,10] Further, persons with TBI also have an increased risk of developing symptoms of psychiatric disorders such as depression,[11] anxiety,[12] substance abuse,[13] aggression,[14,15] and personality problems,[4,12, 16] which also affects re-integration into the community.[17] Moreover, the persons' own perception of their problems may influence how well they reintegrate into the community,[18-20] which demonstrates the importance of using self-reporting assessment tools in TBI outcome research.

While reduced self-reported executive function has been reported within the first year after moderate and severe TBI,[21,22] few studies have reported perceived executive problems beyond this period.[20] The concept of executive function refers to all functions related to goal-directed regulation of thoughts, actions, and emotions; including but not restricted to, problem-solving, monitoring ongoing operations, switching between operations, emotion regulation, initiation of behaviour, and inhibition of non-adaptive behaviour.[23,24] Regulating emotions and actions requires additional processes other than those commonly assessed by performance-based measures (e.g. problem-solving, monitoring ongoing operations, switching between tasks).[25] Hence, a complimentary approach is to assess perceived executive functioning related to everyday problems through questionnaires, such as the Behavior Rating Inventory of Executive Function-Adult Version (BRIEF-A).[26,27] The BRIEF-A assesses goal-directed regulation of thoughts, actions, and emotions, and is one of the most comprehensive measures regarding the number of items and executive domains assessed.[28] However, the few studies that have employed the BRIEF-A as an outcome measure after TBI have had relatively small sample sizes,[21,29,30] been retrospective in design,[29,31] and lacked comparisons with large

demographically matched healthy control groups. Further complicating the issue is that self-reported cognitive complaints may also overlap with emotional problems.[29,32]

A broad assessment is necessary to capture the variety of emotional and behavioural problems that patients experience after TBI.[2] Compared with the general population, a substantially larger proportion of individuals with TBI qualify for an Axis I diagnosis according to DSM-IV, with depression, anxiety, and substance abuse most commonly observed.[12,33] However, people with TBI may also experience a greater degree of sub-clinical symptoms than healthy individuals, which is better illustrated by questionnaires.[21,33] An extensive questionnaire offers a good framework to organize the variety of emotional and behavioural symptoms that are frequently reported after TBI.[33,34] One such questionnaire is the adult version of the Achenbach System of Empirically Based Assessment (ASEBA), which is widely used among psychiatrists, but has never been used as an outcome measure after TBI in adults.

Although self-reported executive problems after TBI may be associated with emotional status,[35] associations are observed with other factors as well. Lower performance on neuropsychological tests has been observed with older age and fewer years of education.[36] However, firm evidence of such an association to self-reported executive function after moderate and severe TBI has not yet been established. A positive relationship has been reported between self-reported executive problems and Glasgow Coma Scale score (GCS),[35,37] but to our knowledge reports of an association with duration of PTA is lacking. While no association between self-reported executive problems and findings on early CT scans is established,[35] focal lesions in the orbitofrontal cortex demonstrated on MRI have been observed to be associated with perceived executive dysfunction.[29] Moreover, TBI and especially traumatic axonal injuries (TAI), typically cause widespread damage localized in fronto-temporal and sub-cortical structures affecting functional neural networks.[38] Especially complex and multidimensional functions as executive functions rely upon network interactions between several cortical, subcortical and cerebellar brain regions with frontal projections.[39-41] Therefore perceived executive functions may be

hypothesized to be vulnerable to TAI.[42-44] To our knowledge, such an association has not yet been reported. Further complicating the picture is that the relationship between self-reported and performance-based executive function after TBI is far from established.[45-47] In cases in which associations were observed, they were in the small to moderate range.[21,45,47,48] Taken together, exploration of associations between demographic factors and injury characteristics, as well as early emotional and cognitive function, and long-term self-reported executive function is still warranted.

Further, development of depression and anxiety after TBI have been observed to be associated with low socioeconomic resources (i.e., fewer years of education),[12,49] while aggression and anti-social personality problems have been found to be associated with age.[12, 33, 34] Evidence of associations between injury severity and later neuropsychiatric problems have been conflicting,[12,33,50,51] with some with some studies reporting no association at all.[52] Furthermore, the occurrence of mood disorders has been related to dysfunction in neural circuits involving cortical and subcortical structures, as well as in neurotransmitter systems.[53] However, only a few studies purporting to examine factors associated with emotional and behavioural problems after TBI have included magnetic resonance imaging (MRI) findings,[54,55] and reviews in the field are inconclusive.[12,33]

The main goal of this prospective study was to delineate the magnitude and profile of self-reported executive and emotional function 2-5 years after moderate and severe TBI. We expected persons with TBI to endorse more problems with executive function (regulation of thoughts, actions, and emotions), and to endorse more symptoms of emotional and behavioural problems (i.e. depression, anxiety, aggression, rule-breaking behaviour) than healthy individuals. Secondly, we aimed to explore a broad array of demographic and injury related factors hypothesized to be associated with self-reported executive and emotional function 2-5 years post-injury. We specifically investigated the predictive value of injury severity measures such as GCS score, length of PTA, and MRI findings recorded in the acute phase, as well as clinical observations during the first year post-injury, such as symptoms of depression, performance-based cognitive function and global outcome.

METHODS

Study design and participants

From October 2004 to July 2008, 236 consecutive patients with moderate and severe TBI according to the Head Injury Severity Scale (HISS) criteria[56] were admitted to the Department of Neurosurgery at St. Olavs Hospital, Trondheim University Hospital, Norway, and registered in a database.[57] Five did not consent to any follow-up. As part of a large follow-up study using advanced MRI for diagnosis and outcome assessment in TBI patients, participants registered in this data base were contacted between February 2009 and August 2010 if they were more than one year post-injury and fulfilled the inclusion criteria: (1) 15-65 years of age at injury; (2) fluency in Norwegian; and (3) Glasgow Outcome Score Extended (GOSE) ≥5. Exclusion criteria were ongoing or pre-injury substance abuse, neurological or psychiatric conditions, or previous moderate to severe TBI.

Of the 231 patients in the database, 51 died, and 85 were excluded because of the age limit (n=40), premorbid or ongoing illness endorsed in the clinical interview during the hospital stay (n=28), not fluent in the Norwegian language (n=4), and GOSE scores <5 (n=13). This left 95 patients eligible for this study, of which 74 (78%) consented (description of patient selection and non-participants in flowchart, appendix, figure 1). Seven were excluded from analysis owing to invalid questionnaire completion, which left 67 TBI survivors for the full analysis.

A subgroup of patients (n = 49) had participated in a previous study with enrolment between October 2004 – October 2007. This study used a neuropsychological test battery to assess cognitive function 3 months post-injury,[57] and these patients were included in the subgroup analysis that investigated the association between subacute neuropsychological test performance and symptoms of depression to self-reported cognitive, emotional, and behavioural function at 2-5 years post-injury.

Sex-, age-, and education-matched healthy control participants were recruited from the family and friends of the patients with TBI, hospital employees, and through

advertisement. Six of 78 recruited controls were excluded because of previously diagnosed psychiatric or neurological conditions (discovered on the day of testing, n=3) or invalid completion of the forms (n=3). As a result, 72 control participants were included.

Assessment between the acute phase and 12 months post-injury

Injury-related variables

GCS score was recorded at or after admittance if the patient deteriorated, or before intubation in cases of pre-hospital intubation. GCS scores of 9-13 were classified as moderate TBI and scores ≤8 were considered severe TBI.[56,57] Duration of PTA was categorized as ≤1 week or >1 week. MRI findings were categorized as the absence or presence of TAI. MRI (1.5 Tesla) was performed at median 10 days post-injury (range = 1-120 days). The scan protocol included T1- and T2-weighted sequences, a T2*-weighted gradient echo sequence, fluid-attenuated inversion recovery (FLAIR) sequences, and diffusion-weighted imaging. MRI parameters and the evaluation procedure have been reported in previous studies.[58,59]

Early cognitive, emotional and global assessment

Global outcome was assessed with the Glasgow Outcome Scale Extended (GOSE) structured interview at 12 months post-injury for all participants recruited from the initial data base (n=66).[60]

The sub-group were assessed at mean 99 ± 10 days post-injury, with performance-based neuropsychological tests grouped into cognitive domains as described in table 1. These tests covered processing speed,[61, 62] attention,[63] memory,[64-66] and executive function.[62,67] T-scores were used in the analysis. These tests have demonstrated adequate validity and reliability.[36] The procedures have been described in previous studies.[10,59] The Vocabulary and Matrix Reasoning sub-tests of the Wechsler Abbreviated Scale of Intelligence (WASI) were used to estimate current IQ.[68] Depressive symptoms were assessed with the Beck Depression Inventory (BDI) at both 3 months (n=47) and 12 months (n=44) post-injury.[69]

Assessment at follow-up (2-5 years post-injury)

Participants completed questionnaires that assessed self-reported executive, emotional, and behavioural problems at mean 2.9 ± 0.9 years post-injury. A few participants were unable to complete all questionnaires. All but one participant were ≥ 18 years of age when completing the questionnaires at follow-up (one was 17 years old). We used a self-report form and an interview to estimate the number of years of education completed at the time of follow-up.

