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Clinical and neuropsychological correlates of major depression following post-traumatic brain injury, a prospective study

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ABSTRACT

Objectives: Major depression disorder (MDD) is the most frequent psychiatric complication after traumatic brain injury (TBI), with a prevalence of 14–77%. The aim of this study was to analyse the psychiatric sequelae of TBI, and to identify the neuropsychological and psychopathological correlates of post-TBI MDD in order to highlight their differences from those of primary MDD.
Methods: This was a longitudinal, prospective, case-control study. Sixteen patients with closed brain injury, and a lesion revealed by computed tomography (CT), were recruited and were evaluated one (T1), three (T3) and six (T6) months after discharge from Neurosurgery Department; the controls were six patients with MDD. The psychiatric symptoms were evaluated using brief psychiatric rating scale (BPRS), Hamilton depression rating scale (HRSD), Beck depression inventory scale (BDI), Hamilton anxiety rating scale (HRSA), global assessment of functioning (GAF) and instrumental activity of daily living (IADL). Neuropsychological profiles were assessed by using neuropsychological tests, focused on memory and frontal-executive functioning.
Results: At T1, MDD was observed in 10 cases (62.5%), a manic episode in 12.5%, and post-traumatic stress disorder in 6.5%. At T3 and T6, MDD was diagnosed in, respectively, eight (50%) and six cases (37.5%). Post TBI MDD had less severe depressive symptoms, showed greater social isolation and hostility and more cognitive deficits in comparison with the control group.
Conclusions: MDD is a frequent TBI complication. Patients with post-TBI MDD have a specific psychopathological profile characterised by a less severe depressive symptomatology and a neuropsychological pattern that is significantly associated with greater deficits in cognitive functions than those with primary MDD.

1. Introduction

Psychiatric disorders seem to be a major cause of disability after traumatic brain injury (TBI) (Bowen et al., 1993; Fann et al., 1995; Levin et al., 1997; Silver et al., 1990, 2001). The prevalence of post-TBI psychiatric sequelae ranges from 34% to 50%, depending on the severity of the trauma (Jorge et al., 2004; O'Donnell et al., 2004).

Major depression disorder (MDD) is the most widely studied psychiatric disorder after TBI. The published rates of axis I disorders in patients with TBI are 14–77% for MDD (Deb et al., 1999; Fann et al., 1995; Fedoroff et al., 1992; Hibbard et al., 1998; Jorge et al., 1993a; Varney et al., 1987), 2–14% for dysthymia (Fann et al., 1995; Fedoroff et al., 1992; Jorge et al., 1993a; Hibbard et al., 1998), 2–17% for bipolar disorder (Varney et al., 1987; Jorge et al., 1993c; Van Reekum et al., 1996; Hibbard et al., 1998), 3–28% for generalised anxiety disorder (Fann et al., 1995; Jorge et al., 1993b; Van Reekum et al., 1996; Hibbard et al., 1998; Deb et al., 1999), 4–17% for panic disorder (Fann et al., 1995; Van Reekum et al., 1996; Hibbard et al., 1998; Deb et al., 1999), 1–10% for phobic disorders (Van Reekum et al., 1996; Hibbard et al., 1998; Deb et al., 1999), 2–15% for obsessive-compulsive disorder (Van Reekum et al., 1996; Hibbard et al., 1998; Deb et al., 1999), 3–27% for

Abbreviations: BDI, Beck depression inventory scale; BPRS, brief psychiatric rating scale; CT, computed tomography; DSM-IV-TRd, iagnostic and statistical manual of mental disorders, fourth edition, text revision; GAF, global assessment of functioning; GCS, Glasgow coma scale; HRS-A, Hamilton anxiety rating scale; HRS-D, Hamilton depression rating scale; IADL, instrumental activity of daily living; IQ, intelligence quotient; MDD, major depression disorder; PTSD, post traumatic stress disorder; SCID-Istruct, ured clinical interview for axis I disorders; SCID II, structured clinical interview for *DSM-IV* Axis II disorders; TBI, traumatic brain injury; TOL, Tower of London test; WCST, Wisconsin card sorting test.

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post-traumatic stress disorder (PTSD) (Van Reekum et al., 1996; Hibbard et al., 1998; Deb et al., 1999; Hibbard et al., 2000; Bryant et al., 2000), 5–28% for substance abuse or dependence (Fann et al., 1995; Van Reekum et al., 1996; Hibbard et al., 1998; Deb et al., 1999), and 1% for schizophrenia (Deb et al., 1999; Koponen et al., 2002).

Furthermore, patients are at high risk of developing depression not only during the acute phase, but also for decades after the TBI (Jorge et al., 2004). Jorge et al. (1993b) investigated the effects of TBI in 66 patients, who were followed up for more than one year. Using the *DSM III-R* diagnostic criteria, 42.4% of the patients were diagnosed as having MDD, and this finding was supported by a large-scale study conducted by Kreutzer et al. (2001) who found that 41.9% of 722 patients had MDD on the basis of the *DSM IV* criteria. Levin et al. (2005) studied a cohort of 125 adults with mild TBI and, reviewing their own earlier work in which they cited a 17% incidence of MDD in subjects with mild TBI one-year after injury, they noted an increased incidence of depression by age, and that this increased by a factor of 7 if there were abnormal cumputed tomography (CT) findings.

