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Neuroimaging correlates of symptom burden and functional recovery following mild traumatic brain injury: A systematic review☆

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A R T I C L E I N F O

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A B S T R A C T

Background: Mild traumatic brain injury (mTBI) represents 95% of all traumatic brain injuries. Despite being classified as "mild," mTBI can lead to persistent symptoms that impact quality of life. Diagnostic and management strategies rely heavily on subjective symptom reporting due to a lack of validated biomarkers. Identifying neuroimaging biomarkers to characterise the pathophysiological features underlying symptom burden and poor recovery is critical for improving mTBI management.
Objective: To synthesise evidence on cross-sectional, longitudinal, and prognostic links between Magnetic Resonance Imaging (MRI) features and mTBI symptom burden and functional recovery.
Methods: The review followed PRISMA guidelines. Systematic searches of MEDLINE, SCOPUS, and Cochrane Library identified mTBI studies with acute MRI data, measures of symptom burden or functional recovery, and at least one follow-up clinical timepoint, covering publications to July 18, 2025. Risk of bias was evaluated using the Quality in Prognostic Studies tool, and findings were synthesised narratively.
Results: Sixty-two of 7,232 articles were included. The review identified heterogeneous evidence across MRI modalities. Structural MRI findings showed limited correlation with clinical outcomes, while changes in white matter and functional connectivity were more strongly associated with symptom burden and recovery. Disruptions of integrative regions and association pathways such as the thalamus, superior longitudinal fasciculus, and cingulate cortex were linked to worse symptom burden and recovery outcomes.
Conclusions: Acute MRI, when contextualised with clinical data, helps delineate correlates of mTBI symptom burden and functional recovery. To strengthen inference, future neuroimaging studies should prespecify and report symptom burden and functional recovery as core endpoints.

Abbreviations: AD, axial diffusivity; ACRM, American Congress of Rehabilitation Medicine; ASL, arterial spin labelling; AUC, area under the curve; BSI, Brief Symptom Inventory; CBF, cerebral blood flow; CDC, Centers for Disease Control and Prevention; CISG, Concussion in Sport Group; DKI, diffusion kurtosis imaging; DTI, diffusion tensor imaging; FA, fractional anisotropy; fALFF, fractional amplitude of low frequency fluctuations; FLAIR, fluid attenuated inversion recovery; GCS, Glasgow Coma Score; GOS-E, Glasgow Outcome Scale Extended; HAM-A, Hamilton Anxiety Rating Scale; HAM-D, Hamilton Depression Rating Scale; HBI, Health and Behaviour Inventory; ICA, independent component analysis; IQR, interquartile range; KAX, axial kurtosis; KFA, kurtosis fractional anisotropy; KRAD, radial kurtosis; LOC, loss of consciousness; MD, mean diffusivity; MK, mean kurtosis; mTBI, mild traumatic brain injury; NCAA-DOD CARE, National Collegiate Athlete Association and U.S. Department of Defense Concussion Assessment, Research, and Education Consortium.

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1. Introduction

Mild traumatic brain injury (mTBI) represents 95 % of all traumatic brain injuries (Feigin et al., 2013, James et al., 2019). The term "concussion" is often used interchangeably with mTBI, and other times as a distinct form of brain injury. There is now consensus that concussion is a form of mTBI (Patricios et al., 2023, Silverberg et al., 2023). Further, in 2018, a statement from the Centers for Disease Control and Prevention recommended using mTBI as the standard terminology to avoid misinterpretation (Lumba-Brown et al., 2018). In line with this recommendation, the term mTBI will be used in the remainder of the paper. While classified as "mild" because they are generally not life-threatening and do not typically result in coma or permanent disability (Sussman et al., 2018), up to 50 % of individuals with such injuries may experience debilitating symptoms and a reduced quality of life 6–12 months after the injury (Feigin et al., 2013, Nelson et al., 2019, Voormolen et al., 2020). Previous research has identified several factors that predict delayed recovery from mTBI, including a pre-existing history of mental health issues or migraines, a higher acute symptom burden, female sex, delayed presentation to a clinician, and/or repeated mTBI (Zemek et al., 2016, Iverson et al., 2017, Emery et al., 2021). However, due to a lack of clinically validated objective biomarkers, the pathophysiological mechanisms contributing to the heterogeneity in mTBI symptom severity and functional recovery outcomes are poorly understood (Silverberg et al., 2020). This means that diagnosing, managing, and determining recovery from mTBI relies on clinical assessment, with subjective symptom reporting playing a crucial role in clinical decision-making (Silverberg et al., 2020). One of the difficulties with this current approach is that subjective reporting can be influenced by contextual factors such as downplaying the injury to return to sport (Meier et al., 2015b, Clark and Stanfill 2019). Additionally, emerging evidence suggests that physiological recovery takes longer than the person noticeably experiences symptoms, possibly resulting in people returning to high-risk activities before the brain fully recovers (Kamins et al., 2017). This highlights the need for objective markers of injury and recovery following mTBI.

Kenzie et al., developed a causal-loop model of mTBI that integrates biomechanical studies, basic science, and clinical evidence. This model illustrates how mTBI induces a pathophysiological cellular environment, which impairs neurological networks and drives symptom complaints and quality of life deficits (Kenzie et al., 2018). The framework provides targets for developing potentially translatable fluid and neuroimaging biomarkers to enhance our understanding of mTBI and improve clinical outcomes for patients. Modern Magnetic Resonance Imaging (MRI) sequences offer promising methods to non-invasively investigate the pathophysiological consequences of mTBI on brain structure and function in patient populations. T1-weighted (T1w) images assess changes in brain structure and volume, while T2-weighted (T2w) and FLuid Attenuated Inversion Recovery (FLAIR) images reveal tissue abnormalities. Susceptibility Weighted Imaging (SWI) and Quantitative Susceptibility Mapping (QSM) allow for the assessment of microbleeds and iron deposition. Functional connectivity can be measured by correlating blood oxygenation level dependent (BOLD) fluctuations using resting-state functional MRI (rs-fMRI). Diffusion-weighted imaging, including Diffusion Tensor Imaging (DTI), facilitates the investigation of altered white matter structure, with more advanced forms such as Diffusion Kurtosis Imaging (DKI) allows one to investigate more complex microstructural changes. Finally, Arterial Spin Labelling (ASL) can map perfusion parameters such as cerebral blood flow (CBF) and cerebral blood volume.

Previous efforts to study mTBI using MRI have largely focused on comparing participants with mTBI against healthy controls. Systematic reviews have highlighted conflicting results across DTI (Asken et al., 2018, Hellewell et al., 2021, Jain et al., 2021, Lindsey et al., 2021), rs-fMRI (Morelli et al., 2021), and ASL (Wang et al., 2023) studies, attributing these inconsistencies to variations in study design, time since mTBI, imaging parameters, image quality, and analysis methods. For susceptibility-based techniques such as SWI and QSM, there appears to be only one prior scoping review (Hageman et al., 2022), and reporting of associations with outcome data was sparse. Many studies, however, treat mTBI samples as a homogeneous group despite documented heterogeneity in symptomology and functional recovery outcomes. Furthermore, studies commonly group acute (0–14 days post-injury), subacute (14 days to 8 weeks post-injury), and chronic (12 + weeks post-injury) mTBI in the same sample for analysis. Finally, reviews to date have focused on a single MRI modality to investigate the effects of mTBI. The multifaceted nature of mTBI suggests that valuable insights may be gained from curating evidence to explore the overlapping nature of MRI findings across multiple modalities.

Given the complexity of mTBI, MRI findings may vary between patients with different levels of symptom severity or between those whose symptoms spontaneously resolve versus those who develop persistent symptoms. To better understand how MRI can provide insights into mTBI symptoms and functional recovery, synthesising the available evidence across various MRI modalities and study designs is essential. mTBI outcomes vary across populations due to differences related to injury mechanisms, sex, life stage, and recovery environments. Synthesising evidence across these heterogeneous groups provides a unique opportunity to identify common neurobiological patterns that may underpin symptom burden and recovery, irrespective of demographic or contextual factors. Examining concurrent and longitudinal imaging features can help identify brain regions that are particularly vulnerable to change after injury, characterise recovery trajectories, and clarify the predictive value of early imaging markers for long-term outcomes. Therefore, this systematic review collates and appraises the literature to address three key questions:

1. How strongly do imaging features correlate with same-visit measures of symptom burden when assessed cross-sectionally (both at acute stage and at later follow-up timepoints)?
2. How do longitudinal changes in imaging features correlate with changes in symptom burden and/or functional recovery over the same timeframe?
3. How do acute imaging features relate to, or predict, follow-up clinical assessments of symptom burden and/or functional recovery?

2. Methods

This review was conducted per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A priori criteria of this review were registered with the International Prospective Register of Systematic Reviews (PROSPERO; CRD42022338069), and the review methodology conformed to Population, Intervention, Comparator, and Outcome (P.I.C.O.) guidelines. Note, studies reporting

ND, no difference; NODDI, neurite orientation dispersion and density imaging; NS, not specified; ODI, orientation dispersion index; PASL, pulsed arterial spin labelling; PCASL, pseudo-continuous arterial spin labelling; PCSI, Post Concussion Symptom Inventory; PCSS, Post Concussion Symptom Scale; PedsQL™, Paediatric Quality of Life Inventory; P-INJ, post-injury; PROMIS, Patient-Reported Outcomes Measurement Information System; QSM, quantitative susceptibility mapping; rCBF, relative cerebral blood flow; RD, radial diffusivity; ReHo, regional homogeneity; ROI, region-of-interest; RPQ, Rivermead Post Concussion Symptoms Questionnaire; rs-fMRI, resting-state functional magnetic resonance imaging; RTP, return to play; SCAT, Sport Concussion Assessment Tool; SWI, susceptibility weighted imaging; TBSS, tract based spatial statistics; T1w, T1 weighted; T2w, T2 weighted; V_{IC}, intracellular volume; V_{ISO}, isotropic volume; WHO, World Health Organization.

MRI findings and neurocognitive outcomes without measurement of symptom burden and/or functional recovery outcomes were beyond the scope of this review.