Self-reported executive function

Self-reported executive function was assessed with the BRIEF-A questionnaire, which consists of 75 items that measure behavioural, emotional, and cognitive aspects of executive function. It features sound psychometric properties,[70,71] good reliability, and large-scale norms.[28,70] Each item is rated on a three-point frequency scale (0 = never; 1 = sometimes; 2 = often). Five items are designed to detect invalid response styles (inconsistencies or negativity). Seventy items generate three composite index scores and nine subscale scores. The subscales Inhibit, Shift, Emotional Control, and Self-Monitor generate the Behavior Regulation Index (BRI), while the subscales Initiate, Working Memory, Plan/Organize, Task Monitor, and Organization of Materials constitute the Metacognitive Index (MI). In addition, a Global Executive Composite (GEC) is calculated from all 70 items. Its clinical range is classified as T-score ≥65.

Emotional and behavioural problems

Self-reported emotional and behavioural problems were assessed with the ASEBA: Adult Self-Report Form (ASR).[72] The ASR consists of one section that measures adaptive functioning (38 items) and one section that measures emotional and behavioural problems (126 items) on a three-point scale (0 = statement not true; 1 = statement sometimes true; 2 = statement very true). Eight syndrome scales are generated: anxious/depressed, withdrawn, somatic complaints, thought problems, attention problems, aggressive behaviour, rule-breaking behaviour, and intrusive behaviour. The form yields three composite scores: total problems, internalizing problems (sum of the scales anxious/depressed, withdrawn, and somatic complaints),

and externalizing problems (sum of the scales aggressive, rule-breaking, and intrusive behaviour). The form also yields six DSM-IV-oriented scales: depressive, anxiety, somatic, avoidant personality, attention deficit hyperactivity disorder (ADHD), and antisocial personality problems. Items considered critical to diagnostic categories in the DSM-IV constitute the critical items scale.

The ASEBA reference manual[72] recommends using raw scores when presenting descriptive data, and borderline range using T-scores as the threshold in research (clinical cut-off). The clinical range is classified as T-score ≥70 and the borderline range is classified as T-score ≥65 for the syndrome scales; the respective ranges are classified as T-score ≥63 and ≥60 for the composite scales.[72] The subscales inattention and hyperactivity/impulsive are set at ≥97th percentile and ≥93rd percentile, respectively.

Ethics

The Regional Committee for Medical Research Ethics approved the study protocol. Written consent was obtained from patients aged ≥16 years at injury and from both participants and their parents if patients were aged <16 years at injury.

Statistical methods

Demographic characteristics, injury severity characteristics, and the different cognitive domains are presented as mean (±standard deviation, SD) for normally distributed data, and otherwise as median with interquartile range (IQR; 25th to 75th percentile). For missing data, we used available case analysis, utilizing all cases for which the variables were present. Independent samples *t*-tests based on 2000 bootstrap samples were used for between-group comparisons (controls vs. patients with TBI). The Kruskal-Wallis test and Mann-Whitney U test were used for non-normally distributed data. Effect sizes were calculated as Cohen's *d* based on pooled variance (d_{pooled}).[73] Cohen defined a *d* of 0.8 as large, 0.5 as medium, and 0.2 as small effect sizes.[74] Proportions were compared using the chi-squared test, the unconditional z-pooled test,[75] and the Newcombe confidence interval.[76,77]

Linear regression analyses were performed with composite scores from BRIEF-A and ASR as dependent variables; pre-injury variables, injury-related variables, neuropsychological test scores at 3 months post-injury, GOSE scores, and BDI were employed as covariates. These covariates were included separately and then adjusted for age at injury and length of education at follow-up. An additional linear regression analysis was performed with main indexes and composite scores from BRIEF-A and ASR as dependent variables, and the presence of TAI employed as a covariate with adjustment for BDI. Pearson's correlation coefficient (r) was used to analyse associations between the main indexes on BRIEF-A and the symptom scales on ASR.

We reported 95% confidence intervals (CIs) where relevant, and two-sided p-values <0.05 were considered statistically significant. P-values between 0.01 and 0.05 should be interpreted with caution owing to multiple hypotheses. Statistical analyses were performed with SPSS 18.0.

RESULTS

Participant characteristics are presented in table 2 for the full sample and in appendix, table 2 for the sub-sample. Individuals with TBI and healthy controls did not differ regarding distribution of sex, age at testing, or years of education. Participants with TBI assessed at 3 months post-injury exhibited significantly lower estimated IQ, and reduced processing speed, memory, and executive function compared with controls. At 2-5 years post-injury a higher proportion of individuals with TBI neither worked nor attended school (18%) compared with controls (6%, difference in proportions: 12%; p=0.03).

Self-reported executive function 2-5 years post-injury

Individuals with TBI reported more problems on all three composite indexes of BRIEF-A (GEC, BRI, and MI) than healthy controls (table 3). Effect sizes were in the moderate range (0.38 – 0.66). More respondents with TBI (18%) reported symptoms in the clinical range on the GEC (difference in proportions; 17%, p<0.001), BRI (8%; difference in proportions, 7%; p=0.02), and MI (20%; difference

in proportions, 18%; $p<0.001$). On the BRI subscales, participants with TBI also reported more difficulties with inhibition, set-shifting, emotional regulation, and self-monitoring, with effect sizes in the medium range. On the MI subscales, individuals with TBI reported more problems with working memory than healthy controls, with 37% reporting working memory problems in the clinical range (difference in proportions, 32%; $p<0.001$).

Emotional and behavioural outcome 2-5 years after TBI

On the ASR adaptive scales, respondents with TBI reported significantly fewer personal strengths than healthy controls. They did not differ from controls with regard to problems in their family relationships or friendships. On the composite scales Total problems, Internalizing problems and Externalizing problems, persons with TBI reported significantly more problems compared with controls (table 4). Effect sizes were in the medium range (0.40-0.68). A greater proportion of individuals with TBI (20%) reported problems in the clinical range on the scales Total problems (difference in proportions, 18%; $p=0.002$), Internalizing problems (24%; difference in proportions, 16%; $p=0.05$), and Externalizing problems (14%; difference in proportions, 12%; $p=0.016$). On the syndrome scales, individuals with TBI also reported more problems with anxiousness/depression, somatic complaints, thought problems, attention problems, and aggressive behaviour than healthy controls. Among the DSM-IV-oriented scales, respondents with TBI reported higher scores for depression, anxiety, somatic problems, and attention problems. They also reported higher scores than controls on critical items (d: 0.84).

Factors associated with executive, emotional, and behavioural problems at follow-up

Fewer years of education predicted endorsement of greater problems on the GEC and BRI, but not on the MI (table 5). TAI on MRI during the early phase predicted more problems on GEC and BRI, while GCS score and duration of PTA did not. However, the association between TAI and the GEC and BRI did not reach statistical significance when adjusted for age and education. Neuropsychological test performance at 3 months post-injury was not associated with any of the BRIEF-A

scales (β ranging from -0.187 to 0.137, p>0.05 for all; see appendix 3 for full overview). Depressive symptoms at 3 months post-injury predicted metacognitive problems (MI) at follow-up, while depressive symptoms 1 year after injury predicted later executive problems on all the main indexes. Lower GOSE score at 12 months post-injury predicted more problems on all main indexes at follow-up.

Younger age at injury predicted more emotional and behavioural problems at follow-up, particularly regarding externalizing problems (table 6). Presence of TAI on early MRI predicted higher scores on ASR Total problems and Internalizing problems. Only the association with Internalizing problems persisted after adjusting for age at injury and length of education. However, the presence of TAI still predicted higher scores on ASR Total problems and Internalizing problems, when adjusting for depressive symptoms 3 months post-injury. More depressive symptoms at both 3 and 12 months post-injury predicted later high scores on ASR Total problems, and depressive symptoms 12 months post-injury predicted both internalizing and externalizing problems at follow-up.

Lower GOSE score at 12 months post-injury predicted later high scores on both ASR Total problems and Internalizing problems when adjusted for age and education. Neuropsychological test performance at 3 months post-injury was not associated with any of the ASR scales (β ranging from -0.086 to 0.588, p>0.05 for all; see appendix table 3 for full overview).

Concurrent status of employment was not associated with any main BRIEF-A index or ASR composite score (β: -5.151 to 2.954, p>0.05 for all). Patients that reported more problems on the ASR symptom scales also reported more problems on the GEC, with correlation coefficients ranging from 0.327 (thought problems) to 0.823 (attention problems; p<0.001 for all). This pattern held true also for the indexes BRI (r: from 0.242 to 0.716, p<0.01 for all) and MI (r: 0.283 to 0.816, p<0.001 for all). An exception was ASR intrusive behaviour, which was associated only with BRI (r: 0.27, p=0.027), and not with GEC (r: 0.20, p=0.112) or MI (r: 0.12, p=0.319; see appendix table 4 for full overview).

DISCUSSION

In this large, prospective longitudinal study, our main aim was to delineate the magnitude and profile of chronic problems with executive, emotional and behavioural function experienced by individuals with moderate to severe TBI 2-5 years post-injury. The present study is one of the largest to use BRIEF-A as an outcome measure after TBI, the first to include the comprehensive questionnaire ASR to assess a wide array of emotional and behavioural problems after TBI, and the first to include a large demographically matched control group.