Mild TBI has also been found to be a risk factor for MDD and generally increased levels of depressive symptoms have been observed in long-term follow-up studies (Levin et al., 2005). Koponen et al. (2002) evaluated the frequency of Axis I and Axis II disorders in a retrospective 30-year follow-up study of 60 patients who had been treated for TBI. These patients were particularly vulnerable to developing depressive disorders, and showed a lifetime prevalence of MDD of 26.7% (Koponen et al., 2002).

Patients experiencing major depressive episodes following a mild TBI have increased levels of anxiety disorder, cognitive deficits and disability in comparison with those who do not develop depression (Jorge et al., 2004; Levin et al., 2001). Jorge et al. (2004) found MDD in 33% of 91 patients who had sustained a TBI, comorbid anxiety in 76.7% and aggressive behaviour in 56.7%. Forty of their patients had sustained a mild TBI, whereas the rest had moderate-severe TBI.

Emotional disturbances are perhaps the most socially and vocationally disruptive sequelae of severe TBI. Patients may experience significant personality changes, becoming childish and dependent, prone to sudden violent outbursts, anxious, or severely depressed. These changes may influence their social relationships and ability to retain employment, and place a great burden on their family members. In particular, aggressive behaviour is one of the most socially and vocationally disruptive consequences of these neuropsychiatric disorders (Tateno et al., 2003).

MDD has also been associated with poorer social functioning at 6- and 12-month follow-up visits, as well as with significantly reduced volumes of left prefrontal grey matter, particularly the ventrolateral and dorsolateral regions (Rao et al., 2010).

The aims of this prospective study were to investigate the prevalence of psychiatric disorders in patients with TBI, to characterise the severity of clinical symptoms and neuropsychological deficits in patients with post-TBI MDD, and to characterise the symptoms of post-traumatic psychiatric disorders in order to reveal any differences between post-TBI and primary MDD.

2. Methods

2.1. Study population

In this longitudinal, prospective case-control study, we studied all of the consecutive patients aged 18–65 years admitted to the Department of Neurosurgery, IRCCS Foundation Ca' Granda, Ospedale Maggiore Policlinico of Milan, Italy, between September 2011 and September 2012 with a closed head injury and a lesion revealed by computed tomography (CT). The inclusion criteria were loss of consciousness for at least 1 min, the presence of post-traumatic amnesia for at least 30 min, and neuroradiological evidence suggesting TBI. Subjects affected by past unstable neurological conditions (coma, stupor, epilepsy, acute meningo-encephalitis, metabolic encephalopathy), pathological conditions of the cardiorespiratory system (cardiac or respiratory failure, cardiogenic shock, pneumothorax), patients with a past psychiatric diagnosis on Axis I or on Axis II and patients with comorbid substance abuse were excluded from the study. The subjects without a CT-detectable lesion were also excluded because they could develop post-concussive disorders, a complex syndrome characterised by an association of somatic symptoms that distinguish it from the psychiatric disorders that are the subject of this study.

The control group, recruited in the same period of TBI subjects, consisted of age- and gender-matched patients with primary recurrent MDD attending the Department of Neuropsychopharmacology and Day Hospital, IRCCS Foundation Ca' Granda, Ospedale Maggiore Policlinico of Milan.

The diagnosis was formulated at admission by expert clinicians using the structured clinical interview for Axis I disorders (SCID-I) (First et al., 1996) and the structured clinical interview for Axis II disorders (SCID-II) (First et al., 1997) based on the criteria of the diagnostic and statistical manual of mental disorders, fourth edition, text revision (DSM-IV-TR) (American Psychiatric Association, 2000).

The patients with TBI were evaluated one month after being discharged from the Neurosurgery Department (T1), and were followed up three (T2) and six months (T3) after the trauma: they underwent CT to monitor the evolution of any parenchymal brain lesions, as well as a diagnostic psychopathological and neuropsychological evaluation.

The control group was also evaluated at the time of enrolment and followed up after one, three and six months.

2.2. TBI severity

The severity of the TBI was assessed using the 24-hour Glasgow coma scale (GCS) (Teasdale et al., 1978): scores of 13–15 were defined as mild head injury, scores of 9–12 as moderate head injury, and scores of 3–8 as severe head injury. Patients with a GCS score of 12–15 who underwent intracranial surgery or presented focal lesions greater than 15 mm were considered as having moderate head injury.

2.3. Neuroimaging

All of the patients with TBI underwent CT immediately after the trauma as part of the standard clinical evaluation in our Department of Neurosurgery. The nature, extent, and location of the traumatic lesions were classified on the basis of the Traumatic Coma Data Bank criteria (Marshall et al., 1983). All of the structural neuroimaging scans were interpreted by a trained neurologist, who was blinded to the results of the psychiatric examination.

2.4. Psychiatric assessment

All of the patients were evaluated using SCID-I (First et al., 1996) and SCID-II (First et al., 1997). The severity of depressive and anxiety symptoms was assessed using the Hamilton rating scale for depression (HRS-D) (Hamilton, 1960), the Beck depression inventory scale (BDI) (Beck et al., 1961) and the Hamilton rating scale for anxiety (HRS-A) (Hamilton, 1959). The patients' global functioning was evaluated using the global assessment of functioning (GAF) (Hall, 1995) and instrumental activity of daily