

Epidemiology and Natural History of Psychiatric Disorders After TBI

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This article outlines the epidemiology of psychiatric disorders in individuals with traumatic brain injury (TBI), with a focus on DSM axis I disorders diagnosed on the basis of structured clinical interview. The epidemiology of psychiatric disorders in the general population is described as a basis for understanding the disorders that occur before and after TBI. For each disorder category, including mood disorders, anxiety disorders, acute stress disorder, post-traumatic stress disorder (PTSD), substance use disorders, psychotic disorders, eating disorders, somatoform disorders, and adjustment disorders, the evidence from retrospective, cross-sectional and prospective studies is reviewed, showing the frequency, time course, and predictors of the disorders. Studies show elevated rates of depressive and anxiety disorders after TBI, most commonly

major depressive disorder and PTSD, usually emerging in the first year postinjury but with delayed onset in severe injury cases. Although individuals with a preinjury history are more likely to develop these disorders, the nature of the disorders may change after injury, and novel psychiatric disorders are also common. Even though the frequency of anxiety disorders diminishes over the years postinjury, depressive disorders are more persistent during postinjury years. Substance use—while high before injury—declines after injury. The frequency of psychotic, eating, somatoform, and adjustment disorders do not exceed population rates.

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For more than a century, traumatic brain injury (TBI) has been associated with changes in psychological functioning, beginning with case reports of traumatic “insanity” and igniting a surge of interest in the role of the brain in personality, behavior, and emotions and the development of idiopathic psychiatric disorders. TBI results in diffuse brain injury, particularly to frontotemporal regions. It causes cognitive, behavioral, and personality changes that in turn can have a major impact on independence, work, study, leisure, and social and personal relationships. Because of the impact of TBI on frontolimbic structures, there is potential for development of organically based psychiatric disorders. Moreover, the experience of disability can have serious psychological consequences. The way a person responds to these impacts will be influenced by the circumstances, severity, and location of the injury, the person’s developmental stage, and preinjury psychosocial adjustment as well as postinjury supports. Psychiatric disorders occur commonly after TBI. We outline the epidemiology and natural history of psychiatric disorders after TBI.

EPIDEMIOLOGY OF PSYCHIATRIC DISORDERS IN THE GENERAL POPULATION

In the U.S. National Comorbidity Survey Replication (N=5,692), 26.2% of respondents received a psychiatric

diagnosis over a 12-month period, and 11.8% received multiple diagnoses. Rates of lifetime disorder were 46.7%, with 40.0% having more than one disorder.^{1,2} Similar rates were obtained in an Australian study, with 20% of respondents meeting *ICD-10* criteria for a psychiatric disorder in the previous 12 months and 8.2% having more than one disorder.³ Almost one-half (45.5%) had a lifetime history of psychiatric disorder. Across all age groups, females had higher rates of 12-month disorders (22%) than males (18%), and rates of disorders declined with age.

METHODOLOGICAL ISSUES IN STUDIES OF PSYCHIATRIC DISORDERS AFTER TBI

The reported frequencies of psychiatric disorder after TBI vary considerably, from 18.3% to 83.3% in the months and years postinjury.^{4,5} This variability is influenced by methods of study recruitment, diagnosis, injury severity, and time postinjury; some studies have made diagnoses in cases up to a decade or more postinjury, relying on retrospective recall of symptoms over many years.

There is variability in the measures used, with some studies using diagnoses documented in medical files and others using gold standard structured clinical interviews. In addition, there are significant challenges in classifying

neuropsychiatric symptoms after TBI. Symptoms commonly associated with TBI, including fatigue, sleep disturbance, irritability, psychomotor slowness, reduced concentration and memory, apathy, and emotional lability, are also characteristic of many psychiatric disorders. Standard classification systems (i.e., *DSM-IV-TR*) employed in TBI psychiatric research do not adequately address the complex neuropsychiatric features of TBI when considering differential diagnoses, specifying only that symptoms of idiopathic psychiatric disorders must not be better explained by a general medical condition.⁶ Thus, potential for misdiagnosis is high.

Most prospective studies have been conducted over only the first year postinjury. Many have predominantly included patients with mild TBI. The vast majority have focused on depression or posttraumatic stress disorder (PTSD). Other studies have examined a range of diagnoses, but many have done so cross-sectionally or retrospectively.