Greater, perceived overall executive problems were reported by TBI individuals compared with healthy controls. This was evident both in terms of group differences and the frequency of individuals reporting problems in the clinical range, corroborating previous studies in TBI populations[21] and other populations with neurological deficits.[29,78] However, group differences did not always indicate symptoms above the clinical cut-off. This observation suggests that sub-clinical problems are commonly experienced within the group as a whole which may add to the total symptom burden for individuals with TBI.

In particular, perceived problems with attentional control and monitoring ongoing operations were frequently reported, supporting previous studies assessing populations with other neurological deficits.[29,78,79] Problem-solving, initiation and task monitoring were not perceived as problematic among individuals with TBI in our study, which is in contrast to a study comprising moderate and severe TBI survivors, where these functions were perceived as most problematic.[21] However, the lack of control group and greater proportion of severe TBI in the prior study[21] make these findings difficult to compare.

We observed that participants with TBI experienced more problems with inhibition, mental flexibility, and emotional regulation. Controlling emotional and behavioural expression is important for social and occupational functioning. However, our respondents with TBI did not report more withdrawal, or problems with social

relations, although these features have been reported in other studies.[12,80] A substantial proportion of moderate TBI in our study may reduce the risk of underestimating their problems due to problems with self-awareness.[81] Although respondents with TBI did not report any problems in their family relationships and friendships, they perceived regulating their emotions and behaviour as prominent problems, which suggests that this area is an important target in post-TBI rehabilitation.

Another important finding was the high burden of internalizing problems among respondents with TBI. They more often reported feeling sad or depressed, which corroborates previous studies.[33,34] The individuals with TBI also reported more problems with externalizing and aggressive behaviour than healthy controls, which is in line with the literature reviewing long-term psychiatric outcome after TBI.[15,49] In our study, persons with TBI did not report more rule-breaking behaviour (lack of empathy, substance abuse, and law-breaking behaviour) or intrusive behaviour, which suggests that the aggression scale encompasses the most prominent post-TBI behavioural problems. The aggression scale on ASR consists of several items related to behavioural control, and we speculate that executive problems (e.g., impaired inhibition and reduced task monitoring/switching)[23] may mediate the behavioural and emotional problems experienced by individuals after TBI.[49]

Our results demonstrated greater perceived problems with emotional regulation among respondents with TBI than healthy controls. Particularly excessive mood swings were commonly reported, which reportedly indicates an increased risk of psychiatric diagnoses.[72] The main concerns reported by participants with TBI were related to perceived negative self-image, indicating that addressing positive re-appraisal of the self-image as important in post-TBI rehabilitation. We believe that the ASR may prove to be valuable as a tool during post-TBI clinical assessment because it incorporates a broad range of symptoms, but that a single mean composite profile does not typify the emotional and behavioural sequelae reported in the TBI population.[33,34]

Factors associated with self-reported executive, behavioural, and emotional problems

One important finding was that self-reported symptoms of depression within the first year post-injury predicted later perceived overall problems with goal-directed cognitive and behavioural regulation, in addition to externalizing and internalizing problems. Notably, the participants had no previous psychiatric disorder, suggesting the depressive symptoms developed secondary to the TBI. Particularly, respondents with TBI that reported depressive symptoms at 12 months post-injury had high risk of experiencing later cognitive and emotional problems, corroborating studies showing that emotional distress affects the extent of self-reported cognitive problems.[29,32] Adaptive problems in every-day life due to the impairments after TBI in combination with the negative thinking typically experienced during depression,[82] may result in a negative spiral, leading to the increase in self-reported depressive symptoms found in our study. We believe that the present study demonstrates that signs of depression should be routinely assessed during rehabilitation, as it seems to be an important warning of future emotional problems.

Extending previous studies, our results also suggest that TAI plays a contributing role in the development of perceived internalizing problems (e.g. anxiety and depression) and behaviour regulation. This association persisted even after adjusting for early self-reported depressive symptoms. TAI is a microscopic strain injury of axons and blood vessels in different predilection locations of the brain, typically causing widespread damage often localized in fronto-temporal and sub-cortical structures,[38] also affecting subcortical structures with frontal projections.[4,5] Neuropathological changes after TBI due to damage to neural circuits involving cortical, sub-cortical and limbic structures may cause changes in neurotransmitter systems, hence also affecting development of mood disorders.[53] In combination with the findings that other measures of injury severity were not associated with later self-reported problems,[35] this suggests that the pathophysiological processes associated with TAI have a distinct effect on later perceived problems with emotional and behavioural regulation as long as 2-5 years after injury. However, both focal and diffuse damage affects the neural pathways necessary for optimal function,[24] and the

group without TAI in our study was small. Hence, some caution should be applied to these findings. Also, age at injury and length of education may have a confounding effect on the association observed with regard to self-reported behaviour regulation. Due to the heterogenetic nature of TBI,[83] larger future studies that distinguish focal damage from TAI are necessary for understanding the neural underpinnings of self-reported executive, emotional, and behavioural problems. Still, our study underscores the clinical importance of early MRI to detect TAI using standard procedures that are easily implemented in the clinic.

Younger age at injury and early symptoms of depression in the present study predicted more self-reported externalizing problems ≤ 2 years post-injury, which is in accordance with previous studies that employed methods of retrospective assessment[14] or cluster analysis.[34] Other reports have indicated that more years of education and higher socioeconomic status are associated with lesser endorsement of emotional and behavioural problems,[34] which was not confirmed in our study. Good access to health services regardless of socioeconomic background and the community welfare system in Norway compared to other countries may contribute to this finding. Further, the aggressive behaviour in participants who were younger at the time of injury could be explained by increased vulnerability to injury in rapidly developing brain areas.[84] The frontal lobe is still maturing during adolescence and young adulthood, rendering functions located therein (e.g., emotional and behavioural regulation) at increased risk following injury.[85,86] Furthermore, age was not associated with symptoms of depression, anxiety, or somatic complaints among individuals with TBI. This suggests the presence of distinct pathways and risk factors in the development of depression and anxiety as opposed to aggression, as others have also indicated.[34]

Respondents with fewer years of education reported more problems with goal-directed cognitive and behavioural regulation. While these functions are important in academic education, our results may reflect both pre-injury characteristics and the ability to complete education after the injury. Reduced global outcome one year post-injury, including less ability to resume social relationships or leisure activities, was

associated with more reported executive and internalizing problems. Experiencing reduced global function may lead to a negative self-image and the increased endorsement of problems. However, the reported executive problems may also reflect cognitive impairment caused by the injury.

In our sub-group analysis, we observed no association between performance-based measures of cognitive function three months post injury and later self-reported executive, emotional and behavioural function, which is in contrast to other studies demonstrating associations between performance-based and self-reported measures of task monitoring and switching.[21,29] The lack of convergence among the data may be explained by the time interval between the assessments, or by different modes of measurement.[85] It has been argued that performance-based measures of executive function provide insight into the efficiency of processing, while rating scales of executive function provide information about success in rational goal pursuit in everyday life.[47] Another explanation is that self-reported cognitive complaints are affected by emotional symptoms[22,29,87] while performance-based measures of executive function are more closely linked to neural damage after TBI.[1,22,29] It is also possible that the assessment methods are complementary and reflecting different neural networks.[29] Given the multifaceted and complex nature of executive dysfunction after TBI, further validation of both performance-based and self-report measures of executive function is needed.

Study limitations

Our main aim was to study how individuals with TBI experience their life after TBI, which also guided the development of the study design. Because we used only self-report questionnaires, we lost any additional information that might have been provided by family members. However, several studies have shown good correspondence between reported symptoms from patients and family members.[1,21,29] Also, the lack of diagnostic interview or a broad concurrent neuropsychological test battery makes our study less optimal for exploring the validity of the BRIEF-A and ASR as proxies for objective cognitive and emotional functioning. Performance-based measures were available for only a sub-group that participated in an earlier

study performed by our research group.[59] These were included in order to explore the association between previous performance-based measures of cognitive function and subsequent self-reported measures. Due to this ad-hoc design, the findings should be interpreted with caution. Moreover, our moderate sample size indicates a need for larger, prospective studies that assess perceived cognitive, emotional, and behavioural problems after moderate and severe TBI.

CONCLUSION

Persons with moderate and severe TBI reported more pronounced difficulties in aspects of executive functions related to attentional control, working memory and emotional regulation, as well as emotional and behavioural problems related to symptoms of depression, anxiety, and aggressive behaviour 2-5 years post injury compared to healthy controls. Both reported symptoms of depression during the first year after injury and the detection of TAI on early MRI was important predictors of later self-reported executive, emotional and behavioural problems. Our findings indicate interplay between demographic, neuropathological and psychological factors during the development of self-reported executive, emotional, and behavioural problems for years after TBI. Hence, early radiological and broad psychological evaluations may give clues as to which patients may be at risk, and for making clinical decisions regarding long-term follow up. In summary, this study yields new information to guide the clinical management of TBI survivors, and provides groundwork for additional clinical research regarding the long-term consequences of TBI.

Declaration of interest:

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REFERENCES

[1] Lannoo E, Colardyn F, Vandekerckhove T, De Deyne C, De Soete G, Jannes J. Subjective complaints versus neuropsychological test performance after moderate to severe head injury. Acta Neurochirurgica (Wien) 1998; 140(3)245-53.