For the purposes of this review – and based on common characteristics across various definitions (Carroll et al., 2004, Carney et al., 2014, Patricios et al., 2023, Silverberg et al., 2023) – mTBI is used to describe brain injuries with the following features:

- A plausible mechanism of injury involving the transfer of direct or indirect external forces to the brain;
- Clinical signs such as Glasgow Coma Scale (GCS; (Jain and Iverson 2020)) score of 13–15, loss of consciousness ≤ 30 min, post-traumatic amnesia ≤ 24 h, gross motor instability, and/or seizure;
- Acute alteration of mental status (i.e. confusion, disorientation, dazed);

Table 1
Search strategy and inclusion/exclusion criteria.

Systematic search strategy		
mTBI-related search terms tbi OR mtbi OR "traumatic brain inj*" OR concuss* OR "sport*-related concussion" OR postconcussion OR "post-concuss*" OR "brain inj*" OR "head impact*"		
AND Imaging search terms "MRI" OR "brain imag*"		
AND Modality search terms "brain plasticity" OR "connectivity" OR "structur*" OR "tract*" OR "perfusion" OR "atlas" OR "diffusion" OR "myelin" OR "relaxom*"		
AND Functional recovery search terms "recovery" OR "symptoms" OR "return to play" OR "return to activity" OR "return to learn" OR "return to work" OR "quality of life" OR "QOL" OR "function" OR participat* OR independ* OR "well-being" or "daily activ*"		
P.I.C.O. framework & study selection criteria		
	Inclusion criteria	**Exclusion criteria**
Participants/population: Males and females of any age diagnosed with mTBI/concussion	Participants who have been diagnosed with mTBI/concussion by a qualified healthcare provider based on criteria consistent with the **American Congress of Rehabilitation Medicine diagnostic criteria for mTBI and/or the Concussion in Sport Group guidelines**	Moderate or severe TBI based on Glasgow Coma Score <13 and/or clinical imaging In vitro models of brain/neuronal/axonal injury Spinal cord injury Subjects with TBI on life support, in a comatose state, and/or subjects that are paralysed
Intervention/exposure: Exposure to direct or indirect biomechanical loading resulting in mTBI/concussion	Examples of biomechanical loading that commonly result in mTBI/concussion diagnosis: falls, sport/physical activity-related collisions, domestic violence/assaults, motor vehicle or workplace accidents, blast exposure	Studies of individuals exposed to repetitive head impacts who are not clinically diagnosed with mTBI/concussion Brain injuries secondary to: ischemia, hypoxia, haemorrhage, cardiovascular complications, chemotherapy, radiation, prenatal complications, penetrating injuries
Comparators/controls: Within-subject longitudinal data, pre-injury baseline measurements, musculoskeletal or trauma injury group, neurologically normal control group, participants receiving standard clinical care, normative data derived from open-source databases	Presence of comparison data	Absence of comparison data
Outcomes: MRI scans and measures of functional recovery	Longitudinal studies with: At least one MRI modality and one measure of functional recovery **collected within the first two weeks post-injury** Minimum of one follow-up timepoint with at least functional recovery data reported	First timepoint collected beyond the first two weeks post-injury No measure of functional recovery Studies that measured neurocognitive or neuropsychological performance alone Cross-sectional studies

MRI – Magnetic Resonance Imaging; mTBI – mild traumatic brain injury.

- Acute physical (i.e. headache, nausea, balance problems, photophobia), cognitive (memory problems, feeling slowed down, difficulty concentrating), or emotional (i.e. uncharacteristic emotional lability or irritability) symptoms that may present immediately or evolve within 72 h post-injury;
- Signs and symptoms are not better explained by a confounding factor (i.e. psychological trauma, alcohol or substance consumption, circulatory disruption); and
- If acute clinical imaging acquired:
  - o Uncomplicated mTBI: clinical criteria above are met and *no* intracranial pathoanatomic features are present on CT/MRI;
  - o Complicated mTBI: clinical criteria are met and intracranial pathoanatomic features (e.g. contusion, haemorrhage, extra-axial lesion, etc.) are present but *do not* require neurosurgical intervention (Williams et al., 1990).

2.1. Search strategy and study selection criteria

Table 1 provides the search terms used to identify studies investigating the relationships between functional recovery outcomes following mTBI and acute/follow-up MRI findings. Using the AND operator, we filtered titles, abstracts, and keywords by combining mTBI-related, imaging-related, modality-related, and functional recovery-related search terms. Additional filtering was applied, when possible, to identify full text original research journal articles written in English. The systematic search returned 8,703 articles (Fig. 1) available online

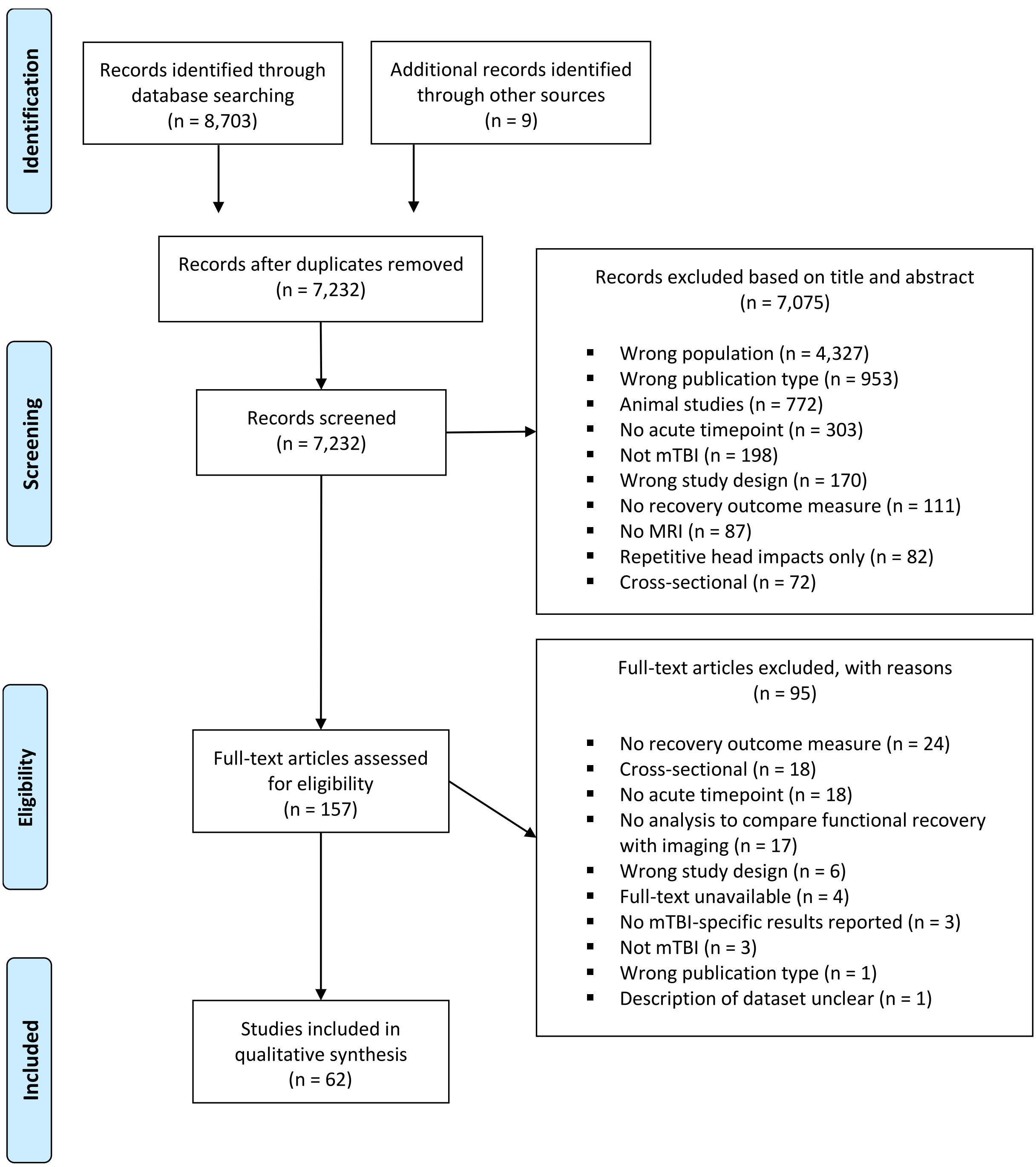

Fig. 1. PRISMA flowchart.

and published from inception through to July 18, 2025, in MEDLINE [EBSCO], SCOPUS, and Cochrane Library [Wiley]. After removal of duplicates, the titles and abstracts of 7,232 studies were blindly screened for inclusion by JM and RM or MP using Rayyan Systematic Review Software. The P.I.C.O. framework and inclusion/exclusion criteria detailed in Table 1 were applied to determine eligibility. To be eligible, studies had to report findings relating to one or more of the research questions of interest (same-visit associations, longitudinal change, or predictive relationships). Blinding was temporarily removed after title and abstract screening to resolve any disagreements about studies requiring full-text screening for eligibility. Blinding was reactivated for full-text screening, and again, disagreements were resolved via discussion.

2.2. Data extraction

For each study, the mTBI definition, study design, sample size and characteristics, MRI sequence(s), scanner type, imaging timepoints, measures of mTBI symptoms and/or functional recovery, and results relating imaging findings to symptom/recovery findings were extracted and reported. Only significant results after multiple comparisons correction were extracted, unless otherwise indicated.

2.3. Risk of bias assessment

The Quality in Prognostic Studies (QUIPS) Tool was used to assess potential sources of bias (Hayden et al., 2006, Hayden et al., 2013). The QUIPS tool was chosen as it was developed to assess risk of bias in observational prognostic factor studies, which aligns well with aims of this review to assess concurrent associations and predictive relationships between imaging features (prognostic factors) and mTBI-related symptom burden or functional recovery (outcomes). Sources of bias were assessed across six domains: study participation, study attrition, prognostic factor measurement, outcome measurement, confounding measurement, and analysis. Each domain was rated as low, moderate, or high risk of bias by appraising an operationalised set of prompting items. For example, items within the study attrition domain include whether reasons for loss to follow-up are provided and whether participants lost to follow-up are adequately described for key characteristics (Hayden et al., 2006, Hayden et al., 2013). Recognising common sources of bias in imaging studies, particular focus was given to transparency in participant enrolment and attrition, image preprocessing, adjusting for key covariates (e.g. age, sex, education, motion, scanner site), and correction for multiple comparisons during risk of bias assessment. JM applied the QUIPs tool to all included studies with a 10 % random check by MP, any disagreements or uncertainty were resolved by discussion.

