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Research paper

# Anxiety and comorbid depression following traumatic brain injury in a community-based sample of young, middle-aged and older adults

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#### ABSTRACT

*Background:* Anxiety is common following a traumatic brain injury (TBI), but who is most at risk, and to what extent, is not well understood.

*Methods:* Longitudinal data from a randomly-selected community sample (Wave 1: 7397, Wave 2: 6621 and Wave 3: 6042) comprising three adult cohorts (young: 20–24 years of age, middle-aged: 40–44, older: 60–64), were analysed. The association between TBI history, anxiety and comorbid depression was assessed, controlling for age, sex, marital/employment status, medical conditions, recent life events, alcohol consumption, social support and physical activity.

*Results:* Thirteen percent of the sample had sustained a TBI by Wave 3, 35% of whom had sustained multiple TBIs. Cross-sectional analyses revealed that clinically-significant anxiety was more common in people who had sustained a TBI. Longitudinal analyses demonstrated an increased risk of anxiety post-TBI, even after controlling for potential demographic, health and psychosocial confounds. Anxiety was more common than depression, although 10% of those with a TBI experienced comorbid anxiety/depression.

*Limitations:* TBIs were not medically confirmed and anxiety and depression were only assessed every four years by self-report, rather than clinical interview. Sample attrition resulted in the retention of healthier individuals at each wave.

*Conclusions:* TBIs are associated with a lifelong increased risk of experiencing clinically-significant anxiety, highlighting the chronic nature of TBI sequelae. Positive lifestyle changes (e.g., increasing physical activity, reducing alcohol consumption) may decrease the risk of anxiety problems in the early years after a TBI. Comorbid anxiety and depression was common, indicating that both should be monitored and treated.

#### 1. Introduction

Anxiety is common following a traumatic brain injury (TBI) (Mallya et al., 2015), with symptoms ranging from subtle changes (e.g., restlessness, irritability) to debilitating levels of tension, fear and worry, which can negatively impact on a person's quality-of-life and everyday functioning (American Psychiatric Association, 2013). Although research has focussed on depression, self-report data indicate comparable rates of clinically-significant levels ('cases') of general anxiety (37%) and depression (38%) following TBI (Osborn et al., 2014, 2016a) and, indeed, that the average levels of anxiety may be higher than depression (King and Kirwilliam, 2011; Ortiz et al., 2004; von Steinbuchel et al., 2010; Wood and Rutterford, 2006). In terms of clinical disorders, people are twice as likely to be diagnosed with an anxiety disorder (e.g., Generalized Anxiety Disorder [GAD], Post-

traumatic Stress Disorder [PTSD]) after a TBI, compared to those without a TBI (Van Reekum et al., 2000). Together, these findings suggest that anxiety following TBI warrants greater attention.

Recent population-based longitudinal research data that controlled for a variety of injury, pre-injury and post-injury characteristics when analysing the data, demonstrated that individuals living in the community have a long-term increased risk of clinically-significant depression if they had sustained a TBI at some time in their life Osborn et al., (in press). However, it is not yet clear if this heightened risk is also true for anxiety. Indeed, little is currently known about the complex interplay between a broad variety of demographic (e.g., age, sex), pre-injury (e.g., history of TBI and mental health problems such as depression), injury (e.g., injury severity, time since injury) and postinjury (e.g., stressful life-events, social support) variables that are potentially associated with anxiety (Vanderploeg et al., 2007; Whelan-

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Goodinson et al., 2010; Wood and Rutterford, 2006). This makes it difficult to identify who is most at risk of experiencing problems with anxiety and, thus, implement targeted interventions.

Moreover, to date, most research into anxiety after a TBI has examined samples that are recruited from clinical settings (e.g., hospitals, rehabilitation centres), rather than sourcing individuals who are living in the community. Clinical samples are more likely to be seriously injured and experience greater physical, cognitive and psychological problems, which may lead to higher reported rates of anxiety and/or depression (Dworkin, 1992). In addition, many people do not seek medical attention following a mild TBI (Corrigan et al., 2010; Setnik and Bazarian, 2007), resulting in a large sub-group who have sustained a TBI, but whose outcomes are often overlooked in the extant literature. Although a few studies have recruited from the general population and demonstrated an increased risk of developing neuropsychiatric problems after a TBI (Anstey, 2004; Silver et al., 2001), their data was cross-sectional rather than longitudinal. Thus, the relationship between a TBI and the anxiety levels of individuals living in the community over the long-term, is not yet known.