[2] Draper K, Ponsford J, Schonberger M. Psychosocial and emotional outcomes 10 years following traumatic brain injury. Journal of Head Trauma Rehabilitation 2007;22(5):278-87.

[3] Himanen L, Portin R, Isoniemi H, Helenius H, Kurki T, Tenovuo O. Longitudinal cognitive changes in traumatic brain injury: a 30-year follow-up study. Neurology 2006; 66(2): 187-92.

[4] Koponen S, Taiminen T, Portin R, Himanen L, Isoniemi H, Heinonen H, Hinkka S, Tenovuo O. Axis I and II psychiatric disorders after traumatic brain injury: a 30-year follow-up study. American Journal of Psychiatry 2002;159(8):1315-21.

[5] Ponsford J, Draper K, Schonberger M. Functional outcome 10 years after traumatic brain injury: its relationship with demographic, injury severity, and cognitive and emotional status. Journal of the International Neuropsychological Society, 2008. 14(2): p. 233-42.

[6] Millis SR, Rosenthal M, Novack TA, Sherer M, Nick TG, Kreutzer JS, High WM Jr, Ricker JH. Long-term neuropsychological outcome after traumatic brain injury. Journal of Head Trauma Rehabilitation 2001; 16(4): 343-55.

[7] Schretlen DJ, Shapiro AM. A quantitative review of the effects of traumatic brain injury on cognitive functioning. Interntational Review of Psychiatry 2003; 15(4): 341-9.

[8] Dikmen SS, Machamer JE, Powell JM, Temkin NR. Outcome 3 to 5 years after moderate to severe traumatic brain injury. Archives of Physical Medicine and Rehabilitation 2003; 84(10): 1449-57.

[9] Spitz G, Ponsford JL, Rudzki D, Maller JJ. Association between cognitive performance and functional outcome following traumatic brain injury: a longitudinal multilevel examination. Neuropsychology 2012; 26(5): 604-12.

[10] Finnanger TG, Skandsen T, Andersson S, Lydersen S, Vik A, Indredavik MSI. Differentiated patterns of cognitive impairment 12 months after severe and moderate traumatic brain injury. Brain Injury 2013,27(13-14):1606-16

[11] Rapoport MJ. Depression following traumatic brain injury: epidemiology, risk factors and management. CNS Drugs 2012; 26(2): 111-21.

[12] Rogers JM, Read CA. Psychiatric comorbidity following traumatic brain injury. Brain Injury 2007; 21(13-14): 1321-33.

[13] West SL. Substance use among persons with traumatic brain injury: a review. NeuroRehabilitation 2011; 29(1): 1-8.

[14] Baguley IJ, Cooper J, Felmingham K. Aggressive behavior following traumatic brain injury: how common is common? . Journal of Head Trauma Rehabilitation 2006; 21(1): 45-56.

[15] Hesdorffer DC, Rauch SL, Tamminga CA. Long-term psychiatric outcomes following traumatic brain injury: a review of the literature. Journal of Head Trauma Rehabilitation 2009; 24(6): 452-9.

[16] Whelan-Goodinson R, Ponsford J, Johnston L, Grant F. Psychiatric disorders following traumatic brain injury: their nature and frequency. Journal of Head Trauma Rehabilitation 2009. 24(5): 324-32.

[17] Ownsworth T, McKenna K. Investigation of factors related to employment outcome following traumatic brain injury: a critical review and conceptual model. Disability and Rehabilitation 2004; 26(13): 765-83.

[18] Bush BA, Novack TA, Malec JF, Stringer AY, Millis SR, Madan A. Validation of a model for evaluating outcome after traumatic brain injury. Archives of Physical Medicine and Rehabilitation 2003; 84(12): 1803-7.

[19] Malec JF, Brown AW, Moessner AM. Personality Factors and Injury Severity in the Prediction of Early and Late Traumatic Brain Injury Outcomes. Rehabilitation Psychology 2004; 49(1): 55-61.

[20] Reid-Arndt SA, Nehl C, Hinkebein J. The Frontal Systems Behaviour Scale (FrSBe) as a predictor of community integration following a traumatic brain injury. Brain Injury 2007; 21(13-14): 1361-1369.

[21] García-Molina A, Tormos JM, Bernabeu M, Junqué C, Roig-Rovira T. Do traditional executive measures tell us anything about daily-life functioning after traumatic brain injury in Spanish-speaking individuals? Brain Injury 2012; 26(6): 864-74.

[22] Schiehser DM, Delis DC, Filoteo JV, Delano-Wood L, Han SD, Jak AJ, Drake AI, Bondi MW. Are self-reported symptoms of executive dysfunction associated with objective executive function performance following mild to moderate traumatic brain injury? Journal of Clinical Experimental Neuropsychology 2011; 33(6): p. 704-14.

[23] Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, Wager TD. The unity and diversity of executive functions and their contributions to complex "Frontal Lobe" tasks: a latent variable analysis. Cognitive Psychology 2000; 41(1): 49-100.

[24] Stuss DT, Functions of the frontal lobes: relation to executive functions. Journal of the International Neuropsychological Society 2011; 17(5): 759-65.

[25] Stuss DT. Traumatic brain injury: relation to executive dysfunction and the frontal lobes. Current Opinion of Neurology 2011; 24(6): 584-9.

[26] Roth R, Isquith P, Gioia G. Behavior Rating Inventory of Executive Function-Adult Version. 2005, Lutz, FL: PAR.

[27] Gioia GA, Isquith PK. Ecological assessment of executive function in traumatic brain injury. Developmental Neuropsychology 2004; 25(1-2): 135-58.

[28] Malloy P, Grace J. A review of rating scales for measuring behavior change due to frontal systems damage. Cognitive Behavioural Neurology 2005; 18(1): 18-27.

[29] Løvstad M, Funderud I, Endestad T, Due-Tønnessen P, Meling TR, Lindgren M, Knight RT, Solbakk AK. Executive functions after orbital or lateral prefrontal lesions: neuropsychological profiles and self-reported executive functions in everyday living. Brain Injury 2012; 26(13-14): 1586-98.

[30] Ragsdale KA, Neer SM, Beidel DC, Frueh BC, Stout JW. Posttraumatic stress disorder in OEF/OIF veterans with and without traumatic brain injury. Journal of Anxiety Disorders 2013; 27(4): 420-426.

[31] Toglia J, Johnston MV, Goverover Y, Dain B. A multicontext approach to promoting transfer of strategy use and self regulation after brain injury: An exploratory study. Brain Injury 2010; 24(4): 664-677.

[32] Jamora CW, Young A, Ruff RM. Comparison of subjective cognitive complaints with neuropsychological tests in individuals with mild vs more severe traumatic brain injuries. Brain Injury 2012; 26(1): 36-47.

[33] Warriner EM, Velikonja D. Psychiatric disturbances after traumatic brain injury: neurobehavioral and personality changes. Current Psychiatry Report 2006; 8(1): 73-80.

[34] Velikonja D, Warriner E, Brum C. Profiles of emotional and behavioral sequelae following acquired brain injury: cluster analysis of the Personality Assessment Inventory. Journal of Clinical Experimental Neuropsychology 2010; 32(6): 610-21.

[35] Chamelian L, Feinstein A. The effect of major depression on subjective and objective cognitive deficits in mild to moderate traumatic brain injury. Journal of Neuropsychiatry and Clinical Neuroscience 2006; 18(1): 33-8.

[36] Lezak MD, Howieson DB, Loring DW. Neuropsychological assessment. 4th ed. 2004: Oxford University Press.

[37] Misic-Pavkov G, Novovic Z, Bozic K, Kolundzija K, Kovacevic SI, Drakip D, Lukic T, Jelkić M Forensic aspect of late subjective complaints after traumatic brain injury. European Review of Medical and Pharmacological Science 2012; 16(13): 1806-13.

[38] Gentry LR, Godersky JC, Thompson B. MR imaging of head trauma: Review of the distribution and radiopathologic features of traumatic lesions. American Journal of Roentgenology 1988; 150(3): 663-672.

[39] Dosenbach NU, Visscher KM, Palmer ED, Miezin FM, Wenger KK, Kang HC, Burgund ED, Grimes AL, Schlaggar BL, Petersen SE. A core system for the implementation of task sets. Neuron 2006; 50(5): 799-812.

[40] Olsen A, Brunner JF, Evensen KA, Garzon B, Landrø NI, Håberg AK. The functional topography and temporal dynamics of overlapping and distinct brain activations for adaptive task control and stable task-set maintenance during performance of an fMRI-adapted clinical continuous performance test. Journal of Cognitive Neuroscience 2013; 25(6): 903-19.

[41] Dosenbach NU, Fair DA, Miezin FM, Cohen AL, Wenger KK, Dosenbach RA, Fox MD, Snyder AZ. Distinct brain networks for adaptive and stable task control in humans. Proceedings of the National Academy of Sciences of the United States of America 2007; 104(26): 11073-8.

[42] Little DM, Kraus MF, Joseph J, Geary EK, Susmaras T, Zhou XJ, Pliskin N, Gorelick PB. Thalamic integrity underlies executive dysfunction in traumatic brain injury. Neurology 2010;74(7): 558-64.