PREINJURY PSYCHIATRIC DISORDERS

There is some evidence to suggest that individuals with TBI have higher than expected rates of preinjury disorder,^{7,8} whereas other findings suggest that rates are generally comparable to the general population.^{9–11} Variability in comparison groups may partially account for this, because the TBI population differs from the general population in certain demographic aspects such as age and gender. Individuals with TBI are more likely to have preinjury alcohol use disorder¹⁰ (Table 1). Alway et al.⁹ found that substance use was the most common preinjury diagnostic class, with 38.5% meeting criteria for alcohol or drug use disorder, which may reflect the relationship between alcohol, risk taking, and injury. Rates of preinjury mood and anxiety disorders were 23.0% and 21.7%, respectively. Preinjury psychotic (4.3%), eating (3.7%), somatoform (0%), and adjustment (9.3%) disorders were relatively rare.

POST-TBI PSYCHIATRIC DISORDERS

Most studies report that rates of psychiatric disorders after TBI are higher than those of the general population, and higher than rates prior to injury^{9–11,17} (Table 1). Studies report elevated frequencies of mood and anxiety disorders that increase throughout the first year postinjury, high comorbidity between disorders, and evidence for different patterns of onset by disorder type.^{4,9–11,18–20} For example, compared with mood disorders, anxiety disorders appear to emerge earlier postinjury.¹⁰ Rates of psychotic, somatoform, eating, and adjustment disorders appear comparable to those of the general population.^{9,10} Postinjury diagnoses differ from those received prior to injury, with a decrease in diagnosis of substance use and an increase in diagnoses of mood and anxiety disorders.^{9,10,17,19}

Results from medical file reviews vary widely, illustrating the limitations of this approach, in which diagnosis depends

on cases presenting to services and on diagnostic methods. In a file review of health plan members in the United States with mild (N=803) or moderate to severe (N=136) TBI, reported rates of psychiatric disorders were 34.0% for mild and 49.1% for moderate to severe TBI respectively during the first year postinjury, 30.2% and 33.0% in the second, and 27.9% and 26.3% in the third.²¹ These figures suggest a decline in disorders over time among those with moderate to severe TBI but not mild TBI.

Smaller file reviews from Denmark²² and New Zealand²³ found much lower rates of 4.0% and 9.3%, respectively. Studies examining postinjury psychiatric disorders retrospectively have reported rates ranging from 48.3% to 83.3%,^{5,17,24,25} implying that psychiatric disorders may continue to emerge after the first year postinjury.

Prospective studies examining a range of psychiatric disorders using structured clinical interviews, mostly limited to the first year postinjury, have reported disorder rates ranging from 18.3% to 60.8% in the first year postinjury. In studies estimating point prevalence, lower rates have been reported in samples with predominantly mild TBI^{4,18} compared with studies including a greater range of diagnoses and injury severity.^{10,11} Only one study, by Alway et al.,⁹ has examined the full spectrum of disorders prospectively over 5 years postinjury. In their sample of predominantly moderate to severe cases of TBI, overlapping with the data set of Gould et al.,¹⁰ 74.5% received a psychiatric diagnosis over the 5 years, commonly emerging within the first year (77.7%). Anxiety, mood, and substance use disorders were the most common diagnostic classes, often presenting comorbidly, and 56.5% experienced a novel diagnostic class not present prior to injury. Disorder frequency ranged between 61.8% and 35.6% over time, with disorder likelihood decreasing by 27.0% with each year postinjury.

MOOD DISORDERS AND TBI

Mood disorders are the most common psychiatric disorder after sustaining a TBI, presenting at rates higher than in the general population.^{4,10,19,20,26} Mood disorders frequently develop without a preinjury psychiatric history^{9–11,18,20,27} and present comorbidly with anxiety disorders in approximately three in four cases.^{10,18,20}

Reported rates of bipolar-type disorders have been relatively low, ranging from 2% to 9% in the first year postinjury.^{10,11,19,28} Major depressive disorders are the most common diagnosis. Prospective studies with predominantly mild TBI samples report fairly consistent point prevalence rates, ranging from 17.0% to 23.1% at 3 months,^{18,28,29} 18.5%–23.2% at 6 months,^{28,30} and 13.9%–18.6% at 12 months^{4,18,28} postinjury.

Results of prospective studies examining the entire first year postinjury and a greater range of injury severity are more variable, with rates ranging from 11.3% to 42.4% for major depressive disorder,^{10,11,19,20,27,28} 1.0% for dysthymia,¹⁰ and 5.3%–19.6% for depression not otherwise

TABLE 1. Frequency of DSM-IV Psychiatric Disorders Among Persons With a Traumatic Brain Injury Compared With the General Population^a