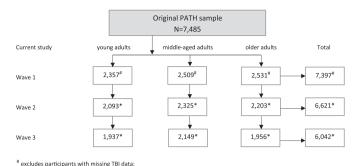
Notwithstanding the fact that anxiety and depression are often experienced, diagnosed, and treated as independent conditions (American Psychiatric Association, 2013), they are also frequently comorbid; both in the general population (Slade et al., 2009) and following a TBI (Bombardier et al., 2010; Jorge et al., 2004; Whelan-Goodinson et al., 2010). In the case of TBI, comorbid anxiety and depression are frequently associated with greater disability, increased service-use and slower recovery (McEvoy et al., 2011), suggesting that they should not be viewed in isolation. Indeed, some studies have reported that, after a TBI, all individuals diagnosed with GAD additionally met the criteria for major depression (Jorge et al., 1993; Van Reekum et al., 1996). Similarly, many people who report experiencing clinically significant anxiety (using self-report scales), also report being depressed (Truelle et al., 2010; Van Der Horn et al., 2013). However, research examining comorbid anxiety and depression following TBI is very limited, particularly in community-based samples; highlighting the need to examine comorbidity in a non-clinical sample.

The current study therefore used data from a randomly-selected community-based sample to address three aims relating to selfreported 'cases' of clinically-significant anxiety and depression. More specifically, it was designed to: (1) examine the prevalence of 'cases' of anxiety in individuals with a TBI, relative to those without a TBI; (2) investigate the prevalence of 'cases' of co-morbid anxiety and depression in those with a TBI, and; (3) use longitudinal analyses to determine whether 'cases' of anxiety are related to having had a TBI, and whether these relationships are independent of potentially confounding demographic (age, sex, marital/employment status), health (depression history, comorbid medical conditions, multiple TBIs, alcohol consumption) and psychosocial (life-events, physical activity, social support) variables.

#### 2. Method

#### 2.1. Participants and procedure

The PATH Through Life Project is an Australian population-based longitudinal study that is assessing adult life-span changes to physical (e.g., medical conditions, substance abuse) and mental (e.g., depression, anxiety) health, cognitive functioning (e.g., memory, attention), and social dynamics (e.g., support, networks). Three cohorts, originally aged 20–24, 40–44 and 60–64 years, were randomly selected from the Canberra and Queanbeyan (Australia) electoral rolls. Electoral registration is compulsory for Australian citizens aged  $\geq 18$  years (over 93% currently enrolled), with the final PATH sample being representative of the 2001 Australian Census data for the region (Anstey et al., 2012). Assessments were conducted every four years (Wave 1 [W1]: 1999–



\* excludes participants with missing TBI data or who were lost to follow-up

Fig. 1. Flow chart of participants, with and without a TBI sustained since birth, partitioned according to age-cohort and wave/successive assessment.

2002, Wave 2 [W2]: 2003–2006, Wave 3 [W3]: 2007–2010, Wave 4 [W4]: 2011-ongoing) in the participant's home or at the Centre for Mental Health Research, Australian National University. After obtaining informed consent, trained interviewers administered the physical and cognitive tests, with the remaining measures completed on a laptop. The PATH project was approved by the Human Research Ethics Committee, Australian National University, and full details of the PATH sample and methodology are outlined in Anstey et al. (2012).

The current sample examined all individuals from the PATH study who reported whether or not they had ever sustained a TBI (W1: N= 7397, W2: N= 6621, and W3: N= 6042), but excluded those whose TBI status could not be determined (approximately 1–2%) because data were missing, or participants had responded 'don't know', 'uncertain' or 'refused'. W4 data were not yet available for all cohorts, consequently it was excluded from the current analysis. The number of participants lost to follow-up between W1 and W3 was low, with 90% of W1 completing W2 and 91% of W2 completing W3; equating to an 82% retention rate across the 8-years. Fig. 1 provides summary details of the full W1 PATH sample (n = 7485) and the samples examined in the current study at each successive wave. Additional summary details for these participants (W1-W3) are provided in the Electronic Supplementary Material, Table S1.

#### 2.2. Measures

The PATH project used a range of measures to collect information relating to a person's overall health and well-being, such as cognitive functioning, physical (blood pressure, lung function) and mental (anxiety, depression) health, drug and alcohol use, personality (e.g., ruminative style, resilience), and levels of pet ownership/volunteering. Variables used in the current study were:

**Socio-demographics**: age (assessment and TBI), education (total years), marital status (married/de-facto, separated/divorced/widowed, never married), and employment status (employed full- or part-time, not in labour force, looking for more work).

**Traumatic brain injury**: determined by the self-reported presence (yes/no) of "a serious injury to the head that interfered with memory, level of consciousness, or caused brain haemorrhaging" (see Osborn et al., (in press) for further details). TBI data were harmonised across assessments in order to determine, at each wave, whether a TBI had been sustained at any time since birth (TBI<sub>lifetime</sub>), in the preceding four years (TBI<sub>recent</sub>), never (TBI<sub>no</sub>), and more than once (TBI<sub>multiple</sub>).

Anxiety and depression: the Goldberg Anxiety Scale (GAS) and Goldberg Depression Scale (GDS) (Goldberg et al., 1988) were used to assess anxiety and depression (respectively) at each wave (W1-W3). Each scale incorporates 9 items and has a total score range of 0–9, with higher scores indicating more symptoms in the preceding month. Clinically significant 'cases' were identified using cut-offs of ≥7 (GAS) and ≥6 (GDS) (Kiely and Butterworth, 2015), creating a binary variable (yes/no). In addition, a lifetime history of depression (categorical

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