[43] Kinnunen KM, Greenwood R, Powell JH, Leech R, Hawkins PC, Bonnelle V, Patel MC, Counsell SJ, Sharp DJ. White matter damage and cognitive impairment after traumatic brain injury. Brain 2011; 134(Pt 2): 449-63.

[44] Scheid R, Walther K, Guthke T, Preul C, von Cramon DY. Cognitive sequelae of diffuse axonal injury. Archives of Neurology 2006; 63(3): p. 418-424.

[45] Chaytor N, Schmitter-Edgecombe M. The ecological validity of neuropsychological tests: a review of the literature on everyday cognitive skills. Neuropsychology Review 2003; 13(4): 181-97.

[46] Chaytor N, Temkin N, Machamer J, Dikmen SS. The ecological validity of neuropsychological assessment and the role of depressive symptoms in moderate to severe traumatic brain injury. Journal of the International Neuropsychological Association 2007; 13(3): p. 377-85.

[47] Toplak ME, West RF, Stanovich KE. Practitioner review: do performance-based measures and ratings of executive function assess the same construct? Journal of Child Psychology and Psychiatry 2013; 54(2): 131-43.

[48] Chaytor N, Schmitter-Edgecombe M, Burr R. Improving the ecological validity of executive functioning assessment. Archives of Clinical Neuropsychology 2006; 21(3): 217-227.

[49] Kim E, Lauterbach EC, Reeve A, Arciniegas DB, Coburn KL, Mendez MF, Rummans TA, Coffey EC; ANPA Committee on Research. Neuropsychiatric complications of traumatic brain injury: a critical review of the literature (a report by the ANPA Committee on Research). Journal of Neuropsychiatry and Clinical Neuroscience 2007; 19(2): 106-27.

[50] Dikmen SS, Bombardier CH, Machamer JE, Fann JR, Temkin NR. Natural history of depression in traumatic brain injury. Archives of Physical Medicine and Rehabilitation 2004; 85(9): 1457-64.

[51] Holsinger T, Steffens DC, Phillips C, Helms MJ, Havlik RJ, Breitner JC, Guralnik JM, Plassman BL. Head injury in early adulthood and the lifetime risk of depression. Archives of General Psychiatry, 2002. 59(1): p. 17-22.

[52] Vaishnavi S, Rao V, Fann JR. Neuropsychiatric problems after traumatic brain injury: unravelling the silent epidemic. Psychosomatics 2009; 50(3): 198-205.

[53] Jorge R, Robinson RG. Mood disorders following traumatic brain injury. International Review of Psychiatry 2003; 15(4): 317-27.

[54] Jorge RE, Acion L, Starkstein SE, Magnotta V. Hippocampal volume and mood disorders after traumatic brain injury. Biological Psychiatry 2007; 62(4): 332-8.

[55] Levin HS, Brown SA, Song JX, McCauley SR, Boake C, Contant CF, Goodman H, Kotrla KJ. Depression and posttraumatic stress disorder at three months after mild to moderate traumatic brain injury. Journal of Clinical Experimental Neuropsychology 2001; 23(6): 754-69.

[56] Stein SC, Spettell C. The Head Injury Severity Scale (HISS): a practical classification of closed-head injury. Brain Injury 1995; 9(5): 437-444.

[57] Teasdale, G., & Jennett, B. (1974). Assessment of coma and impaired consciousness. A practical scale. Lancet, 2(7872), 81-84. doi: S0140-6736(74)91639-0 [pii].

[58] Skandsen T, Kvistad KA, Solheim O, Strand IH, Folvik M, Vik A. Prevalence and impact of diffuse axonal injury in patients with moderate and severe head injury: a cohort study of early magnetic resonance imaging findings and 1-year outcome. Journal of Neurosurgery 2010b; 113; 3; 556-563. doi: 10.3171/2009.9.JNS09626

[59] Skandsen T, Finnanger TG, Andersson S, Lydersen S, Brunner, JF, Vik A. Cognitive Impairment 3 months after moderate to severe traumatic brain injury: a prospective follow-up study. Archives of Physical Medicine and Rehabilitation 2010a; 19; 12; 1904-1913. doi: S0003-9993(10)00756-2 [pii]10.1016/j.apmr.2010.08.021

[60] Wilson JT, Pettigrew LE, Teasdale GM. Structured interviews for the Glasgow Outcome Scale and the extended Glasgow Outcome Scale: guidelines for their use. Journal of Neurotrauma, 1998. 15(8): p. 573-585.

[61] Smith A. Symbol Digit Modality Test, Ninth printing 2002, (SDMT) Manual. 1982: Los Angeles: Western Psychological Services.
[62] Delis DC, Kaplan E, Kramer J. Delis Kaplan Executive Function System. 2001: San Antonio, TX: The Psychological Corporation.
[63] Conners CK, Staff M. Conners' Continuous Performance Test II (CPT II) Computer Program for Windows, Technical Guide and Software Manual. 2000: Toronto, ON: Multi-Health Systems Inc.
[64] Delis DC, Kramer JH, Kaplan E, Ober BA. California Verbal Learning Test, Second edition (CVLT-II). Adult Version, Manual: San Antonio, TX: The Psychological Corporation; 2000.
[65] Trahan DE, Larrabee GJ, Continous Visual Memory Test. 1988: Odessa, FL: Psychological Assessment Resources.
[66] Meyers JE, Meyers KR. Rey Complex Figure test and Recognition Trial: Professional Manual. 1995: Odessa, FL: Psychological Assessment Resources.
[67] Heaton RK. Wisconsin Card Sorting Test, Computer Version -2 Research Edition. 1993: Odessa, FL: Psychological Assessment Resources, Inc.
[68] Wechsler D. Wechsler Abbreviated Scale of Intelligence Scale. 1999: San Antonio, TX: The Psychological Corporation.
[69] Beck AT, Rush A J, Shaw BF. et al., Cognitive therapy of depression. 1979, New York: Guilford Press.
[70] Waid-Ebbs JK, Wen PS, Heaton SC, Donovan NJ, Velozo C. The item level psychometrics of the behaviour rating inventory of executive function-adult (BRIEF-A) in a TBI sample. Brain Injury 2012; 26(13-14): 1646-57.
[71] Roth RM, Lance CE, Isquith PK, Fischer AS, Giancola PR. Confirmatory Factor Analysis of the Behavior Rating Inventory of Executive Function-Adult Version in Healthy Adults and Application to Attention-Deficit/Hyperactivity Disorder. Archives of Clinical Neuropsychology 2013; 28(5): 425-434.
[72] Achenbach TM, Rescorla LA. Manual for the ASEBA Adult Forms & Profiles. 2003. Burlington VT, USA: University of Vermont, Research Center for Children, Youth and Families
[73] Grissom RJ, Kim JJ, Effect Sizes for Research. A Broad Practical Approach. 2005: Lawrence Erlbaum Associates, Inc.
[74] Cohen J. Statistical Power Analysis for the Behavioral Sciences. 2nd ed. 1988: Hillsdale, NJ: Erlbaum.
[75] Lydersen S, Fagerland MW, Laake P. Recommended tests for association in 2 x 2 tables. Statistics in Medicine 2009; 28(7): 1159-75.
[76] Altman D, Bryant T, Gardner S. (ed). Statistics with Confidence: Confidence intervals and statistical guidelines. 2000: John Wiley & Sons.
[77] Fagerland MW, Lydersen S, Laake P. Recommended confidence intervals for two independent binomial proportions. Statistical Methods in Medical Research. 2011.
[78] Rabin, L.A., et al., Self- and informant reports of executive function on the BRIEF-A in MCI and older adults with cognitive complaints. Archives of Clinical Neuropsychology 2006; 21(7): p. 721-32.
[79] Rotenberg-Shpigelman S, Rapaport R, Stern A, Hartmen-Maeir A. Content validity and internal consistency reliability of the Behavior Rating Inventory of Executive Function-Adult Version (BRIEF-A) in Israeli adults with attention-

deficit/hyperactivity disorder. Israeli Journal of Occupational Therapy 2008; 17(2): 77-96.

[80] Hoofien D, Gilboa A, Vakil E, Donovick PJ. Traumatic brain injury (TBI) 10-20 years later: a comprehensive outcome study of psychiatric symptomatology, cognitive abilities and psychosocial functioning. Brain Injury 2001; 15(3): 189-209.

[81] Prigatano GP. Impaired self-awareness after moderately severe to severe traumatic brain injury. Acta Neurochirurgica Supplemental 2005; 93: 39-42.

[82] Seel RT, Macciocchi S, Kreutzer JS. Clinical considerations for the diagnosis of major depression after moderate to severe TBI. Journal of Head Trauma Rehabilitation 2010; 25(2):99-112.

[83] Maas AI, Stocchetti N, Bullock R. Moderate and severe traumatic brain injury in adults. Lancet Neurology 2008; 7(8): 728-41.

[84] Johnston MV. Neurotransmitters and vulnerability of the developing brain. Brain Development 1995; 17(5): 301-6.

[85] Cicerone K, Levin H, Malec J, Stuss D, Whyte J. Cognitive rehabilitation interventions for executive function: moving from bench to bedside in patients with traumatic brain injury. Journal of Cognitive Neuroscience 2006; 18(7): 1212-22.

[86] Stuss DT. Science mirroring reality: an improbable journey into the functions of the frontal lobes. Archives of Clinical Neuropsychology 2013; 28(1): 1-8.