Disorder Category Diagnosis	Lifetime Preinjury Disorders					12-Month Postinjury Disorders				
	N	%	Population Rate (%)	χ^2	p	N	%	Population Rate (%)	χ^2	p
Any disorder	54	52.9				62	60.8			
Recalculated rate of any disorder ^b	42	41.2	45.1		n.s.	38	37.3	19.5	20.36	0.001
Mood disorder	24	23.5				43	42.2			
Recalculated rate of mood disorder ^c	17	16.7	12.6		n.s.	32	31.4	5.5	132.35	0.001
Major depressive disorder	14	13.7	10.9		n.s.	30	29.4	4.2	159.66	0.001
Dysthymic disorder	4	3.9	1.5		n.s.	1	1.0	1.0		n.s.
Bipolar disorder	0	0.0	1.5		n.s.	2	2.0	1.1		n.s.
Depressive disorder not otherwise specified	7	6.9	—			20	19.6	—		
Mood disorder not otherwise specified	1	1.0	—			1	1.0	—		
Anxiety disorder	22	21.6				45	44.1			
Recalculated rate of anxiety disorder ^d	12	11.8	17.8		n.s.	16	15.7	11.1		n.s.
Social phobia	8	7.8	7.8		n.s.	3	2.9	4.2		n.s.
Posttraumatic stress disorder (PTSD)	2	2.0	5.8		n.s.	13	12.7	3.6	24.26	0.001
Panic disorder with/without agoraphobia	2	2.0	3.3		n.s.	2	2.0	1.8		n.s.
Agoraphobia without panic disorder	0	0.0	1.4		n.s.	0	0.0	0.6		n.s.
Obsessive-compulsive disorder (OCD)	0	0.0	4.1		n.s.	1	1.0	3.1		n.s.
Generalized anxiety disorder	1	1.0	5.1		n.s.	2	2.0	1.7		n.s.
Anxiety disorder not otherwise specified	6	5.9	—			36	35.3	—		
Specific phobia	6	5.9	—			7	6.9	—		
Substance-induced anxiety disorder	1	1.0	—			1	1.0	—		
Acute stress disorder	0	0.0	—			1	1.0	—		
Substance use disorder	35	34.3	31.9		n.s.	12	11.8	8.65		n.s.
Alcohol abuse	16	15.7	23.8		n.s.	4	3.9	5.0		n.s.
Alcohol dependence	12	11.8	5.5	7.89	0.005	2	2.0	2.4		n.s.
Drug abuse	1	1.0	6.8		n.s.	4	3.9	1.5		n.s.
Drug dependence	4	3.9	4.6		n.s.	2	2.0	1.2		n.s.
Adjustment disorders	8	7.8	2.0–8.0 ^e			5	5.0	2.0–8.0 ^e		
With depressed mood	5	4.9	—			2	2.0	—		
With anxious mood	0	0.0	—			1	1.0	—		
With mixed anxious and depressed mood	3	2.9	—			2	2.0	—		
Psychotic disorders	4	3.9	—			2	2.0	0.4–0.7 ^f		
Schizophrenia	1	1.0	0.4 ^g			1	1.0	—		
Substance-induced psychotic disorder	3	2.9	—			1	1.0	—		
Eating disorders	5	5.0	—			3	3.0	0.5 ^h		
Anorexia nervosa	2	2.0	1.9 ⁱ			1	1.0	<0.1 ^h		
Bulimia nervosa	1	1.0	2.9 ⁱ			1	1.0	0.4 ^h		
Eating disorder not otherwise specified	2	2.0	5.3 ⁱ			1	1.0	—		
Somatoform disorders	0	0.0	0.2–2.0 ^j			0	0.0	5.7–16.6 ^k		

^a Adapted with permission from Cambridge University Press, 2011.¹⁰^b The data indicate the sum of all substance use disorders and the recalculated rates for mood disorders and anxiety disorders.^c The data indicate the sum of frequency rates for major depressive disorder, dysthymic disorder, and bipolar disorder only.^d The data indicate the sum of frequency rates for social phobia, PTSD, panic disorder with or without agoraphobia, agoraphobia without panic disorder, OCD, and generalized anxiety disorder only.^e The data indicate the prevalence of adjustment disorder as reported in *DSM-IV-TR*;⁶ statistical comparisons were not conducted.^f The data indicate that the 1-year population rate of psychotic disorders was from *ICD-10* ratings of Australian males;¹² statistical comparisons were not conducted.^g Lifetime prevalence of schizophrenia was obtained from a global systematic review;¹³ statistical comparisons were not conducted.^h One-year population rates for eating disorders were obtained from a New Zealand population study;¹⁴ statistical comparisons were not conducted.ⁱ Lifetime population rates for eating disorders were obtained from an Australian female twin study;¹⁵ statistical comparisons were not conducted.^j The lifetime prevalence rate of somatoform disorders is shown as reported in *DSM-IV-TR*;⁶ statistical comparisons were not conducted.^k The 1-year population rate for somatoform disorder was obtained from a German study;¹⁶ statistical comparisons were not conducted.