3. Results

Screening of titles and abstracts resulted in 157 full-text articles assessed for eligibility. During full-text screening, a search of reference lists identified nine further studies for consideration. In total, 62 studies were included in the qualitative synthesis for this review (Fig. 1).

3.1. Study characteristics

A description of the mTBI definition used, mTBI and control cohort details, MRI sequences and scanners, and whether multi-site data was used is provided for each study in Table 2.

All studies adopted an observational cohort design. Across 62 studies, 35 examined paediatric and/or young adults (university-age) with mTBI (Henry et al., 2011, Meier et al., 2015a, Meier et al., 2016, Churchill et al., 2017, Manning et al., 2017, Meier et al., 2017, Koch et al., 2018, McCuddy et al., 2018, Murdaugh et al., 2018, Stephens et al., 2018, Churchill et al., 2019a, Churchill et al., 2019b, Wang et al., 2019, Baker et al., 2020, Mayer et al., 2020a, Meier et al., 2020, Muftuler et al., 2020, Stephenson et al., 2020, Ware et al., 2020, Wu et al., 2020, Bobholz et al., 2021, Fleck et al., 2021, Chung et al., 2022, Mayer et al., 2022, Ware et al., 2022, Brown et al., 2023, Mayer et al., 2023a, Mayer et al., 2023b, Onicas et al., 2023, Ware et al., 2023, Sicard et al., 2024, van der Horn et al., 2024, Onicas et al., 2025), with the remaining 27 studies evaluating effects of mTBI in consecutive adult patients presenting to emergency departments, trauma centres, or outpatient facilities (Yuh et al., 2014, Sours et al., 2015a, Sours et al., 2015b, Strauss et al., 2016, Dall'Acqua et al., 2017, Palacios et al., 2017, Evans et al., 2018, Studerus-Germann et al., 2018, Madhavan et al., 2019, Yin et al., 2019, D'Souza et al., 2020, Stenberg et al., 2021, Zhuo et al., 2021, Huovinen et al., 2022, Palacios et al., 2022, Cai et al., 2023, Ekdahl et al., 2023, Gugger et al., 2023, Li et al., 2023, Pinto et al., 2023, Woodrow et al., 2023, Xu et al., 2023, Li et al., 2024, Moen et al., 2024, Richter et al., 2024, Walter et al., 2024, Zhuo et al., 2024). Twenty of the 35 paediatric/young adult studies were specifically focused on sports-related mTBI (Henry et al., 2011, Meier et al., 2015a, Meier et al., 2016, Churchill et al., 2017, Manning et al., 2017, Meier et al., 2017, Koch et al., 2018, McCuddy et al., 2018, Murdaugh et al., 2018, Stephens et al., 2018, Churchill et al., 2019a, Churchill et al., 2019b, Wang et al., 2019, Meier et al., 2020, Muftuler et al., 2020, Wu et al., 2020, Bobholz et al., 2021, Chung et al., 2022, Bertò et al., 2024, Churchill et al., 2025).

Comparators/control cohorts reported across the studies included age and sex-matched healthy controls (Sours et al., 2015a, Sours et al., 2015b, Strauss et al., 2016, Dall'Acqua et al., 2017, Palacios et al., 2017, Studerus-Germann et al., 2018, Madhavan et al., 2019, Yin et al., 2019, Baker et al., 2020, D'Souza et al., 2020, Mayer et al., 2020a, Stephenson et al., 2020, Wu et al., 2020, Bobholz et al., 2021, Stenberg et al., 2021, Zhuo et al., 2021, Mayer et al., 2022, Palacios et al., 2022, Cai et al., 2023, Gugger et al., 2023, Li et al., 2023, Mayer et al., 2023a, Mayer et al., 2023b, Pinto et al., 2023, Woodrow et al., 2023, Xu et al., 2023, Richter et al., 2024, van der Horn et al., 2024, Zhuo et al., 2024), matched healthy contact sport athletes (Meier et al., 2015a, Meier et al., 2016, Manning et al., 2017, Meier et al., 2017, Murdaugh et al., 2018, Churchill et al., 2019b, Wang et al., 2019, Meier et al., 2020, Wu et al., 2020, Bobholz et al., 2021, Chung et al., 2022, Mayer et al., 2023b) matched healthy non-contact sport athletes (Henry et al., 2011, Churchill et al., 2017, Koch et al., 2018, McCuddy et al., 2018, Stephens et al., 2018, Churchill et al., 2019a, Churchill et al., 2019b, Muftuler et al., 2020, Chung et al., 2022, Mayer et al., 2023b), patients with isolated upper/lower extremity orthopaedic injury (Mayer et al., 2020a, Ware et al., 2020, Fleck et al., 2021, Ware et al., 2022, Brown et al., 2023, Ekdahl et al., 2023, Onicas et al., 2023, Ware et al., 2023, Sicard et al., 2024, Zhuo et al., 2024, Onicas et al., 2025) or within-subject longitudinal data (Yuh et al., 2014, Evans et al., 2018, Huovinen et al., 2022, Bertò et al., 2024, Li et al., 2024, Moen et al., 2024, Walter et al., 2024, Churchill et al., 2025). A single study had pre-injury MRI data (Churchill et al., 2025). Approximately half of controls/comparators were assessed at a single timepoint, while the remainder were assessed at multiple timepoints after injury.

Twenty-three studies used data from registered research initiatives including: A-CAP (Ware et al., 2020, Ware et al., 2022, Onicas et al., 2023, Ware et al., 2023, Onicas et al., 2025), TRACK-TBI (Yuh et al., 2014, Palacios et al., 2017, Evans et al., 2018, Palacios et al., 2022, Cai et al., 2023), NCAA-DOD-CARE (Wang et al., 2019, Meier et al., 2020, Wu et al., 2020, Bobholz et al., 2021, Chung et al., 2022, Bertò et al., 2024), CENTER-TBI (Pinto et al., 2023, Woodrow et al., 2023, Richter et al., 2024), PEDCARE (Brown et al., 2023, Sicard et al., 2024) and the Trondheim mTBI Study (Stenberg et al., 2021, Moen et al., 2024). Twenty-one studies analysed data collected across multiple sites (Evans et al., 2018, Madhavan et al., 2019, Wang et al., 2019, Mayer et al., 2020a, Meier et al., 2020, Ware et al., 2020, Wu et al., 2020, Bobholz et al., 2021, Chung et al., 2022, Palacios et al., 2022, Ware et al., 2022, Cai et al., 2023, Mayer et al., 2023b, Onicas et al., 2023, Pinto et al., 2023, Ware et al., 2023, Woodrow et al., 2023, Bertò et al., 2024, Moen

Table 2
Summary of studies meeting inclusion for review.

Authors	mTBI definition	mTBI cohort details	Control cohort details	MRIsequence(s)	Multi-site?	Scanner(s)
Henry et al. (2011)	NS	University level male football players presenting to team physician or physiotherapist n =16 22.08 ± 1.72 years	Athletes with no history of mTBI n = 8 22.81 ± 1.53 years	DTI	N	Siemens Trio 3T
Yuh et al. (2014)	ACRM	Patients presenting to emergency department CT/MRI-negative n = 44 31.2 ± 9.5 years F: 17; M: 27 CT/MRI-positive n = 32 33.9 ± 12.0 years F:9; M: 23	Age and sex matched healthy controls with no history of drug/alcohol abuse, neuropsychiatric illness, or previous TBI n = 50 28.7 ± 9.2 years F: 18; M: 32	DTI	N	GE Signa EXCITE 3T
Meier et al. (2015a)	NS	Male university football athletes n = 17 20.57 ± 1.20 years	Uninjured male university football athletes n = 27 20.65 ± 1.43 years	ASL	N	GE Discovery MR750 3T
Sours et al. (2015a)	GCS 13–15 and mechanism of injury consistent with trauma and a positive admission head CT or altered mental status and/or loss of consciousness.	mTBI with persistent symptoms n = 15 50.2 ± 13.9 years F: 7; M: 8 mTBI without persistent symptoms n = 17 34.2 ± 16.5 years F: 4; M: 13	Neurologically intact age and sex matched controls n = 31 37.3 ± 17.1 years	rs-fMRI	N	Siemens Tim Trio 3T
Sours et al. (2015b)	Same as above	mTBI with persistent symptoms n = 12 46.3 ± 14.1 years F: 6; M: 6 mTBI without persistent symptoms n = 16 33.3 ± 15.3 years F: 4; M: 12	Neurologically intact age and sex matched controls n = 28 39.3 ± 17.2 years F: 12; M: 16	PASL	N	Siemens Tim Trio 3T
Meier et al. (2016)	CISG	University athletes n = 40 20.12 ± 1.4 years F: 10; M: 30	Healthy university contact-sport athletes n = 46 20.31 ± 1.5 years F: 16; M: 30	DTI	N	GE Discovery MR750 3T
Strauss et al. (2016)	GCS 13-15, LOC <20 mins, PTA <24 hours	Patients presenting to emergency department n = 39 38.5 [min: 24; max: 64] years F: 16; M: 10	Healthy controls n = 40 38.85 [min: 20; max: 60] years F: 19; M: 21	DTI	N	Philips Achieva 3T
Churchill et al. (2017)	CISG	University athletes n = 27 20.0 ± 1.8 years F: 14; M:13	Age, sex, and mTBI history matched healthy university athletes with no mTBI in last 6 months n = 27 20.1 ± 2.0 years F: 14; M:13	rs-fMRI, DTI	N	Siemens Magnetom Skyra 3T

(continued on next page)

Table 2 (*continued*)