[87] Funderud I, Lindgren M, Løvstad M, Endestad T, Voytek B, Knight RT, Solbakk AK. Differential Go/NoGo activity in both contingent negative variation and spectral power. PLoS One 2012; 7(10): e48504. doi: 10.1371/journal.pone.0048504

Table 1. Overview of performance-based neuropsychological tests assessing cognitive function in the sub-sample grouped into cognitive domains 3 months after TBI.

Neuropsychological tests			Reference
Motor function			
Grooved Pegboard,	Dominant hand		[29]
Information processing speed			
Delis Kaplan Executive Function System:		(D-KEFS)	(220)
Trail Making Test	Condition 2 (number sequencing)	(TMT)	
	Condition 3 (letter sequencing)		
Color-Word Interference Test	Condition 1 (color naming)	(CWIT)	
	Condition 2 (word reading)		
Symbol Digit Modality Test	Oral version	(SDMT)	[38]
	Written version		
Attention			
Conners' Contiuous Performance Test II		(CPT-II)	[40]
Visual memory			
Continuous Visual Memory Test		(CVMT)	[42]
Rey-Osterrieth Complex Figure Test*		(ROCF)	[43]
Verbal memory			
California Verbal Learning Test - II		(CVLT-II)	[41]
Executive function			
Wisconsin Card Sorting Test computer version		(WCST)	[44]
Verbal Fluency Test (D-KEFS)	Condition 1 (letter fluency),		[39]
	Condition 3 (category change)		
TMT (D-KEFS)	Condition 4 (Number-Letter Sequencing)		
CWIT (D-KEFS)	Condition 3 (Inhibition)		
	Condition 4 (Inhibition/Switching)		
Tower Test (D-KEFS)			

Table 2. Description of participants: demographics, injury severity characteristics, and clinical observations at 1 and 2-5 years after moderate and severe TBI: global outcome and employment.

Variable	*n*	Persons with TBI		*n*	Controls		*p*-value
Demographics at injury							
Male sex (n, %)	67	48	(72)	72	55	(76)	0.593 *
Age (mean, range)	67	29	(15-63)				
Injury related variables							
Mechanisms of Injury	67						
Traffic accident (n, %)		33	(49)				
Fall (n, %)		27	(40)				
Ski accident (n, %)		2	(3)				
Other (n, %)		5	(9)				
GCS score (median, IQR)	67	9	(7)				
HISS grade; moderate TBI (n, %)	67	39	(58)				
PTA <1 week (n, %)	66	37	(55)				
Early MRI findings	65						
EDH only (n, %)		1	(2)				
Pure TAI (n, %)		17	(25)				
Cortical contusions (n, %)		16	(24)				
Cortical contusions/TAI (n, %)		30	(45)				
Global outcome 12 months post-injury							
GOSE score (median, IQR)	66	7.0	(2)				
Demographics at follow-up							
Age (mean, range)	67	32	(17-65)	72	33	(13)	0.683 †
Years post-injury (mean, SD)	67	2.9	0.8				
Years education (mean, range)	67	12	(9-18)	72	12	(2)	0.979 †
Occupation	67			72			0.025 ‡
Unemployed/no school (n, %)		12	(18)		4	(6)	
Employed or at school (n, %)		55	(82)		68	(94)	

GCS = Glasgow Coma Scale; GOSE: Glasgow Outcome Scale Extended; IQR = inter quartile range; PTA = post-traumatic amnesia; SD = standard deviation; TAI = traumatic axonal injury; TBI = traumatic brain injury

* Pearson's Chi-squared test

† Independent samples *t*-test

‡ Unconditional z-pooled test

Table 3. Self-reported executive function on BRIEF-A at 2 – 5 years after moderate and severe traumatic brain injury compared to healthy controls*

BRIEF – A (T-scores)	Persons with TBI n=67		Controls n= 72		Mann-Whitney test	Effect size
	Mean	SD	Mean	SD	p-value	*d*†
Global scales						
Global Executive Composite (GEC)	51.40	(11.94)	46.19	(7.28)	**0.003**	0.53
Behavior regulation Index (BRI)	50.69	(11.13)	44.51	(7.28)	**<0.001**	0.66
Metacognitive Index (MI)	51.81	(11.90)	48.02	(7.57)	**0.029**	0.38
Behavioral and emotional regulation scales						
Inhibit	51.84	(10.57)	47.72	(8.87)	**0.014**	0.42
Shift	49.52	(11.04)	44.64	(7.01)	**0.003**	0.53
Emotional regulation	51.61	(11.45)	44.88	(7.81)	**<0.001**	0.69
Self-monitor	47.87	(10.70)	44.54	(7.74)	**0.039**	0.36
Metacognitive Index Scales						
Initiate	51.87	(11.68)	48.61	(9.86)	0.079	0.30
Working Memory	57.48	(13.01)	47.89	(7.91)	**<0.001**	0.89
Plan/organize	50.54	(11.00)	47.61	(7.45)	0.071	0.31
Task Monitoring	50.97	(11.90)	48.88	(7.27)	0.217	0.21
Organization of materials	46.60	(11.54)	48.49	(8.35)	0.268	-0.19

Higher T-scores indicate more problems.

* Central tendency and variance given as mean and SD.

† Cohen's *d*

Table 4. Self-reported adaptive function, personal strengths and psychological problems on ASR at 2 – 5 years after moderate and severe traumatic brain injury compared to healthy controls.

Adult Self-Report	Persons with TBI n=66		Controls n= 71		Mean difference (95 % CI) †		t-test	Effect size
	Mean	SD	Mean	SD	Lower	Upper	p	*d*‡
Adaptive scores*								
Personal strengths	16.18	(3.18)	17.39	(3.09)	-2.26	-0.15	**.025**	**.39**
Mean adaptive	49.61	(5.44)	50.15	(4.32)	-2.21	1.13	.523	.11
Relation to friends	9.82	(2.00)	10.00	(1.82)	-0.82	0.46	.580	.09
Relation to family	1.57	(0.44)	1.49	(0.37)	-0.06	0.22	.246	-.20
Composite scales								
Total problems	39.17	(26.08)	26.13	(16.67)	5.57	20.51	**.001**	**.60**
Internalizing problems	12.44	(9.81)	7.08	(5.42)	2.64	8.07	**<.001**	**.68**
Externalizing problems	9.05	(8.59)	6.24	(5.05)	0.40	5.22	**.023**	**.40**
Critical Items	4.95	(3.64)	2.46	(2.22)	1.46	3.52	**<.001**	**.83**
Syndrome scales								
Anxious/depressed	6.48	(6.29)	3.34	(3.26)	1.43	4.87	**<.001**	**.63**
Withdrawn	2.27	(2.22)	1.75	(1.93)	-0.17	1.27	.139	.25
Somatic complaints	3.68	(2.81)	2.00	(2.08)	0.84	2.52	**<.001**	**.68**
Thought problems	2.09	(2.26)	1.01	(2.25)	0.31	1.84	**.006**	**.48**
Attention problems	7.73	(5.37)	4.96	(3.72)	1.19	4.32	**.001**	**.60**
Aggressive behavior	4.76	(4.55)	2.01	(2.46)	1.49	4.00	**<.001**	**.75**
Rule-breaking behavior	2.70	(3.49)	2.21	(2.12)	-0.50	1.47	.331	.17
Intrusive behavior	1.59	(1.96)	2.01	(1.89)	-1.07	0.23	.200	-.22
DSM-IV oriented scales								
Depression	5.02	(4.52)	2.70	(2.47)	1.06	3.56	**<.001**	**.64**
Anxiety	3.12	(2.67)	2.00	(2.00)	0.32	1.92	**.007**	**.47**
Somatic	2.21	(2.17)	1.30	(1.57)	0.28	1.55	**.005**	**.48**
Avoidant personality problems	2.32	(2.02)	2.11	(1.88)	-0.45	0.86	.538	.11
ADHD problems	7.20	(4.86)	4.85	(3.69)	0.88	3.82	**.002**	**.54**
Inattention	3.88	(2.81)	2.37	(2.10)	0.67	2.36	**.001**	**.61**
Hyperactivity/impulsivity	3.32	(2.53)	2.48	(2.21)	0.04	1.64	**.040**	**.35**
Antisocial personality problems	3.50	(4.44)	2.66	(2.73)	-0.41	2.11	.182	.23

Central tendency and variance measured in mean and SD (raw scores). Higher scores indicate more problems.

* Higher scores indicate *better* function

† Results from t-test based on 2000 bootstrap samples.

‡ Cohen's *d*

Table 5. Demographic and clinical factors during 1th year post-injury associated with self-reported executive function (BRIEF-A) 2-5 years after moderate and severe TBI.