specified.^{10,11} Among studies examining rates of major depressive disorder at multiple time points within the first year, the timing of onset and course of disorder have been variable. Studies involving predominantly mild TBI cases suggest that major depressive disorder onset occurs within 3 months following injury,^{20,27,28} whereas a more recent study focusing on moderate to severe injuries reported that onset is more common 6–12 months postinjury.¹⁰ These findings suggest that those with more severe injuries may show more delayed onset of symptoms. In their 5-year prospective study of individuals with moderate to severe TBI, Alway et al.⁹ found that rates of mood disorders were highest in the first year (40%) postinjury but remained significantly elevated over population rates at 27.7% in the fifth year postinjury. Major depressive disorder was the most common diagnosis, presenting at rates between four and six times (18.7%–28.3%) those in the general population (4.2%) over the 5-year period. A subsyndromal variant of major depressive disorder, diagnosed as depressive disorder not otherwise specified, was the next common mood disorder (6.5%–15.8%), while dysthymia (0.0%–2.0%) and bipolar disorder (0.0%–3.1%) were relatively rare. Reported rates of depressive disorders from studies with retrospective or cross-sectional designs vary from 12.1% to 61.1% for major depressive disorder, 0%–14% for dysthymia, and 0.0%–16.7% for bipolar-type disorders.^{5,7,17,24,25,31} Findings generally indicate poor disorder resolution,^{17,24,31} although others have found decreasing⁷ and stable²⁴ rates of predominantly major depressive disorder with greater time postinjury.

ANXIETY DISORDERS AND TBI

Preinjury Anxiety Disorders

As in the general population, anxiety disorders are a common class of preinjury psychiatric disorder, with reported lifetime rates ranging from 8.8% to 21.6%.^{5,10,17,20}

Postinjury Anxiety Disorders

Although anxiety symptoms are common following TBI, relatively few studies have examined a range of anxiety diagnoses concurrently. Reported rates range from 19% to 50% over variable postinjury periods.^{5,7,10,17,32} Most anxiety disorders appear to be novel and highly comorbid with mood disorders.^{10,17,18} In their overlapping prospective studies, Gould et al.¹⁰ and Alway et al.⁹ found that anxiety disorder not otherwise specified was the most common anxiety diagnosis (10.3%–34.2%), especially in the first year postinjury, frequently characterized by subthreshold PTSD and/or generalized anxiety disorder symptoms. Cases of PTSD-like anxiety not otherwise specified commonly did not meet the PTSD avoidance criterion, whereas cases of generalized anxiety disorder-like anxiety not otherwise specified had clinically significant anxiety symptoms confined to a major depressive episode, precluding a concurrent generalized anxiety disorder diagnosis. This suggested that, following

moderate to severe TBI, subthreshold PTSD or generalized anxiety disorder presentations might precede full diagnoses. PTSD was the second most common anxiety disorder (5.0%–13.2%), exceeding 12-month rates in the general population (3.5%) each year postinjury.³³ Other anxiety disorders, including panic disorder (2.0%–3.3%), agoraphobia (0.7%–1.0%), obsessive-compulsive disorder (OCD; 0.0%–2.6%), and generalized anxiety disorder (0.0%–3.3%), were relatively uncommon and presented at rates comparable to those in the general population;³³ only one case of substance-induced anxiety disorder has been documented.^{10,17} Research on specific anxiety disorder diagnoses are considered below.

Acute Stress Disorder and PTSD

TBI is frequently caused by a traumatic event such as a motor vehicle accident or assault, and such events are also common precipitants of acute stress disorder and PTSD. However, there has been considerable debate as to whether acute stress disorder or PTSD can develop after TBI due to injury-related loss of consciousness and amnesia. However it has been proposed that acute stress disorder and PTSD may occur following mild TBI where loss of consciousness and posttraumatic amnesia are brief, resulting in partial or full encoding of the traumatic event.³⁴ Nonetheless, acute stress disorder and PTSD cases have been reported across the full range of TBI severity.^{10,35,36}

Rates of acute stress disorder following mild TBI have ranged from 4.6% to 21.2%.^{37–39} Some evidence suggests that acute stress disorder frequently progresses to PTSD following mild TBI. Harvey and Bryant³⁸ found that of 79 motor vehicle accident victims with mild TBI, 14% developed acute stress disorder within the first month postinjury and 24% had PTSD at 6 months postinjury. Remarkably, 82% of acute stress disorder cases had PTSD at 6 months and 73% at 2 years postinjury. Of studies including individuals with moderate and severe TBI, Whelan-Goodinson et al.¹⁷ found 11% of 100 cases retrospectively reported acute stress disorder symptoms up to 5 years previously, whereas Gould et al.¹⁰ prospectively found only one case of acute stress disorder, which progressed into PTSD between 6 and 12 months postinjury.