Authors	mTBI definition	mTBI cohort details	Control cohort details	MRIsequence(s)	Multi-site?	Scanner(s)
Dall'Acqua et al. (2017)	European Federation of Neurological Society	Patients presenting to emergency department n = 49 34.9 ± 12.4 years F: 31; M: 18	Sex, age, and education matched healthy controls n = 49 35.0 ± 12.1 years F: 31; M: 18	rs-fMRI, DTI	N	Philips Ingenia 3T
Manning et al. (2017)	NS	Adolescent male ice hockey players presenting to sports medicine clinic n = 17 13.3 ± 0.6 years	Age matched healthy ice hockey players n = 26 13.0 ± 1.0 years	rs-fMRI, DTI, MRS	N	Siemens Tim Trio 3T
Meier et al. (2017)	CISG	University athletes n = 43 20.29 ± 1.31 years F: 9; M: 34	Healthy university contact-sport athletes n = 51 20.26 ± 1.44 years F: 16; M: 35	rs-fMRI	N	GE Discovery MR750 3T
Palacios et al. (2017)	ACRM	Patients presenting to hospital n =75 32.36 ± 9.50 years	Age and education matched controls with no history of mTBI and/or neuropsychiatric disorders n = 47 28.90 ± 9 years	rs-fMRI	N	GE Signa EXCITE 3T
Evans et al. (2018)	ACRM	Patients presenting to emergency department n = 45 11.6 ± 4.1 years F: 12; M: 33	Within-subject longitudinal data	VIBE T1w, HASTE, SWI	Y	3T scanners across vendors
Koch et al. (2018)	NS	Male high school and university football athletes n = 28 17.7 (95% CI: 17.2-18.3) years	Athletes without mTBI n = 28 17.9 (95% CI: 17.3-18.5) years	QSM	NS	NS
McCuddy et al. (2018)	CISG	University athletes n = 43 20.29 ± 1.31 years F: 9; M: 34	Age and sex matched healthy athletes n = 51 20.26 ± 1.44 years F: 16; M: 35	rs-fMRI	N	GE Discovery MR750 3T
Murdaugh et al. (2018)	GCS 13-15, LOC < 5 min	Adolescent male football players presenting to sports medicine clinic n = 16 15.99 ± 1.18 years	Age matched players from the same team with no history of mTBI n = 12 15.77 ± 1.23 years	rs-fMRI, DTI	N	Siemens Trio 3T
Stephens et al. (2018)	A witnessed blow to the head or body with subsequent onset of at least 2 mTBI symptoms, LOC <15 min, PTA <24 hours, and GCS 13-15	Adolescent athletes presenting to mTBI clinic n = 15 15.6 ± 1.2 years F:4; M:11	Adolescent athletes with no history of mTBI n = 15 15.2 ± 1.7 years F: 5; M: 10	PCASL	N	Philips 3T
Studerus-Germann et al. (2018)	GCS 13-15, LOC < 30 min, PTA < 24 h and/or alteration in mental status at time of injury	Patients presenting to emergency department n = 30 35.0 ± 13.4 years F:14; M: 16	Age and sex matched healthy controls n = 20 43.2 ± 14.4 years F:10; M:10	T1w, Fast gradient T2w, SWI	N	Siemens MAGNETOM Verio 3T
Churchill et al. (2019a)	Events where athletes sustained direct or indirect contact to the head with the presence of signs and/or symptoms	Athletes presenting to university sports medicine clinic n = 33 20.5 ± 1.7 years F: 17; M: 16	Age, sex and mTBI history matched healthy athletes n = 33 20.3 ± 2.0 years F: 17; M: 16	Single-shell DTI, Multi-shell-NODDI	N	Siemens MAGNETOM Skyra 3T

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Table 2 (*continued*)

Authors	mTBI definition	mTBI cohort details	Control cohort details	MRIsequence(s)	Multi-site?	Scanner(s)
Churchill et al. (2019b)	CISG	Athletes presenting to university sports medicine clinic n = 24 20.0 ± 1.9 years F: 13; M: 11	Age, sex and mTBI history matched healthy athletes n = 122 20.3 ± 2.0 years F: 60; M: 62	rs-fMRI, ASL, DTI	N	Siemens MAGNETOM Skyra 3T
Madhavan et al. (2019)	NS	Patients presenting to hospital n = 91 23.4 ± 8.8 years F: 42; M: 49	Age and sex matched healthy controls n = 23 25.1 ± 8.7 years F:12; M: 11	rs-fMRI	Y	GE Signa MR750 3T
Wang et al. (2019)	NCAA-DoD CARE	University athletes and military service academy students presenting to team medical professional n = 24 18.96 ± 1.20 years F: 5; M: 19	Age, sex, sport and premorbid level of intelligence matched healthy contact sport controls n = 24 19.33 ± 1.52 years F: 5; M:19	ASL	Y	Siemens 3T Trio or GE Discovery MR750 3T
Yin et al. (2019)	WHO	Patients presenting to emergency department n = 33 37.7 ± 13.6 years F: 12; M: 21	Age, sex, and education matched healthy controls with no history of neurological or psychiatric disorder n = 31 37.5 ± 12.2 years F: 9; M: 22	DTI	N	GE 750 3T
Baker et al. (2020)	CISG	Adolescent patients presenting to mTBI clinic n = 26 15.1 ± 1.1 years F: 11; M: 15	Age matched healthy controls n = 13	DTI	N	NS
D'Souza et al. (2020)	ACRM	Adult patients presenting to tertiary health-care centre n = 60 30.40 ± 10.34 years	Age and sex matched healthy controls n = 60 30.82 ± 7.39 years	rs-fMRI	N	Siemens Skyra 3T
Mayer et al. (2020a)	ACRM, WHO, CISG	Paediatric patients presenting to emergency department Site 1 n = 151 14.3 ± 2.5 years F: 68; M: 83 Site 2 n = 136 12.5 ± 2.7 years F: 45; M: 91	Site 1 Age, education, and sex matched typically developing healthy controls n = 106 14.5 ± 2.5 years F: 47; M: 59 Site 2 Orthopaedic injury limited to upper or lower extremity fractures with no recent history of mTBI and similar age and sex distribution n = 71 12.4 ± 2.4 years F: 24; M: 47	T1w, T2w, SWI, T2*w, FLAIR	Y	Siemens MAGNETOM Skyra 3T or Phillips 3T
Meier et al. (2020)	NCAA-DoD CARE	University athletes presenting to team medical professional n = 92 19.18 ± 1.16 years F: 14; M: 78	Age, sex, institution, sport, race/ethnicity, mTBI history, premorbid verbal intellectual functioning, years of participation, status as a starter, and head impact exposure matched non-injured contact sport controls n = 82 19.20 ± 0.90 years F: 15; M: 67	rs-fMRI	Y	Siemens MAGNETOM Prisma 3T or Siemens MAGNETOM Trio 3T or GE Discovery MR750 3T

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Table 2 (*continued*)

Authors	mTBI definition	mTBI cohort details	Control cohort details	MRIsequence(s)	Multi-site?	Scanner(s)
Mufuler et al. (2020)	CDC HEADS UP	Male high school and university football athletes n = 96 18.06 ± 1.5 years	Athletes without mTBI matched based on demographics and neurocognitive performance n = 82 18.37 ± 1.7 years	DKI	N	GE MR750 3T
Stephenson et al. (2020)	ACRM, CISG	Children and adolescents presenting to emergency department and urgent care n = 158 14 [IQR 12-16] years F: 60; M:75	Age and sex matched healthy controls n = 135 15 [IQR 13-16] years F:71; M: 87	rs-fMRI	N	Siemens 3T Trio
Ware et al. (2020)	Blunt head trauma resulting in at least one of following: 1) observed LOC <30 mins; 2) GCS ≥13; or 3) at least two acute signs of mTBI symptoms	Children and adolescent presenting to emergency department within 24 hours of injury n = 132 12.57 ± 2.64 years F: 45; M: 87	Children with orthopaedic injury to the upper or lower extremity n = 69 12.37 ± 2.41 years F: 22; M: 47	DTI	Y	Siemens 3T Trio or Philips Achieva 3T
Wu et al. (2020)	NCAA-DoD CARE	University athletes n = 82 18.87 ± 0.93 years F: 13; M: 69	Age, sex, education and premorbid verbal intellectual functioning matched controls Total n = 137 Contact sport controls n = 68 18.82 ± 1.26 years F: 14; M: 54 Non-contact sport controls n = 69 19.20 ± 1.22 years F: 14; M: 55	DTI	Y	Siemens MAGNETOM 3T Tim Trio or Siemens Prisma 3T
Bobholz et al. (2021)	NCAA-DoD CARE	University athletes presenting to team medical professional n = 99 19.29 ± 1.00 years F: 17; M: 82	Age, sex, sport and premorbid level of intelligence matched healthy contact sport controls: n = 91 19.42 ± 1.29 years F: 20; M:71 Matched non-contact sport controls: n = 95 19.83 ± 1.19 years F: 18; M:77	T1w MPRAGE (Siemens) or T1w BRAVO (GE)	Y	Siemens MAGNETOM Prisma 3T or Siemens MAGNETOM Trio 3T or GE Discovery MR750 3T
Fleck et al. (2021)	Head trauma involving blunt force or acceleration/ deceleration injury with GCS ≥14 with either LOC <30 min or alteration of mental state at time of injury	Adolescents presenting to emergency department Total n = 43 11-16 years	Patients with isolated extremity orthopaedic injury and no suggestion of mTBI Sample size NS	DTI	N	Philips 3T
Stenberg et al. (2021)	WHO	Patients presenting to emergency department n = 178 Median 28.1 [IQR: 18.1-38.1] years F: 65; M: 113	Age, sex, education-matched community controls n = 78 Median 27.6 [IQR: 17.6-37.6] years F: 30; M: 48	DTI	N	3T Siemens Skyra
Zhuo et al. (2021)	GCS 13–15, mechanism of injury consistent with trauma, evidence of physical trauma to the head, and either (a) a positive admission CT or (b) reported loss	mTBI with persistent symptoms @ 6 months: n = 30 46.6 ± 15.6 years F: 11; M: 19	Neurologically intact volunteers aged 18-70 from the local community n = 34 39.0 ± 18.0 years F: 16; M: 18	T1w	N	Siemens Tim Trio 3T

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Table 2 (*continued*)

