INPLASY PROTOCOL

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Conflicts of interest:

None declared.

INTRODUCTION

Review question / Objective: This review aims to determine the prevalence and characteristics of empathic functioning in adults with an acquired brain injury (ABI). Specifically, the review will aim to answer the following questions:

1. What is the prevalence of empathy deficits after ABI?

Empathy in adults with acquired brain injury: a protocol for systematic review and meta-analysis

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Review question / Objective: This review aims to determine the prevalence and characteristics of empathic functioning in adults with an acquired brain injury (ABI). Specifically, the review will aim to answer the following questions:

- 1. What is the prevalence of empathy deficits after ABI?
- 2. To what extent does self-reported total, cognitive and affective empathy differ between participants with ABI and neurotypical controls?
- 3. Are there any gender differences in self-reported empathic functioning after ABI?

Information sources: Ovid MEDLINE, ProQuest, PsycINFO, Scopus, and Web of Science. Additional studies may be identified by hand-searching, included scanning the reference list of included studies. Unpublished studies will be sought.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 November 2022 and was last updated on 09 December 2022 (registration number INPLASY2022110125).

- 2. To what extent does self-reported total, cognitive and affective empathy differ between participants with ABI and neurotypical controls?
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Rationale: The loss of empathy after an acquired brain injury (ABI) is reported to be one of its most frequent and devastating

consequences (Hillis, 2020; O'Keeffe et al., 2020). Several brain regions implicated in empathic processing are vulnerable to brain injury, namely ventromedial prefrontal areas, as well as right cortical and limbic regions (Leigh et al., 2013; Shamay-Tsoory et al., 2004). When empathic functioning is compromised, survivors of brain injury often struggle to maintain interpersonal relationships across family, work and community contexts (Saxton et al., 2013; Williams et al., 2020; Yeates et al., 2016), increasing the risk of social isolation and poor mental health (Salas et al., 2018, 2021).

The most consistent finding in the literature is that adults with moderate-to-severe traumatic brain injury (TBI) report low affective empathy compared to healthy, matched controls (de Sousa et al., 2010, 2011, 2012; Neumann et al., 2014; Rushby et al., 2013, 2016; Spikman et al., 2012; Williams & Wood, 2010; Wood & Williams, 2008), although several studies have not found significant differences (Driscoll & Krueger, 2012; Nijsse et al., 2019; Osborne-Crowley et al., 2020). TBI patients also report greater difficulties in cognitive empathy relative to controls (de Sousa et al., 2010; Neumann et al., 2014; Spikman et al., 2012; Eslinger et al., 1996). Overall, these difficulties appear unrelated to time since injury, injury severity (Williams & Wood, 2010) or neurocognitive deficits (Osborne-Crowley et al., 2020; Wearne et al., 2021). Low empathy has also been documented in non-TBI-related ABIs, including low-grade glioma (Herbet et al., 2015), subarachnoid haemorrhage (Brand et al., 2015; Buunk et al., 2017) and stroke (Hillis, 2014).

To date, the nature of empathic deficits after ABI has not been well characterised. Most studies have relied on small samples and prevalence estimates vary widely. For example, low affective empathy is reported to occur in 23 – 71% of TBI patients (versus 14 – 34% matched controls; de Sousa et al., 2010, 2011, 2012; Osborne-Crowley et al., 2020; Williams & Wood, 2010; Wood & Williams, 2008; Zupan et al., 2018), with estimates of cognitive empathy deficits ranging from 34 – 50% (versus 18% HCs; de Sousa et al., 2010; Zupan et al., 2018). In

addition, much research to date has only examined a single dimension of empathy, despite contemporary theoretical models emphasizing both cognitive and affective components (e.g., Bird & Viding, 2014). This is inconsistent with other clinical research. which has documented selective deficits (e.g., cognitive and/or affective) across a variety of conditions, including schizophrenia (Horan et al., 2015), autism spectrum disorder (Song et al., 2019). borderline personality disorder (Harari et al., 2010) and eating disorders (Kerr-Gaffney et al., 2019). Finally, although gender differences in empathy ability are consistently found in normative samples, these are yet to be quantified in ABI. To address these issues, the following is proposed as the first systematic review of empathy after acquired brain injury.

Condition being studied: Empathy is the ability to feel, share and understand another's emotional experiences, whilst maintaining awareness that the emotional source originates outside oneself (Eklund & Meranius, 2021). Empathy is considered integral to interpersonal relationships, permitting affiliative bonding and sensitive responding to others' needs (Decety et al., 2016; Manusov et al., 2020). Conversely, a lack of empathy has been linked to social dysfunction, such as aggressive behaviour (Blair, 2010; Eisenberg, 2000) and psychopathy (van Dongen, 2020).

Although definitions vary, there is a general consensus that empathy includes both affective and cognitive components (e.g., Preston & de Waal, 2002). Affective empathy refers to viscerally sharing another's emotion, whilst cognitive empathy denotes the ability to recognize and understand that emotion (Decety & Jackson, 2004). Evidence suggests that these are distinct, separable processes. Affective empathy is thought to occur via automatic mechanisms, including perception (e.g., recognizing facial expressions) and mimicry/embodiment (e.g., spontaneous facial mimicry of another's emotional expression). Conversely, cognitive empathy likely reflects higher-level effortful processing, permitting mentalizing, perspective-taking and self-other distinction (Shamay-Tsoory et al., 2009). However, these neural circuits appear to overlap and interact as well. Indeed, optimal empathic functioning has been posited to involve flexible coactivation of cognitive and affective components, according to an individual's goals in a given context (Weisz & Cikara, 2021).