Most studies of PTSD have focused on mild TBI samples. Findings suggest that mild TBI may increase risk of PTSD following injury^{18,40} and result in higher frequency of delayed-onset PTSD characterized by onset more than 6 months posttrauma.⁴¹ Reported rates have varied from 12.0% to 12.7% at 3 months,^{18,29,40} 14%–24% at 6 months,^{42,43} 2.4%–15.0% at 12 months,^{4,18} and 22% at 2 years³⁸ postinjury.

There is greater variability in frequencies of PTSD from studies of moderate to severe TBI. For example, Bryant et al.⁴⁰ reported a rate of 27.1% at 6 months postinjury using *DSM-III-R* criteria. However, studies assessing the full first year postinjury have reported lower frequencies (i.e., 0.0%–12.7%) using *DSM-IV-TR* criteria, which require that PTSD

symptoms result in clinically significant distress.^{10,11,19} Results of retrospective studies indicate that PTSD may emerge or persist years or decades following injury. Frequencies range from 0% to 19%,^{17,24,25} but may be inflated due to retrospectively assessed symptoms over long periods. One cross-sequential study found that PTSD frequency decreased with time postinjury.⁷

Few studies have reported on the timing of onset and course of PTSD. In their prospective study of 85 individuals with moderate to severe TBI (78.8% male), Alway et al.⁴⁴ found that 17.6% developed injury-related PTSD over the first 4 years postinjury, none of whom had PTSD prior to injury. PTSD onset peaked between 6 and 12 months postinjury. The majority of PTSD cases (66.7%) had a delayed onset, which for a third was preceded by subsyndromal symptoms in the first 6 months postinjury. PTSD frequency increased over the first year postinjury, remained stable during the second year, and gradually declined thereafter. The majority with PTSD experienced a chronic symptom course, and all developed one or more comorbid psychiatric disorders, with mood, other anxiety, and substance use disorders being the most common. Although shorter post-traumatic amnesia was associated with presence of PTSD, greater TBI severity did not prevent PTSD from evolving. Patients with PTSD also exhibited poorer functional outcomes and quality of life after TBI.⁴⁵

Generalized Anxiety Disorder

The frequency of generalized anxiety disorder after TBI is unclear. Some findings in both mild TBI and moderate to severe TBI samples suggest generalized anxiety disorder is one of the most common anxiety disorders after TBI, occurring in 13.4%–27.3% of cases;^{5,17–19,31} in other findings the diagnosis is the least common,^{4,10,24,25} with rates of 1%–2%. Differences in application of diagnostic criteria, particularly the requirement for symptoms to be present for 6 months prior to diagnosis, might account for these discrepancies. Rates of generalized anxiety disorder in retrospective studies are generally higher than reported in the first year postinjury; in studies examining periods up to 9 years postinjury, reporting rates range from 17% to 27.3%.^{5,17} However, lower rates (i.e., 1.7%–9.0%) have been reported in studies examining decades-long periods.^{24,25}

Panic Disorder

Rates of postinjury panic disorder (with or without agoraphobia) vary considerably across studies. Panic disorder appears more common following mild TBI. In moderate to severe TBI samples, rates appear to increase with time postinjury, possibly in response to increased self-awareness of anxiety-based physiological symptoms.⁴⁶ To illustrate, prospective studies have reported frequencies at 12 months postinjury of 7.5%–9%^{4,18} in mild TBI samples, versus 0.0%–2.0%^{10,11,19} for moderate–severe samples. For the latter TBI group, Alway et al.⁹ reported rates ranging from 2.0% to 3.3% up to 5 years postinjury. Retrospective and cross-sectional

studies report rates ranging from 6.0% to 16.7% over the first 9 years^{5,17} and 8.3%–14.0% up to 48 years^{24,25} postinjury.

Social Phobia

To qualify for a diagnosis of social phobia, anxiety symptoms need to be contextually disproportionate,⁶ which is important when assessing individuals with TBI, who may present with appropriate disability-related anxiety in social settings. Of the few studies examining social phobia in TBI samples, reported frequencies appear similar to the general population, with relative stability with time postinjury. However, it is not clear whether these stable rates reflect patterns of continuing or new onset disorders over time. To illustrate, in a prospective study by Bryant and colleagues,¹⁸ rates of social phobia at 3 and 12 months post mild TBI were 6.1% and 9%, respectively. Rates ranging between 0.0% and 5.3% have been reported in prospective studies examining the first 12 months following mild to severe TBI.^{10,11} Alway et al.⁹ reported a small increase over 5 years postinjury, with a peak of 6% at 4 years, dropping to 3% at 5 years. Retrospective studies have reported rates ranging from 5% to 7% in samples up to 48 years postinjury.^{17,24,25}