Dependent variable		Regression coefficient for worse outcome, unadjusted				Regression coefficient for worse outcome, adjusted*			
Independent variables	**N**	**R2**	**Estimate**	**95% CI**	**p-value**	**R2**	**Estimate**	**95% CI**	***p*-value**
Global Executive Composite									
Age at injury	67	0.049	-0.405	-0.850 to 0.040	0.074				
Years of education at injury	67	0.067	-3.076	-5.934 to -0.219	**0.035**				
PTA duration (1 week)	66	0.000	-1.103	-11.832 to 14.038	0.856	0.114	-1.273	-14.425 to 11.880	0.847
GCS score	67	0.003	-0.421	-2.279 to 1.437	0.652	0.098	-0.011	-1.861 to 1.838	0.990
Presence of TAI	65	0.063	14.140	0.279 to 28.002	**0.046**	0.150	10.616	-3.164 to 24.396	0.129
Presence of TAI adjusted for BDI 3 months post-injury	48	0.048	12.012	-2.957 to 26.980	0.113				
BDI 3 months post injury	48	0.066	1.442	-0.192 to 3.075	0.082	0.117	1.579	-0.010 to 3.167	0.051
BDI 1 year post injury	45	0.277	2.224	1.105 to 3.343	**<0.001**	0.337	2.070	0.941 to 3.199	**0.001**
GOSE score 1 year post injury	67	0.087	-6.720	-12.161 to -1.279	**0.016**	0.231	-9.280	-14.945 to -3.615	**0.002**
Behaviour Regulation Index									
Age at injury	67	0.040	-0.159	-0.352 to 0.033	0.103				
Years of education	67	0.063	-1.277	-2.496 to -0.059	**0.040**				
PTA duration (1 week)	66	0.003	-1.148	-6.691 to 4.396	0.680	0.109	-1.806	-7.351 to 3.738	0.517
GCS score	67	0.005	-0.229	-1.030 to 0.572	0.570	0.089	-0.069	-0.870 to 0.733	0.864
Presence of TAI	65	0.059	6.677	0.721 to 12.633	**0.029**	0.143	5.313	-0.648 to 11.275	0.080
Presence of TAI adjusted for BDI 3 months post-injury	49	0.129	6.314	0.286 to 12.343	**0.040**				
BDI 3 months post injury	49	0.043	0.478	-0.195 to 1.152	0.159	0.160	0.546	-0.108 to 1.200	0.099
BDI 1 year post injury	45	0.326	1.046	0.583 to 1.509	**<0.001**	0.381	0.979	0.513 to 1.443	**<0.001**
GOSE score 1 year post injury	67	0.087	-2.910	-5.241 to -0.578	**0.015**	0.216	-3.954	-6.417 to -1.490	**0.002**
Metacognitive Index									
Age at injury	67	0.048	-0.247	-0.520 to 0.026	0.075				
Years of education	67	0.053	-1.665	-3.410 to 0.080	0.061				
PTA duration (1 week)	66	0.000	0.242	-7.670 to 8.1559	0.951	0.099	-0.796	-8.740 to 7.148	0.842
GCS score	67	0.002	-0.192	-1.335 to 0.950	0.737	0.086	0.063	-1.080 to 1.206	0.913
Presence of TAI	65	0.047	7.501	-1.036 to 16.038	0.084	0.130	5.475	-2.964 to 13.961	0.202
Presence of TAI adjusted for BDI 3 months post-injury	49	0.107	5.825	-3.438 to 15.088	0.212				

BDI 3 months post injury	49	0.055	0.968	-0.037 to 1.972	0.059	0.169	1.027	0.041 to 2.014	**0.042**
BDI 1 year post injury	45	0.200	1.136	0.437 to 1.834	**0.002**	0.248	1.029	0.318 to 1.741	**0.006**
GOSE score 1 year post injury	67	0.068	-3.653	-7.009 to -0.298	**0.033**	0.197	-5.244	-8.796 to -1.692	**0.004**

* adjusted for age at injury and years of education prior to the injury

BDI = Beck Depression Inventory; BRIEF-A = Behavioral Rating Inventory for Executive Function – Adult version; CI = Confidence Interval; GCS = Glasgow Coma Scale; GOSE = Glasgow Outcome Scale Extended; PTA = post-traumatic amnesia; TAI = traumatic axonal injury; TBI = traumatic brain injury

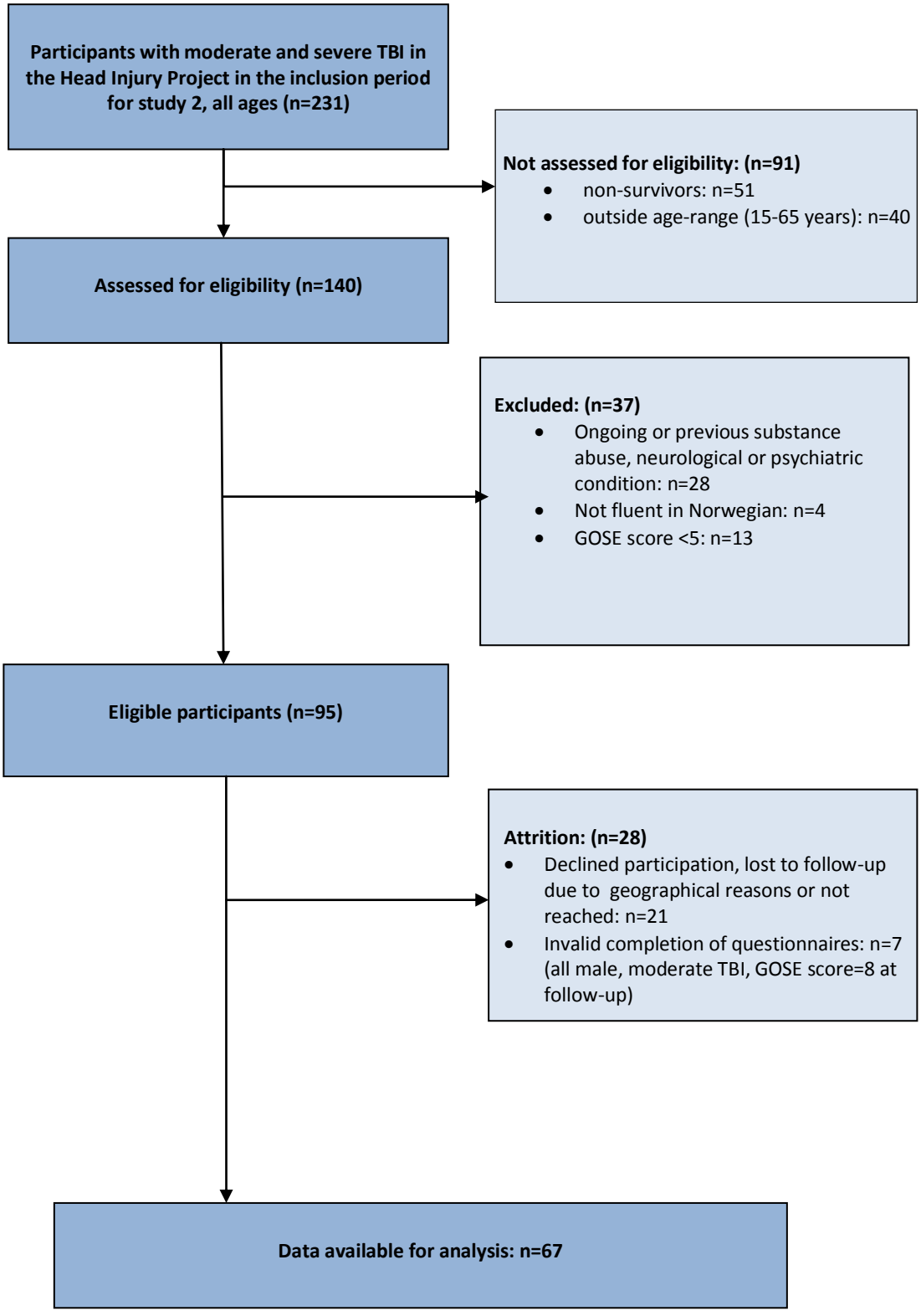
Table 6. Demographic and clinical factors during 1th year post-injury associated with self-reported emotional and behavioural problems (ASR) 2-5 years after moderate and severe traumatic brain injury (TBI).