As such, empathy is subject to regulatory and motivational processes (Decety & Holvoet, 2021). In particular, well-regulated empathic arousal is thought to result in empathic concern (i.e., feelings of sympathy and compassion; Decety et al., 2016), which in turn increases the likelihood of prosocial behaviour and sensitive responding (Brethel-Haurwitz et al., 2020). Conversely, poorly regulated empathic arousal may be more likely to lead to personal distress (Eisenberg et al., 2013), an aversive state of negative arousal consistently linked to avoidance behaviour (Grynberg & López-Pérez, 2018), hostility (Contardi et al., 2016) and internalizing symptoms (MacDonald & Price, 2019). Thus, empathic concern and personal distress may play an important role in predicting socio-emotional functioning. The current review will aim to address these empathy-related components, as well as affective and cognitive dimensions of empathy.

METHODS

Search strategy: This review will conform to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 (Page et al., 2021). A systematic search of five electronic databases will be conducted: Ovid MEDLINE, ProQuest, PsycINFO, Scopus, and Web of Science. Studies will be included if they assess empathy using a validated self-report measure(s) in an acquired brain injury sample. There will be no limitations to publication date or status, however the search will be restricted to English language only. Additional inclusion criteria are listed below. Searches will be re-run shortly before the final analyses and any further studies identified will be retrieved for inclusion.

Example search strategy: (empath* OR interpersonal reactivity OR emotion* contagion OR experience sharing OR theory of mind OR mentali?ing OR perspective taking OR social cogniti*) AND ((brain OR head OR craniocerebral OR cranial OR cerebr*) Adj2(injur* OR trauma* OR incident OR accident OR damage OR concussi* OR brain ischemi* OR stroke OR diffuse axonal injur* OR tbi OR abi OR abd)).

Participant or population: This review will include studies with an adult population (mean age between 18 – 70 years old) with an acquired brain injury (ABI). ABI is defined as any brain injury incurred after birth, excluding degenerative disease. It comprises traumatic brain injury (TBI, i.e., injury caused by external force to the head) and non-TBI, such as cerebral vascular accident, aneurysm, brain tumour and hypoxia. Children and adolescents (70 years old) and participants with neurodegenerative disease, as this does not fit our target definition of ABI.

Intervention: Not applicable.

Comparator: A comparator group of adults (aged 18 – 70) without brain injury.

Study designs to be included: Inclusion: cross-sectional, longitudinal, intervention (if pre-treatment data available). Exclusion: qualitative studies, case studies, review articles.

Eligibility criteria: In addition to the above, studies selected for inclusion will be limited to a) English language, b) with full-text availability and c) the presence of a control group.

Information sources: Ovid MEDLINE, ProQuest, PsycINFO, Scopus, and Web of Science. Additional studies may be identified by hand-searching, included scanning the reference list of included studies. Unpublished studies will be sought.

Main outcome(s): Empathy ability, as measured by any validated self-report tool.

Additional outcome(s): Sample age, gender and injury type (e.g., traumatic brain injury, stroke).

Data management: Covidence software will be used to manage all stages of the data screening and extraction process. After removal of duplicates, the lead author will initially screen titles and abstracts against the inclusion/exclusion criteria outlined above. The remaining records will then be full text screened. At each stage of the screening process, a second author will independently screen 40% of the records for inclusion in the review. Reasons for excluding studies will be recorded, as well as the level of agreement between the two researchers. Conflicts will be resolved via discussion and/or input from an additional reviewer.

Data will be manually extracted by the lead author and checked by a second author. Study authors will be contacted to clarify uncertainties or obtain missing data. Data extracted will include:

- Study title, author, journal and year of publication
- Study aim
- Study funding sources and any reported conflicts of interest
- Participant recruitment method and setting
- Sample size, age, gender composition
- Injury characteristics (e.g., injury type, time since injury)
- Comparator group characteristics (e.g., demographic information, type of control group)
- Measure/s of empathy used in the study
- Mean (SD) empathy levels for ABI sample and comparator group.

Quality assessment / Risk of bias analysis:

The quality of individual studies will be appraised according to the Joanna Briggs Institute Critical Appraisal Tools (Joanna Briggs Institute, 2017).

Strategy of data synthesis: Sample characteristics, nature and severity of injury and empathy measurement will be summarized for ABI participants and controls. Where studies have used similar measures and conceptualisations of

empathy, results will be pooled and quantitative analysis carried out. Meta-analysis will be conducted using the Comprehensive Meta-Analysis Software (CMA) and the software programme R using the "Metafor" package (Viechtbauer, 2010). Hedges' g will be used to estimate the magnitude of the standardized difference between mean empathy scores for the ABI and control groups. A random-effects model is planned, as heterogeneity in effect sizes across studies is expected.

Subgroup analysis: If sufficient quantities of studies are found, the review may additionally analyse individual components of empathy (e.g., cognitive empathy, affective empathy) and associated constructs (e.g., empathic concern, personal distress). The review also aims to compare empathic functioning between males and females, as gender-based differences in self-reported empathy have consistently been found in community samples. If possible, stratified analysis will be used to explore heterogeneity in effect estimates according to the measures used.

Sensitivity analysis: Not applicable.

Language restriction: English.

Country(ies) involved: Australia.

Keywords: acquired brain injury, empathy, systematic review, neuropsychology.

Dissemination plans: The results will be presented as a journal article.

Contributions of each author:

Author 1 - Emily Clements - Conceptualisation of the review, literature search, study screening, data extraction, quality assessment, data analysis, first draft of the manuscript and approval of the final manuscript.

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