Specific Phobia

Traumatic experiences associated with the injury or acute hospitalization may precipitate phobic reactions. Specific phobia should be diagnosed only after evaluating the context of the phobic reaction and considering PTSD as a differential diagnosis.⁴⁶ Rates of specific phobia appear comparable to that in the general population. Only one participant (0.8%) in the study by Deb et al.⁴ had an *ICD-10* diagnosis of specific phobia at 12 months postinjury. Two other prospective studies reported higher rates (5.3 and 6.9%) of *DSM-IV-TR* specific phobia over the first 12 months following mild–severe TBI.^{10,11} Alway et al.⁹ reported a peak rate of 6% at 1 year, dropping to 4% in years 3 and 4 and 0% in year 5. Retrospective studies have reported rates of specific phobia ranging from 5.6% to 7.0% postinjury,^{5,17} with slightly higher rates (8.3%–10.0%) in studies covering several decades postinjury.^{24,25}

OBSESSIVE-COMPULSIVE DISORDER

OCD is relatively uncommon in the general population, and most findings suggest it remains so after TBI. Three prospective studies have reported low rates of OCD within the first 12 months post-TBI: 4%¹⁸ and 1.2%⁴ in mild samples and 1%¹⁰ in moderate–severe samples. Alway et al.⁹ reported low frequencies of OCD (0.0%–2.6%) that were maintained over the first 5 years postinjury. Most retrospective studies have found similarly low rates of OCD.^{5,17,25} The exception is the retrospective study of Hibbard et al.,²⁴ in which 15% were diagnosed as having OCD, according to the *Structured Clinical Interview for DSM-IV Axis I Disorders*, an average of 8 years postinjury. One possible explanation for such a discrepancy is that TBI-related behaviors (e.g., checking due to

memory problems) could be misattributed as symptoms of OCD, artificially inflating rates of diagnosis.

SUBSTANCE USE DISORDERS AND TBI

Preinjury Substance Use Disorders

Relative to the general population, high rates of substance use disorder are reported in TBI samples prior to injury. This is not surprising given that TBI and substance use disorders share common risk factors (e.g., male gender and young age), and substance intoxication is a leading contributor to accident-related injury.⁴⁷ Gould et al.¹⁰ reported preinjury lifetime frequencies of 34.3% for any substance use disorder and 27.5% for alcohol dependence or abuse. Rates of alcohol dependence were twice those in the general population (11.8% versus 5.5%), whereas overall rates of substance use disorder were comparable to a demographically similar population sample (34.3% versus 31.9%). Slightly higher rates of preinjury substance use disorder (41.0%) were found in a retrospective Australian study, with 36.0% having an alcohol-related disorder.¹⁷ Hibbard et al.²⁴ found a similar rate in the United States of 40% for any substance use disorder, whereas one Finnish study found much lower rates of alcohol-related disorders (8.3%), possibly reflecting different cultural patterns of alcohol consumption.²⁵

Postinjury Substance Use Disorders

The reported frequencies of substance use disorders after TBI are generally lower than preinjury rates. This is particularly so during the first year postinjury, when abstinence from alcohol is commonly advised and individuals may be hospitalized for extended periods. Studies examining predominantly mild TBI samples report rates of 4.9% for alcohol dependence⁴ and 9.3% for any substance-use disorder¹⁸ at 12 months postinjury. Rates of alcohol-related disorder during the first year following mild to severe TBI are quite variable, ranging from 5.9% to 19.2%, whereas rates of drug-related disorder are more comparable (2.6%–5.9%).^{10,11,19} Evidence from cross-sectional and retrospective studies suggests that substance use disorders may increase in the years following injury.^{7,17} However a prospective study of moderate–severe TBI found that alcohol and drug abuse, while common preinjury (38.5%), peaked at 17.8% in the second year postinjury but dropped to 9.6%–11.8% in years 3–5, thereby not exceeding general population rates.⁹ Overall substance abuse is less of a problem after injury than it is before.