Dependent variable		Regression coefficient for worse outcome, unadjusted				Regression coefficient for worse outcome, adjusted*			
Independent variables	**N**	**R2**	**Estimate**	**95% CI**	**p-value**	**R2**	**Estimate**	**95% CI**	***p*-value**
ASR Total problems									
Age at injury	66	0.116	-0.640	-1.081 to -0.199	**0.005**				
Years of education at injury	66	0.032	-2.157	-5.143 to 0.828	0.154				
PTA duration (1 week)	64	0.000	-0.796	-14.013 to 12.420	0.905	0.155	4.782	-8.259 to 17.823	0.466
GCS score	66	0.000	0.085	-1.823 to 1.993	0.929	0.141	0.761	-1.090 to 2.613	0.414
Presence of TAI	64	0.076	16.085	1.822 to 30.347	**0.028**	0.185	12.728	-1.276 to 26.733	0.074
Presence of TAI adjusted for BDI 3 months post injury	46	0.315	15..524	1.772 to 29.277	**0.028**				
BDI 3 months post injury	46	0.235	2.845	1.303 to 4.388	**0.001**	0.331	2.868	1.375 to 4.362	**<0.001**
BDI 1 year post injury	43	0.401	2.683	1.662 to 3.705	**<0.001**	0.440	2.518	1.481 to 3.554	**<0.001**
GOSE score 1 year post injury	66	0.020	-3.308	-9.087 to 2.471	0.257	0.210	-7.371	-13.303 to -1.440	**0.016**
ASR Internalizing problems									
Age at injury	66	0.023	-0.106	-0.281 to 0.068	0.228				
Years of education	66	0.006	-0.343	-1.481 to 0.795	0.550				
PTA duration (1 week)	64	0.001	0.495	-4.416 to 5.405	0.841	0.041	1.380	-3.783 to 6.544	0.595
GCS score	66	0.000	0.006	-0.712 to 0.724	0.986	0.027	0.118	-0.623 to 0.859	0.752
Presence of TAI	64	0.075	5.986	0.668 to 11.303	**0.028**	0.097	5.548	0.055 to 11.041	**0.048**
Presence of TAI adjusted for BDI 3 months post injury	46	0.200	6.714	0.641 to 12.787	**0.031**				
BDI 3 months post injury	46	0.110	0.794	0.114 to 1.474	**0.023**	0.137	0.803	0.110 to 1.496	**0.024**
BDI 1 year post injury	43	0.306	0.922	0.490 to 1.354	**<0.001**	0.316	0.886	0.436 to 1.337	**<0.001**
GOSE score 1 year post injury	66	0.040	-1.764	-3.916 to 0.387	0.106	0.104	-2.768	-5.145 to -0.392	**0.023**
ASR Externalizing problems									
Age at injury	66	0.128	-0.221	-0.365 to -0.077	**0.003**				
Years of education	66	0.042	-0.819	-1.797 to 0.159	0.099				
PTA duration (1 week)	64	0.000	0.001	-4.373 to 4.375	1.000	0.174	2.029	-2.239 to 6.297	0.345
GCS score	66	0.001	-0.058	-0.686 to 0.570	0.853	0.157	0.171	-0.434 to 0.776	0.574
Presence of TAI	64	0.023	2.915	-1.859 to 7.689	0.227	0.146	1.630	-3.037 to 6.297	0.488

Presence of TAI adjusted for BDI 3 months post injury	46	0.298	3.525	0.485 to 1.414	0.106				
BDI 3 months post injury	46	0.255	0.917	0.446 to 1.388	**<0.001**	0.369	0.934	0.485 to 1.383	**<0.001**
BDI 1 year post injury	43	0.403	0.761	0.472 to 1.049	**<0.001**	0.446	0.718	0.426 to 1.010	**<0.001**
GOSE score 1 year post injury	66	0.002	-0.307	-2.228 to 1.613	0.750	0.178	-1.450	-3.442 to 0.542	0.151

* adjusted for age at injury and years of education prior to the injury

ASR = Adult Self Report (ASEBA); BDI = Beck Depression Inventory; CI = Confidence Interval; GCS = Glasgow Coma Scale; GOSE = Glasgow Outcome Scale Extended; PTA = post-traumatic amnesia; TAI = traumatic axonal injury; TBI = traumatic brain injury



Appendix, Figure 1.
Flow-chart illustrating sample selection and description of non-participants.

Appendix, Table 2: Description of participants in the subgroup analysis: demographics, injury severity characteristics, and clinical observations at 3 months, 1year and 2-5 years after moderate and severe TBI: cognitive function, emotional function, global outcome and employment.

Variable	*n*	Persons with TBI		*n*	Controls		*p*-value
Demographics							
Male sex (n, %)	49	35	(71)	28	24	(86)	0.593 *
Age at injury (mean, range)	49	30	(14-63)				
Injury related variables							
GCS score (median, IQR)	49	9	(6)				
HISS grade; moderate TBI (n, %)	49	28	(57)				
PTA <1 week (n, %)	48	23	(47)				
Early MRI findings	48						
EDH only (n, %)		1	(2)				
Pure TAI (n, %)		10	(20)				
Cortical contusions (n, %)		14	(29)				
Cortical contusions/TAI (n, %)		23	(48)				
Neuropsychological assessment (3 months post-injury)							
Days post-injury (mean, SD)	49	99	(10)				
Estimated IQ (mean, SD)	47	106	(16)	26	119	(12)	0.001 †
Processing speed (mean, SD)	46	44.5	(10.2)	26	53.0	(4.8)	<0.001†
Attention (mean, SD)	46	49.9	(4.9)	26	51.6	(4.3)	0.124 †
Memory (mean, SD)	46	42.6	(10.0)	26	48.2	(8.3)	0.016 †
Executive function (mean, SD)	47	47.3	(7.6)	26	53.1	(4.8)	0.001 †
Depressive symptoms and global outcome1st year post-injury							
BDI 3 months post-injury (mean, SD)	47	5.5	(4.4)				
BDI 12 months post-injury (mean, SD)	44	6.7	(6.4)				
GOSE score 12 months post-injury (median, IQR)	49	7.0	(2)				
Demographics at follow-up							
Years post-injury (mean, SD)	49	3.2	1.0				
Age (mean, range)	49	34	(17-65)	28	34	(19-64)	0.895 †
Years education (mean, range)	49	12	(9-18)	28	12	(9-18)	0.630 †
Occupation	49			27			

Unemployed/no school (n, %)	10	(20)	1	(4)
Employed or at school (n, %)	55	(82)	26	(96)

Abbreviations: BDI = Beck Depression Inventory; GCS = Glasgow Coma Scale; GOSE: Glasgow Outcome Scale Extended; IQ = Intelligence Quotient; IQR = inter quartile range; PTA = post-traumatic amnesia; SD = standard deviation; TAI = traumatic axonal injury; TBI = traumatic brain injury

* Pearson's Chi-squared test

† Independent samples *t*-test

Appendix, Table 3. Associations between main composite scores on BRIEF-A and ASR 2-5 years after moderate and severe TBI, and neuropsychological test performance 3 months post-injury*

Dependent variable			Regression coefficient for worse outcome		
Independent variable	N	R2	Estimate	95 % Confidence Interval	p-value
BRIEF-A GEC					
Processing speed	47	0.015	-0.143	-0.492 to 0.205	0.413
Attention	47	0.001	-0.077	-0.831 to 0.678	0.839
Memory	46	0.008	0.112	-0.268 to 0.491	0.556
Executive function	48	0.012	-0.167	-0.626 to 0.291	0.467
BRIEF-A BRI					
Processing speed	47	0.015	-0.138	-0.470 to 0.194	0.408
Attention	47	0.006	-0.187	-0.887 to 0.513	0.594
Memory	46	0.004	0.074	-0.285 to 0.433	0.679
Executive function	48	0.011	-0.155	-0.592 to 0.281	0.478
BRIEF-A MI					
Processing speed	47	0.010	-0.115	-0.454 to 0.224	0.497
Attention	47	0.000	0.011	-0.723 to 0.745	0.976
Memory	46	0.013	0.137	-0.225 to 0.500	0.449
Executive function	48	0.009	-0.146	-0.591 to 0.299	0.513
ASR Total problems					
Processing speed	46	0.000	0.059	-0.753 to 0.872	0.883
Attention	46	0.000	0.065	-1.627 to 1.756	0.939
Memory	46	0.046	0.588	-0.229 to 1.405	0.154
Executive function	47	0.002	0.145	-0.933 to 1.223	0.788
ASR Internalizing problems					
Processing speed	46	0.010	0.106	-0.209 to 0.421	0.501
Attention	46	0.000	0.043	-0.620 to 0.705	0.897
Memory	46	0.060	0.260	-0.054 to 0.575	0.102
Executive function	47	0.008	0.126	-0.291 to 0.543	0.545
ASR Externalizing problems					
Processing speed	46	0.001	-0.033	-0.291 to 0.225	0.798
Attention	46	0.002	-0.086	-0.628 to 0.456	0.750
Memory	46	0.020	0.125	-0.138 to 0.388	0.344
Executive function	47	0.000	0.024	-0.318 to 0.367	0.887

* given in T-scores

Abbreviations: ASR = Adult Self-Report, BRIEF-A = Behavior Rating Inventory of Executive Function, BRI = Behavior Regulation Index, GEC = Global Executive Composite, MI = Metacognitive Index, TBI = Traumatic Brain Injury

Appendix, Table 4: Associations between main indexes on BRIEF-A and symptom scales on ASR at 2-5 years after moderate and severe TBI.

ASR Symptom Scales	BRIEF-A Global Executive Composite (GEC)		BRIEF-A Behavior Regulation Index (BRI)		BRIEF-A Metacognitive Index (MI)	
	r	p-value	r	p-value	r	p-value
Anxious/depressed	0.75	<0.001	0.70	<0.001	0.72	<0.001
Withdrawn	0.59	<0.001	0.55	<0.001	0.57	<0.001
Somatic complaints	0.51	<0.001	0.50	<0.001	0.47	<0.001
Thought problems	0.44	<0.001	0.43	<0.001	0.41	0.001
Attention problems	0.86	<0.001	0.77	<0.001	0.83	<0.001
Aggressive behavior	0.62	<0.001	0.72	<0.001	0.49	<0.001
Rule-breaking behavior	0.44	<0.001	0.40	0.001	0.43	<0.001
Intrusive behavior	0.20	0.112	0.27	0.027	0.12	0.319

Abbreviations: ASR = Adult Self-Report, BRIEF-A = Behavior Rating Inventory of Executive Function, BRI = Behavior Regulation Index, GEC = Global Executive Composite, MI = Metacognitive Index, TBI = Traumatic Brain Injury