Authors	mTBI definition	mTBI cohort details	Control cohort details	MRIsequence(s)	Multi-site?	Scanner(s)
	of consciousness and/or post-traumatic amnesia.	mTBI without persistent symptoms @ 6 months n = 23 38.6 ± 15.7 years F: 4; M: 19				
Chung et al. (2022)	NCAA-DoD CARE	Male university football players n = 24 19.7 ± 1.1 years	Male non-contact sport controls with no history of mTBI or repetitive head impacts n = 28 19.7 ± 1.4 years Male football players with repetitive head impact exposure but no mTBI during study period n = 26 19.3 ± 1.2 years	DTI	Y	Siemens MAGNETOM 3T
Huovinen et al. (2022)	WHO	Consecutive mTBI patients presenting to outpatient clinic Uncomplicated mTBI: n = 75 Median 38.0 years F: 37; M: 38 Complicated mTBI: n = 38 Median 41.5 years F: 12; M: 26	Within-subject longitudinal data	T1w, T2w, SWI, FLAIR	N	Siemens MAGNETOM 3T
Mayer et al. (2022)	ACRM, CISG, WHO	Paediatric patients presenting to emergency department n = 204 14.5 ± 2.9 years F: 83; M: 121	Age and sex matched healthy controls n = 173 14.2 ± 2.8 years F: 73; M: 100	DTI	N	Siemens Trio Tim 3T
Palacios et al. (2022)	ACRM	Patients presenting to trauma centre n = 391 34.6 ± 12.5 years F: 132; M 259	Age, sex, education matched friends or family of cases n = 148 33.6 ± 11.4 years F: 48; M: 100	DTI	Y	3T scanners across vendors
Ware et al. (2022)	WHO	Children presenting to emergency department n = 362 12.30 ± 2.45 years	Children with orthopaedic injury to the upper or lower extremity due to blunt force trauma n = 198 12.44 ± 2.23 years	DTI	Y	GE MR750 3T, Siemens Prisma 3T, Siemens Skyra
Brown et al. (2023)	CISG	Children presenting to emergency department n = 66 Median 12.88 [IQR: 11.80-14.36] years F: 31; M: 35	Children with orthopaedic injury to the upper or lower extremity n = 29 Median 12.49 [IQR: 11.18-14.01] F: 12; M: 17	DTI	N	NS
Cai et al. (2023)	ACRM	Patients presenting to trauma centre mTBI with emotional resilience n = 94 36.1 ± 13.4 years F: 20; M: 74 mTBI with neuropsychiatric distress n = 78 35.1 ± 11.7 years	Demographically matched uninjured healthy controls n = 148	DTI	Y	3T scanners across vendors

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Table 2 (*continued*)

Authors	mTBI definition	mTBI cohort details	Control cohort details	MRIsequence(s)	Multi-site?	Scanner(s)
		F: 33; M: 45				
Ekdahl et al. (2023)	WHO	Consecutive patients presenting to emergency department n = 15 25.1 ± 6.5 years F: 7; M: 8	Patients with orthopaedic injury to the upper or lower extremity n = 15 27.5 ± 7.4 years F: 11; M: 4	rs-fMRI	N	Philips Ingenia 3T
Gugger et al. (2023)	NS	Adults presenting to trauma centre n = 35 Median 29.0 [IQR: 23.0-43.0] years F: 8; M: 27	Demographically matched healthy controls with no history of TBI, pre-existing neuropsychiatric disorder, or current pregnancy n = 35 Median 31 [IQR: 23.0-34.0] years F: 13; M: 22	DTI	N	Siemens Prisma 3T
Li et al. (2023)	Closed head injury, LOC <30 min, initial GCS >13, and normal CT	Patients presenting to hospital n = 70 37.97 ± 12.24 years F: 47; M: 23	Demographically matched healthy controls n = 70 36.66 ± 12.04 years F: 47; M: 23	rs-fMRI, DTI	N	Siemens MAGNETOM Prisma 3T
Mayer et al. (2023a)	ACRM, CISG, WHO	Paediatric patients presenting to emergency department n = 208 14.4 ± 2.9 years F: 84; M: 124	Age and sex matched paediatric healthy controls n = 176 14.2 ± 2.9 years F: 74; M: 102	T1w	N	Siemens Trio Tim 3T
Mayer et al. (2023b)	ACRM, CISG, WHO, NCAA-DoD CARE	Paediatric patients presenting to emergency department n = 235 14.3 ± 2.9 years F: 98; M: 137 University athletes n = 97 20.3 ± 1.1 years F: 16; M: 71	Age and sex matched paediatric healthy controls n = 211 13.9 ± 3.0 years F: 94; M: 117 Age and sex matched contact sport controls n = 82 20.4 ± 1.4 years F: 17; M: 70 Age and sex matched non-contact sport controls n = 87 20.7 ± 1.2 years F: 17; M: 70	T1w	Y	3T scanners across vendors
Onicas et al. (2023)	WHO	Children presenting to emergency department n = 386 12.34 ± 2.41 years F: 146; M: 240	Children with orthopaedic injury to the upper or lower extremity due to blunt force trauma n = 199 12.50 ± 2.20 years F: 88; M: 111	rs-fMRI	Y	3T scanners across vendors
Pinto et al. (2023)	Clinical diagnosis of TBI with GCS 13-15	Patients presenting to hospital mTBI with incomplete recovery @ 6 months n = 87 46.2 ± 17.1 years F: 31; M: 56 mTBI with complete recovery @ 6 months n = 92 37.9 ± 15.5 years F: 26; M: 66	Matched healthy controls n = 85 42.9 ± 11.7 years F: 35; M: 49	DTI	Y	3T scanners across vendors

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Table 2 (*continued*)

Authors	mTBI definition	mTBI cohort details	Control cohort details	MRIsequence(s)	Multi-site?	Scanner(s)
Ware et al. (2023)	WHO	Children presenting to emergency department n = 360 12.27 ± 2.44 years F: 137; M: 223	Children with orthopaedic injury to the upper or lower extremity due to blunt force trauma n = 196 12.43 ± 2.23 years F: 87; M: 109	DTI	Y	GE MR750 3T, Siemens Prisma 3T, Siemens Skyra
Woodrow et al. (2023)	Clinical diagnosis of TBI with GCS 13-15	Patients presenting to hospital within 24 hours of injury n = 108 F: 39; M: 69	Matched healthy controls n = 76 F: 30; M: 46	rs-fMRI	Y	3T scanners across vendors
Xu et al. (2023)	WHO	Patients presenting to emergency department with post-traumatic headache n = 36 37.64 (Standard error: 2.08) years F: 17; M: 19	Matched healthy controls n = 34 34.85 (Standard error: 1.87) years F: 20; M: 14	T1w	N	GE MR750 3T
Bertò et al. (2024)	NCAA-DoD CARE	University athletes presenting to team medical professional n = 47 (42 unique athletes) 18.77 ± 0.84 years F: 8; M 34	Within-subject longitudinal data	DTI	Y	Siemens MAGNETOM Prisma 3T or Siemens MAGNETOM Tim Trio 3T
Li et al. (2024)	ACRM	mTBI with post-traumatic headache n = 48 39.0 ± 11.05 years F: 21; M: 27 mTBI without post-traumatic headache n = 46 42.13 ± 11.98 years F: 25; M: 21	Within-subject longitudinal data	PCASL	N	Philips Ingenia 3T
Moen et al. (2024)	Clinical diagnosis of TBI with GCS 13-15	Consecutive TBI patients presenting to hospital mTBI subsample: n = 158 Median 27.7 [IQR: 21.7-42.5] years F: 55; M: 103	Within-subject longitudinal data	FLAIR, DWI, T2*GRE, SWI	Y	Siemens scanners ranging from 1T to 3T
Richter et al. (2024)	Clinical diagnosis of TBI with GCS 13-15	Patients presenting to hospital n = 153 Median 44 [min: 20; max: 70] years F: 66; M: 87	Healthy volunteers n = 157 Median 39 [min: 21; max: 68] years F: 67; M: 89	DTI	Y	3T scanners across vendors
Sicard et al. (2024)	CISG	Children presenting to emergency department within 48 hours of injury n = 70 13.05 ± 2.02 years F: 33; M: 37	Children with orthopaedic injury to the upper extremity due to blunt force or physical trauma n = 29 12.59 ± 1.97 years F: 12; M: 17	PASL	N	Siemens MAGNETOM Biograph MR 3T
van der Horn et al. (2024)	ACRM, CISG	Paediatric patients presenting to emergency department n = 200 14 [IQR: 12-16] years	Age and sex matched paediatric healthy controls n = 176 14 [IQR: 12-16] years	rs-fMRI	N	Siemens Tim Trio 3T

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Table 2 (*continued*)

Authors	mTBI definition	mTBI cohort details	Control cohort details	MRIsequence(s)	Multi-site?	Scanner(s)
		F: 81; M: 119	F: 77; M: 99			
Walter et al. (2024)	ACRM	Patients presenting to trauma centre n = 32 36.8 ± 13.8 years F: 7; M 25	Within-subject longitudinal data	T1w, FLAIR	N	Siemens Prisma Fit 3T
Zhuo et al. (2024)	GCS 13-15, positive CT or documented LOC, amnesia, and/or evidence of facial trauma	Patients presenting to trauma centre n = 44 34.5 ± 11.3 years F: 20; M 24	Matched healthy controls n = 18 35.5 ± 12.3 years F: 13; M 5 Orthopaedic injury controls n = 19 37.3 ± 13.8 years F: 7; M 12	T1w, T2w, DTI	N	Siemens Prisma 3T
Churchill et al. (2025)	CISG	Athletes presenting to university sports medicine clinic n = 33 20.1 ± 2.3 years F: 18; M: 15	Pre-injury baseline and within-subject longitudinal data	ASL, DTI	N	Siemens MAGNETOM Skyra 3T
Onicas et al. (2025)	WHO	Children presenting to emergency department n = 385 12.35 ± 2.41 years F: 145; M: 240	Children with orthopaedic injury to the upper or lower extremity due to blunt force trauma n = 198 12.49 ± 2.17 years F: 87; M: 111	rs-fMRI	Y	3T scanners across vendors

ACRM – American Congress of Rehabilitation Medicine; ASL – Arterial Spin Labelling; CDC – Centers for Disease Control and Prevention; CISG – Concussion in Sport Group; DKI – Diffusion Kurtosis Imaging; DTI – Diffusion Tensor Imaging; DWI – Diffusion Weighted Imaging; FLAIR – FLuid Attenuated Inversion Recovery; GCS – Glasgow Coma Score; IQR – interquartile range; LOC – loss of consciousness; mTBI – mild traumatic brain injury; NCAA-DOD CARE – National Collegiate Athlete Association and U.S. Department of Defense Concussion Assessment, Research, and Education Consortium; NS – not specified; PASL – Pulsed Arterial Spin Labelling; PCASL – Pseudo-Continuous Arterial Spin Labelling; PTA – post-traumatic amnesia; QSM – Quantitative Susceptibility Mapping; rs-fMRI – resting-state functional MRI; SWI – Susceptibility Weighted Imaging; T1w – T1 weighted; T2w – T2 weighted; WHO – World Health Organisation.

et al., 2024, Richter et al., 2024, Onicas et al., 2025).