PSYCHOTIC DISORDERS AND TBI

Preinjury Psychotic Disorders

Fann et al. have proposed that individuals with a genetic susceptibility to schizophrenia have a greater chance of sustaining a TBI.²¹ However, studies using structured clinical interviews suggest that preinjury psychotic disorders are not common. Results range from 0.0% to 4.3% for

preinjury over the lifetime, with most cases substance-induced psychotic disorders.^{9,10,17,25}

Postinjury Psychotic Disorders

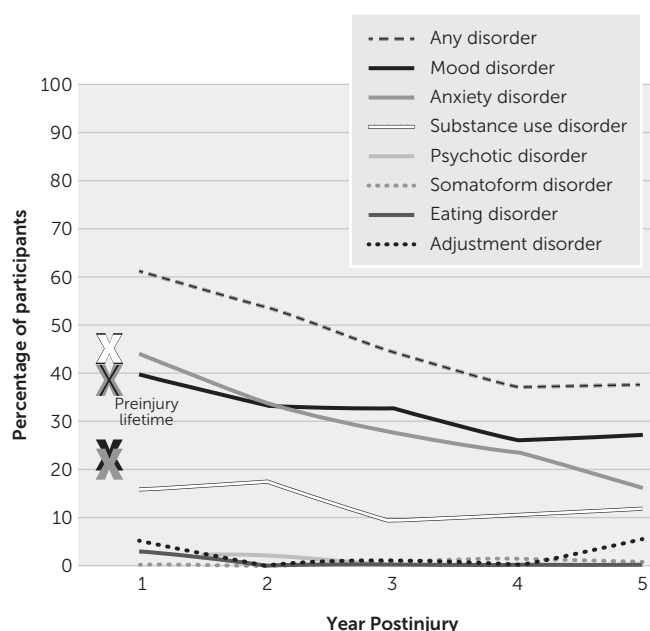
The co-occurrence of TBI and psychotic disorder is rare, yet it is associated with substantial disability. Some have proposed that TBI may cause psychosis (i.e., psychotic disorder due to a TBI) due to apparent clinical and neurobiological differences between posttraumatic psychoses and idiopathic psychotic disorders.⁴⁸ For example, persecutory delusions and auditory hallucinations are the most frequent postinjury psychotic sequelae, with low rates of negative symptoms (e.g., anhedonia), diverging from the symptom profile common to schizophrenia.^{49,50} Onset ranges widely, with one case-control study reporting a mean onset latency of 54.7 months postinjury.⁵⁰

Other findings suggest that postinjury psychotic sequelae are relatively indistinguishable from idiopathic psychotic disorders.⁵¹ One study has suggested that TBI may precipitate the development of schizophrenia in those with a genetic susceptibility,⁵⁰ with a meta-analysis reporting a 60% increase in risk for schizophrenia after TBI.⁵² However, most of these findings are based on case reports (e.g., Fujii and Ahmed)⁴⁹ or population-based studies using medical records to ascertain diagnoses (e.g., Fann et al.²¹ and Orlovskaya et al.²²). A 5-year prospective study following moderate to severe TBI found all postinjury cases had a preinjury history of psychosis.⁹

Findings of prospective studies have reported relatively low rates of psychotic disorders consistent with population rates. Deb and colleagues⁴ reported one case of *ICD-10* schizophrenia at 12 months postinjury in a predominantly mild TBI sample. Following complicated mild to severe TBI, Gould et al.¹⁰ found three cases of substance-induced psychotic disorder (using *DSM-IV-TR* criteria) and one case of schizophrenia. Extending this study, Alway et al.⁹ found no novel cases of schizophrenia and declining rates of psychotic disorder over time, with three, two, one, and one case in the second, third, fourth, and fifth years postinjury (0.9%–3.0%), respectively. Diaz et al.¹⁹ found one case of novel delusional disorder, as diagnosed with *DSM-IV-TR* criteria, in a study of 33 participants with severe TBI, assessed on average 18 months following injury. Findings from retrospective studies over many years confirm the relatively stable frequency of psychotic disorder with time postinjury.^{17,25}

EATING DISORDERS AND TBI

The limited studies to date indicate that postinjury eating disorders present at rates comparable to those in the general population, commonly in the context of a preinjury history. In Gould and colleagues,¹⁰ prospective study, 4.9% had had an eating disorder prior to injury, with 2.9% experiencing a continuation or recurrence of the disorder in the 12 months following injury. Extending this study, Alway et al.⁹ found

FIGURE 1. Frequency of Psychiatric Disorders During the First Five Years After TBI^a

^a For further details on the frequency of psychiatric disorders over the first 5 years, see Alway et al.⁹

only one eating disorder case (0.7%) in the second year and no cases in years 3–5 postinjury. Similarly, in retrospective studies van Reekum et al.⁵ reported one case (5.5%) of anorexia nervosa with preinjury onset, whereas Whelan-Goodinson et al.¹⁷ found a preinjury rate of 2%, with 1% still satisfying diagnostic criteria following injury.