3.2. Risk of bias

Risk of bias was assessed using the QUIPS tool. Consistent with guidance from the developers, no single summary score is presented for each study; instead, domain-level ratings are presented in Table 3 to highlight patterns across sources of bias. Overall, 40 studies demonstrated moderate to high risk of bias across two or more domains. The most frequent concerns related to incomplete reporting of participant enrolment and attrition, and inadequate handling of confounding variables. Many studies described attrition due to imaging quality control but did not provide information for other reasons of drop out. Additionally, several studies analysed subsamples of larger cohorts without clearly outlining enrolment or demonstrating representativeness. While most studies recruited demographically matched control groups (e.g. age, sex, education, mTBI history), adjustment for demographic or other key covariates in statistical models was inconsistent. Although voxel-wise multiple comparisons correction was commonly applied, fewer studies adjusted for the number of imaging-clinical associations tested, often citing limited sample sizes. It was also often largely unclear whether the authors responsible for data analysis were blinded. We observed a trend toward lower risk of bias in more recent studies, particularly those that were multi-site, preregistered, or accompanied by protocol papers. Sixteen of the 20 studies with $\leq$ 1 domain rated as moderate or high risk of bias were published since 2023, including four with low risk of bias across all domains.

3.3. Clinical outcomes

3.3.1. Symptomology and quality of life

In this review, 19 instruments were used to assess mTBI symptom burden (see Tables 4–7). The most common instruments were: Rivermead Post-Concussion Symptoms Questionnaire (RPQ; 16 studies; (King et al., 1995)); Sports Concussion Assessment Tool (SCAT) symptom questionnaire (2nd edition: 1 study, 3rd edition 11 studies; (2009, 2013)), Post-Concussion Symptom Scale (PCSS; 7 studies; (Lovell and Collins 1998)); Post-Concussion Symptom Inventory (PCSI; 7 studies; (Sady et al., 2014)); and Health and Behaviour Inventory (HBI; 5 studies, (Ayr et al., 2009)). Most studies assessed clinical symptomology on the same day as the neuroimaging session. The remaining studies assessed symptomology within 2–3 days of the scan session. Four studies directly assessed the quality-of-life following mTBI using the Paediatric Quality of Life Inventory (Varni et al., 2001) or the Sickness Impact Profile (Bergner et al., 1976).

Seven studies used symptom data for subgroup/phenotype analysis within the mTBI sample. Relationships between cognitive, emotional, and somatic symptom subscales and neuroimaging findings were evaluated in three studies. The four remaining studies compared neuroimaging results for mTBI participants with low versus high symptom burden, participants with/without cognitive intolerance or post-traumatic headache, and mTBI participants demonstrating neuropsychiatric distress versus those with emotional resilience.

3.3.2. Definitions of recovery

There was significant heterogeneity in the operational definitions of mTBI recovery status across studies in this review (see Tables 4–7). The number of days until becoming asymptomatic, returning to play (RTP), or returning to work was used as a measure of time until functional recovery in nine studies. Recovery status was measured with the Glasgow Outcome Scale – Extended (GOS-E; (Wilson et al., 2021) either at 3–4 months post-injury (P-INJ) in five studies, or at six months P-INJ in a further seven studies. Fifteen studies differentiated recovered mTBI participants (those with resolved symptoms) from participants with persistent symptoms using available symptom data. However, the criteria used for classifying recovery status varied across studies. Six studies determined persistent symptom status at six months P-INJ based on features consistent with ICD-10 criteria (World Health Organization 2004). Three studies used simple thresholds to define persistent symptom status. The first study based persistent symptom status on the symptom count being > 1 at six weeks P-INJ, the second study used a total PCSS symptom score of > 8 for females and > 6 for males, the third study defined persistent symptoms as ≥ 3 symptoms with score ≥ 3. Seven studies implemented standardized change metrics (z-score based) to establish persistent status. Five studies compared post-injury symptom scores to premorbid symptom reports, and the final three compared against ratings from the control group (Mayer et al., 2020b).

3.4. Imaging findings

This section synthesises evidence across neuroimaging modalities that investigate brain structure, white matter organisation, functional connectivity, and perfusion in relation to mTBI symptom burden and functional recovery. Fig. 2 illustrates the most common MRI modalities and analytical strategies included in this review. Tables 4–7 summarise study-level details by modality: structural/SWI (Table 4; 13 studies); 2) diffusion-weighted imaging (Table 5; 31 studies); resting-state BOLD fMRI (Table 6; 19 studies); and ASL (Table 7; 8 studies). Within each table, results from investigations of paediatric and university-aged cohorts are grouped together due to ongoing neurodevelopment (Johnson et al., 2009, Somerville 2016) with cohorts of consecutive adult patients grouped separately. Below, key findings relevant to the research questions of this review are organised by imaging modality.

3.4.1. Same-visit imaging-symptom associations

Structural and SWI: Associations between imaging features and symptom measures acquired during the same-visit were largely null (Koch et al., 2018, Mayer et al., 2020a, Bobholz et al., 2021, Mayer et al., 2023a, Walter et al., 2024). Exceptions were higher enlarged white matter perivascular spaces relating to higher RPQ symptom scores at 14 days P-INJ and an inverse relationship between predicted brain-age difference and acute clinical risk score (Mayer et al., 2023b, Zhuo et al., 2024).

Diffusion MRI: Same-visit results are mixed. Several whole-brain/tract-based spatial statistics studies report null findings (Henry et al., 2011, Murdaugh et al., 2018, Yin et al., 2019, Muftuler et al., 2020). Reduced fractional anisotropy (FA) or axial diffusivity (AD) within association tracts corresponds with higher symptom burden, and greater mean diffusivity (MD) relates to higher same-day symptoms (Manning et al., 2017, Baker et al., 2020, Ware et al., 2020). Microstructural patterns relate to clinical phenotypes and composite clinical severity scores at acute visits (Churchill et al., 2019b, Mayer et al., 2022, Brown et al., 2023).

Resting-state fMRI: Several analyses report no same-visit associations (Manning et al., 2017, Meier et al., 2017, Ekdahl et al., 2023, van der Horn et al., 2024), while others indicate reduced global or within-network connectivity aligns with greater symptom burden (McCuddy et al., 2018, Churchill et al., 2019b, Madhavan et al., 2019, D'Souza et al., 2020). Multiple studies highlight differences in within-thalamic, thalamo-cortical, and thalamo-subcortical connectivity correlate with

Table 3
Risk of bias assessment using Quality in Prognostic Studies (QUIPS) Tool.

Authors	Study Participation	Study Attrition	Prognostic Factor Measurement	Outcome Measurement	Study Confounding	Statistical Analysis and Reporting
Henry et al. (2011)	Yellow	Red	Yellow	Green	Red	Yellow
Yuh et al. (2014)	Green	Yellow	Green	Green	Yellow	Yellow
Meier et al. (2015a)	Green	Red	Green	Green	Yellow	Yellow
Sours et al. (2015a)	Green	Red	Green	Green	Yellow	Yellow
Sours et al. (2015b)	Green	Red	Green	Green	Red	Yellow
Meier et al. (2016)	Yellow	Red	Green	Green	Yellow	Yellow
Strauss et al. (2016)	Green	Red	Green	Green	Yellow	Green
Churchill et al. (2017)	Yellow	Yellow	Green	Green	Yellow	Green
Dall'Acqua et al. (2017)	Green	Yellow	Green	Green	Yellow	Green
Manning et al. (2017)	Yellow	Yellow	Green	Green	Yellow	Green
Meier et al. (2017)	Yellow	Red	Green	Green	Yellow	Green
Palacios et al. (2017)	Green	Red	Green	Green	Yellow	Green
Evans et al. (2018)	Green	Yellow	Yellow	Green	Green	Yellow
Koch et al. (2018)	Yellow	Yellow	Green	Green	Yellow	Green
McCuddy et al. (2018)	Yellow	Red	Green	Green	Yellow	Green
Murdaugh et al. (2018)	Green	Yellow	Green	Green	Yellow	Green
Stephens et al. (2018)	Green	Yellow	Green	Yellow	Yellow	Green
Studerus-Germann et al. (2018)	Green	Red	Green	Green	Yellow	Green
Churchill et al. (2019a)	Yellow	Yellow	Green	Green	Yellow	Green
Churchill et al. (2019b)	Yellow	Yellow	Green	Green	Yellow	Green
Madhavan et al. (2019)	Green	Yellow	Green	Green	Green	Green
Wang et al. (2019)	Green	Red	Green	Green	Yellow	Green
Yin et al. (2019)	Green	Red	Green	Green	Yellow	Green
Baker et al. (2020)	Yellow	Red	Yellow	Yellow	Yellow	Yellow
D'Souza et al. (2020)	Green	Red	Green	Green	Yellow	Yellow
Mayer et al. (2020a)	Green	Yellow	Green	Green	Yellow	Green
Meier et al. (2020)	Green	Yellow	Green	Green	Green	Green
Muftuler et al. (2020)	Green	Yellow	Green	Green	Yellow	Green
Stephenson et al. (2020)	Green	Yellow	Green	Green	Green	Green
Ware et al. (2020)	Green	Yellow	Yellow	Green	Green	Green
Wu et al. (2020)	Green	Red	Green	Green	Green	Green
Bobholz et al. (2021)	Green	Yellow	Green	Green	Green	Green
Fleck et al. (2021)	Green	Red	Green	Green	Red	Yellow
Stenberg et al. (2021)	Green	Yellow	Green	Green	Green	Green
Zhuo et al. (2021)	Green	Yellow	Green	Green	Yellow	Green
Chung et al. (2022)	Green	Red	Green	Green	Yellow	Green
Huovinen et al. (2022)	Green	Green	Green	Green	Yellow	Yellow
Mayer et al. (2022)	Green	Green	Green	Green	Yellow	Green
Palacios et al. (2022)	Green	Yellow	Green	Green	Green	Green
Ware et al. (2022)	Green	Red	Green	Green	Green	Green
Brown et al. (2023)	Green	Yellow	Green	Green	Green	Green
Cai et al. (2023)	Green	Yellow	Green	Green	Yellow	Green
Ekdahl et al. (2023)	Yellow	Yellow	Green	Green	Yellow	Green
Gugger et al. (2023)	Green	Yellow	Green	Green	Yellow	Green
Li et al. (2023)	Green	Yellow	Green	Green	Yellow	Green
Mayer et al. (2023a)	Green	Green	Green	Green	Yellow	Green
Mayer et al. (2023b)	Green	Yellow	Green	Green	Green	Yellow
Onicas et al. (2023)	Green	Green	Green	Green	Green	Green
Pinto et al. (2023)	Green	Yellow	Green	Green	Green	Green
Ware et al. (2023)	Green	Yellow	Green	Green	Green	Green
Woodrow et al. (2023)	Green	Yellow	Green	Green	Yellow	Green
Xu et al. (2023)	Green	Red	Green	Green	Green	Green
Berto et al. (2024)	Green	Yellow	Green	Yellow	Yellow	Green
Li et al. (2024)	Yellow	Red	Green	Green	Yellow	Green
Moen et al. (2024)	Green	Yellow	Green	Green	Green	Green
Richter et al. (2024)	Green	Green	Green	Green	Green	Green
Sicard et al. (2024)	Green	Green	Green	Green	Green	Green
van der Horn et al. (2024)	Green	Green	Green	Green	Yellow	Green
Walter et al. (2024)	Green	Red	Green	Green	Red	Yellow
Zhuo et al. (2024)	Green	Green	Green	Green	Yellow	Green
Churchill et al. (2025)	Green	Yellow	Green	Green	Green	Green
Onicas et al. (2025)	Green	Green	Green	Green	Green	Green