SOMATOFORM DISORDERS AND TBI

As in the general population, somatoform disorders appear relatively uncommon after TBI, although only three studies have examined this diagnosis. A prospective study found no cases prior to or 12 months following complicated mild to severe injury,¹⁰ with an extension of this study up to 5 years postinjury revealing rates of 0.0%–1.9%.⁹ A retrospective study reported one case (1%) each of preinjury and novel postinjury somatoform disorder.¹⁷

ADJUSTMENT DISORDERS AND TBI

Many would consider the process of injury-related adjustment to be sufficiently stressful to trigger an adjustment disorder in some individuals. However, only two studies used a structured clinical interview to examine adjustment disorders occurring after TBI. In a prospective study examining a complicated mild to severe TBI sample, the frequency of adjustment disorder was 7.8% prior to injury and 5% in the first 12 months following injury.¹⁰ Extending this study prospectively to 5 years postinjury Alway et al.⁹ reported similarly low frequencies (0.0%–5.9%) (Figure 1).

FACTORS ASSOCIATED WITH PSYCHIATRIC DISORDERS AFTER TBI

Understanding the risk factors associated with the development and course of psychiatric disorders after TBI may assist in prevention and/or identification of management strategies. Likely contributory factors include demographic or personal factors (i.e., genetic susceptibility and preinjury disorder), injury-related changes, and posttraumatic adaptive issues.

In regard to demographic factors, some studies have found that older age increases risk for anxiety^{43,53,54} and mood disorders^{27,28} and younger age increases risk for substance use disorders.^{9,54} Alway et al.⁹ found the likelihood of disorder increased with age up to 30 years and declined with age thereafter. This may explain why other studies have found no significant association of age with psychiatric disorder after TBI.^{7,20,24} Female gender has been associated with increased risk of anxiety^{7,24,53} and mood disorders^{7,29,54} in some studies but not others.^{4,9,11,25} Two studies found that male gender increased risk of postinjury substance use disorder.^{7,9} Lower education has emerged as a risk factor for depression in some studies^{4,54} but not others;^{20,53} it does not appear to be associated with the development of postinjury anxiety disorders.^{24,54} Lower education has also been associated with increased likelihood of substance use disorder.⁹

Although rates of postinjury psychiatric disorders appear elevated for all individuals, the presence of a preinjury psychiatric history is the strongest risk factor for postinjury psychiatric disorders in general and for each of the diagnostic categories of mood, anxiety, and substance use disorders.^{4,9,21,24,53} The timing of onset of postinjury disorders may also vary according to preinjury psychiatric status. Alway et al.⁹ found that cases of postinjury disorder with a preinjury history were significantly more likely than novel cases to present in the first year postinjury (85.1% versus 59.5%). Nevertheless, Alway et al.⁹ also showed that while individuals with a preinjury psychiatric history were significantly more likely to develop a postinjury disorder, two-thirds of these cases developed a diagnostic class not present prior to injury; 37.0% had preinjury diagnostic class only, 27.2% novel diagnostic class only, and 35.8% both a preinjury and novel diagnostic class. Furthermore, the majority without a psychiatric history also developed a disorder postinjury. Therefore, psychiatric presentations after TBI do not merely represent a continuation of preinjury disorders into the postinjury period.^{9,10}

Even though rates of mood and certain anxiety disorders appear to be somewhat higher in moderate to severe TBI samples, previous studies have found no evidence to suggest that TBI severity influences risk for postinjury psychiatric disorders.^{7,9,25,54} Although the presence and severity of bodily injury in general does not appear related to psychiatric disorders after TBI,^{20,54} one previous study found that sustaining a limb injury increased risk of psychiatric disorder by 6.4 times at 12 months postinjury,⁵³ and this

association was confirmed by Alway et al.⁹ The reduced independence, pain, and longer periods of physical rehabilitation and hospitalization associated with sustaining a limb injury may increase distress, heightening vulnerability to psychiatric disorders. Therefore, individuals with limb injuries may require additional support to adjust to the impact of their injury. Time postinjury has also been identified as a predictive factor, with one study finding a 27% decrease in the likelihood of a psychiatric disorder with each year postinjury.⁹ Several studies have shown the presence of psychiatric disorders to be associated with poor functional outcomes and lower quality of life.^{45,55}

CONCLUSIONS

Individuals with TBI show significantly elevated rates of depressive and anxiety disorders, most commonly major depressive disorder and PTSD, which are most likely to emerge in the first year postinjury, although severe injury may be associated with more delayed onset. Although individuals with a preinjury history of psychiatric disorders are more likely to develop these disorders, the nature of the disorders may change after injury, and many individuals also develop novel psychiatric disorders. While the frequency of anxiety disorders diminishes, depressive disorders are more persistent postinjury. Substance use, while high before injury, declines after injury. Studies to date suggest that the frequency of psychotic, eating, somatoform, and adjustment disorders among persons with TBI do not exceed population rates.

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