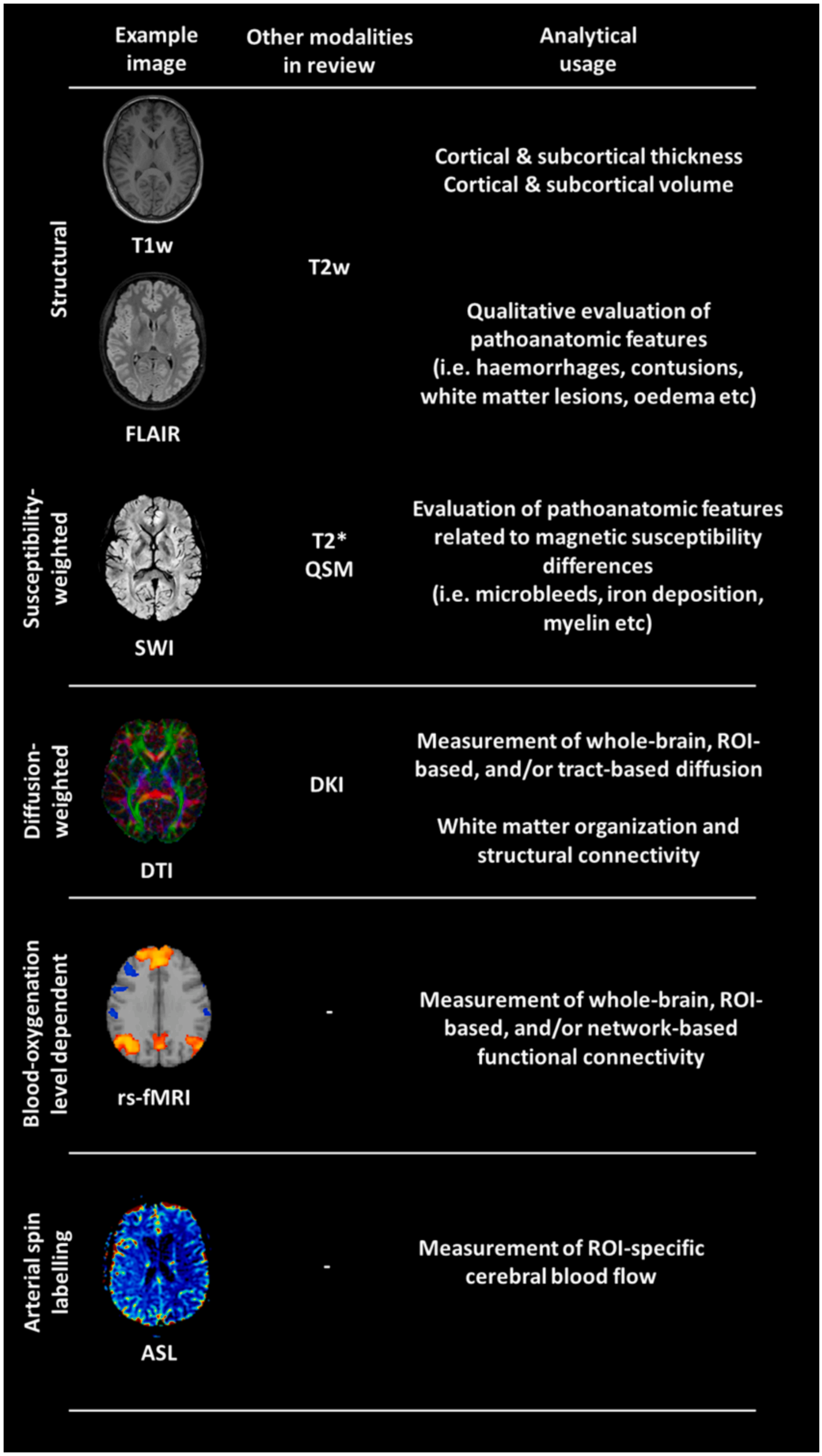

Fig. 2. Summary of MRI modalities used across studies. T1w – T1-weighted; T2w – T2-weighted; FLAIR – Fluid Attenuated Inversion Recovery; SWI – Susceptibility Weighted Imaging; QSM – Quantitative Susceptibility Mapping; DTI – Diffusion Tensor Imaging; DKI – Diffusion Kurtosis Imaging; rs-fMRI – Resting-state Functional MRI; ASL – Arterial Spin Labelling.

Table 4
Results from studies using structural and/or Susceptibility Weighted Imaging grouped by cohort age.

Authors	MRI sequence(s)	Imaging analysis	Imaging timepoints	Measure of symptoms or functional recovery	What does imaging tell us about symptoms and/or functional recovery?
Paediatric and young adult cohort studies					
Evans et al. (2018)	T1w, T2w, FLAIR, SWI	Presence or absence of lesions	2 weeks P-INJ No control group	HBI symptom scores	Presence of extra-axial (but not intra-axial) lesions predicted *lower* HBI cognitive symptoms @ 3 months P-INJ
Koch et al. (2018)	QSM	ROI analysis of susceptibility	24 hours P-INJ, 8 days P-INJ, 6 months P-INJ Controls completed 3 timepoints @ same intervals	SCAT3 symptom scores, days until RTP	No correlation between global or subregional susceptibility and SCAT3 symptom scores @ 24 hours P-INJ Delayed RTP positively associated with greater susceptibility measured @ 24 hours P-INJ within the R cingulum, L inferior fronto-occipital fasciculus, L/R inferior longitudinal fasciculus and L/R superior longitudinal fasciculus (r(s) = 0.58 to 0.67)
Mayer et al. (2020a)	T1w, T2w, SWI, T2*w, FLAIR	Pathoanatomic features of mTBI based on radiological common data elements	7 days P-INJ, 3-4 months P-INJ Orthopaedic injury controls completed 2 timepoints @ same intervals	Parent and child PCSI and HBI symptom scores, PedsQL™ scores	No main effect or interaction effect between MRI findings and PCSI or HBI symptom reports @ ~ 1 week or ~3/4 months P-INJ No main effect or interaction effect between MRI findings and PedsQL™ scores @ ~3/4 months P-INJ
Mayer et al. (2023a)	T1w	Cortical thickness surface maps and ROI volumes for	7 days P-INJ, 4 months P-INJ	PCSI symptom scores and 5P risk score,	ND cortical thickness symptomatic mTBI or asymptomatic mTBI vs controls @ 7 days or 4 months P-INJ

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Table 4 (*continued*)

		the bilateral hippocampi and subcortical structures	Controls completed 2 timepoints @ same intervals	Persistent symptom status @ 4 months P-INJ	ND hippocampal volume symptomatic mTBI vs asymptomatic mTBI @ 7 days or 4 months P-INJ A random forest model using 5P risk score, clinical symptom data and cortical thickness of the rostral middle frontal gyrus and volume of the hippocampi classified mTBI vs control more accurately than a model using only 5P risk score and clinical symptom data (AUC = 0.815 vs 0.731; balance accuracy = 0.746 vs 0.707, sensitivity = 0.732 vs 0.729, specificity = 0.761 vs 0.686)
Bobholz et al. (2021)	T1w	Vertex-wise cortical thickness and cortical volume	24-48 hours P-INJ, Asymptomatic, 7 days post-RTP, 6 months P-INJ Controls completed 4 timepoints @ same intervals	SCAT3 symptom scores, days until asymptomatic	ND in subcortical volumes within the thalamus, hippocampus, or dorsal striatum in mTBI when symptomatic (24-48 hours P-INJ) or asymptomatic
Mayer et al. (2023b)	T1w	T1w images were used to estimate brain age and calculate predicted age difference	Paediatric cohort: 7 days P-INJ, 4 months P-INJ University cohort: ≤2 days P-INJ, asymptomatic, 7 days post-RTP Controls completed 2-3 timepoints @ same interval	Paediatric cohort: PCSI symptom scores and 5P risk score University cohort: SCAT3 symptom score	Negative association between 5P risk score and predicted age difference in paediatric cohort @ 7 days P-INJ No association between predicted age difference and SCAT3 symptom scores in university-aged mTBI cohort @ ≤2 days P-INJ, asymptomatic, or 7 days post-RTP timepoints
Adult cohort studies					

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Table 4 (*continued*)

Studerus-Germann et al. (2018)	T1w, T2w, SWI	Presence or absence of microbleeds	3 days P-INJ, 3 months P-INJ, 1 year P-INJ Single timepoint for controls	PCSS scores	↑ PCSS total symptom score and fatigue, difficulty concentrating and difficulty remembering scores observed in mTBI participants with microbleeds than those without microbleeds @ 1 year P-INJ[†] Number of microbleeds @ 3 days P-INJ in the mTBI group positively associated with greater PCSS total symptom score and PCSS cognitive/emotional items @ 3 months and 1 year P-INJ[†]
Zhuo et al. (2021)	T1w	Subcortical volumes	≤10 days P-INJ, 1 month P-INJ, 6 months P-INJ Single timepoint for controls	GOS-E scores, RPQ symptom scores, presence of persistent symptoms @ 6-months P-INJ	ND subcortical volumes within mTBI without persistent symptoms @ 6 months @ any timepoint ↓ thalamic volume within mTBI with persistent symptoms @ 6 months from ≤10 days P-INJ to 6 months P-INJ ↓ volume from ≤10 days P-INJ to 6 months P-INJ within the thalamus, hippocampus, amygdala, and putamen associated with ↓ GOS-E (r(s) = 0.49 to 0.56) and ↑ RPQ symptom scores (r(s) = -0.43 to -0.55) @ 6 months P-INJ
Huovinen et al. (2022)	T1w, T2w, SWI, FLAIR	Pathoanatomic features of mTBI based on radiological common data elements	10 days P-INJ No control group	RPQ symptom scores, GOS-E score, time to return to work	↑ days to full return to work and RPQ symptom scores in complicated mTBI vs uncomplicated mTBI ↑ days to full return to work in complicated mTBI with >1 traumatic intracranial lesion vs complicated mTBI with 1 lesion ↑ days to full return to work in complicated mTBI with subdural haemorrhages, subarachnoid haemorrhages, or cerebral contusions vs complicated mTBI with other types of lesions
Xu et al. (2023)	T1w	Cortical thickness and cortical surface area	≤7 days P-INJ, 1 month P-INJ Controls completed 2 timepoints @ same intervals	Head Impact Test symptom score	↑ % change in left anterior cingulate cortex (r = 0.33) and left insula (r = 0.41) from ≤7 days to 1 month P-INJ positively associated with ↑ % change in Head Impact Test symptom scores
Moen et al. (2024)	FLAIR, T2*GRE, SWI, DWI[‡]	Presence or absence of TAI	≤5 days P-INJ No control group	Disability status based on GOS-E	Presence of TAI @ ≤5 days P-INJ not a predictor of disability status @ 3 months P-INJ No association between number or volume of TAI @ ≤5 days P-INJ and disability status @ 3 months P-INJ

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Table 4 (*continued*)

				score ≤6 @ 3 months P-INJ	Presence of contusion or extra-axial hematoma ≤5 days P-INJ predictive of disability status @ 3 months P-INJ but wide odds ratio estimates (95% confidence interval range: 3.48 to 223.86)
Walter et al. (2024)	T1w, FLAIR	Enlarged perivascular space counts	~14 days P-INJ No control group	Recovery status based on GOS-E <8 score @ 3 months P-INJ, RPQ and BSI symptom scores, SWLS and ISI scores	No association between enlarged perivascular space counts and RPQ, BSI, SWLS, or ISI scores @ any timepoint after correcting for multiple comparisons ↑ count of enlarged perivascular spaces associated with incomplete recovery @ 6 months P-INJ (odds ratio = 0.94, 95% CI: 0.88-0.99) No association between count of enlarged perivascular spaces @ 6 months P-INJ and incomplete recovery @ 6 months
Zhuo et al. (2024)	T1w, T2w	Automatic quantification of enlarged perivascular space counts	~14 days P-INJ, 6-12 months P-INJ Single timepoint for controls	RPQ symptom scores and PSQI scores	↑ enlarged perivascular spaces within white matter @ 14 days P-INJ associated with ↑ RPQ symptom scores (r = 0.47) @ same timepoint ↑ enlarged perivascular spaces within white matter @ 14 days P-INJ in mTBI with memory problems based on RPQ scores vs mTBI without memory problems @ 14 days and 6-12 months P-INJ Multivariable model including volume of enlarged perivascular spaces @ 14 days P-INJ predictive (AUC = 0.84) of mTBI with memory problems @ 6-12 months P-INJ

† – no multiple comparisons correction reported; ‡ – DWI included here as part of a clinical radiological assessment; AUC – area under the curve; BSI – Brief Symptom Inventory; DWI – Diffusion Weighted Imaging; FLAIR – FLuid Attenuated Inversion Recovery; GOS-E – Glasgow Outcome Scale Extended; HBI – Health and Behaviour Inventory; ISI – Insomnia Severity Index; mTBI – mild traumatic brain injury; ND – no difference; PCSI – Post Concussion Symptom Inventory; PCSS – Post Concussion Symptom Scale; PedsQL™ – Paediatric Quality of Life Inventory; P-INJ – post-injury; PSQI – Pittsburgh Sleep Quality Index; QSM – Quantitative Susceptibility Mapping; ROI – region-of-interest; RTP – return to play; RPQ – Rivermead Post Concussion Symptoms Questionnaire; SCAT – Sport Concussion Assessment Tool; SWI – susceptibility weighted imaging; SWLS – Satisfaction With Life Survey; TAI – traumatic axonal injury; T1w – T1 weighted; T2w – T2 weighted.

Table 5
Results from studies using diffusion-weighted imaging approaches grouped by cohort age.

Authors	MRI sequence(s)	Imaging analysis	Imaging timepoints	Measure of symptoms or functional recovery	What does imaging tell us about symptoms and/or functional recovery?
Paediatric and young adult cohort studies					
Henry et al. (2011)	DTI	Voxel-wise analysis of FA, MD, AD maps	3 days P-INJ, 6 months P-INJ Controls completed 2 timepoints	PCSS scores	ND in number of regions showing altered FA within mTBI group based on total number of symptoms reported
Meier et al. (2016)	DTI	ROI-based analysis of FA maps	2 days P-INJ, 1 week P-INJ, 1 month P-INJ Single timepoint for controls	HAM-D and HAM-A scores, days until RTP	↑ FA within L superior longitudinal fasciculus @ ~48 hours P-INJ associated with ↑ days until RTP (Spearman's correlation = 0.44) ↑ FA within L superior longitudinal fasciculus @ 1 month P-INJ associated with ↑ days until RTP (Spearman's correlation = 0.52)
Churchill et al. (2017)	DTI	Whole-brain voxel-wise FA and MD analysis	≤7 days P-INJ, RTP Single timepoint for controls	SCAT3 symptom scores, days until RTP	No association between difference in FA or MD between mTBI timepoints (RTP – ≤7 days P-INJ) and number of days to RTP
Manning et al. (2017)	DTI	TBSS of FA, MD, AD, and RD maps	≤3 days P-INJ, 3 months P-INJ Single timepoint for controls	SCAT3 and PCSS symptom scores, days until RTP	↓ AD within the superior longitudinal fasciculus @ ≤3 days P-INJ strongly associated with SCAT3 symptom score @ same timepoint (*r* = -0.747) No association between diffusion changes @ 3 months P-INJ and symptom scores @ ≤3 days P-INJ or 3 months P-INJ
Murdaugh et al. (2018)	DTI		≤7 days P-INJ, 3-4 weeks P-INJ	PCSS symptom scores	No association between isotropic diffusion changes and PCSS symptom scores @ ≤7 days or 3-4 weeks P-INJ

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		Diffusion connectometry analysis	Controls completed 2 timepoints at same interval		
Churchill et al. (2019a)	Single-shell DTI, Multi-shell-NODDI	Voxel-wise analysis of FA, AD, RD maps derived from DTI and ODI, V_{ISO} and V_{IC} maps from NODDI	≤7 days P-INJ, RTP Single timepoint for controls	SCAT3 symptom scores, days until RTP	↓ FA and ↑ AD, RD and ODI within the superior longitudinal fasciculus from ≤7 days P-INJ to RTP was strongly associated with ↑ acute symptom severity and ↑ RTP times
Churchill et al. (2019b)	DTI	Voxel-wise analysis of FA and MD maps	≤6 days P-INJ, RTP, 1 year P-INJ Single timepoint for controls	Clinical severity composite score combining SCAT3 symptom scores and days until RTP	↑ FA within external capsule @ ≤7 days P-INJ, RTP, and 1 year P-INJ strongly associated with ↑ clinical severity score (Spearman's correlations = 0.62 to 0.7) ↑ FA within cerebral peduncle @ ≤7 days P-INJ and 1 year P-INJ strongly associated with ↑ clinical severity score (Spearman's correlations = 0.62 to 0.7) ↑ FA @ ≤7 days P-INJ and ↑ MD @ 1 year P-INJ within anterior corona radiata strongly associated with ↑ clinical severity score (Spearman's correlations = 0.65 to 0.69)
Muftuler et al. (2020)	DKI	TBSS analysis of KFA, MK, KRAD, KAX, FA, MD, RD, and AD maps	≤2 days P-INJ, 1 week P-INJ, 2 weeks P-INJ, 6 weeks P-INJ Controls completed 4 timepoints at same intervals	SCAT3 symptom scores, days until asymptomatic	No association between DKI metrics @ any timepoint and SCAT3 symptom scores @ ≤2 days P-INJ No association between DKI metrics @ any timepoint and number of days until asymptomatic
Baker et al. (2020)	DTI	TBSS of FA maps	1 week P-INJ, 3 weeks P-INJ	Cognitive intolerance	No association between FA values and symptoms of cognitive intolerance @ 1 week P-INJ

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			Single timepoint for controls	based on PCSS symptom scores	↓ FA within genu of corpus callosum, longitudinal fasciculi, and ascending/descending tracts @ 3 weeks P-INJ associated with ↑ symptoms of cognitive intolerance @ 3 weeks P-INJ
Ware et al. (2020)	DTI	Automated tractography of FA and MD maps	10 days P-INJ Single timepoint for orthopaedic injury controls	Parent and Child HBI symptom scores	↑ MD within corpus callosum genu (forceps minor) and R uncinate fasciculus @ ≤10 days P-INJ associated with ↑ child HBI symptom scores @ ≤10 days P-INJ ↓ FA within R inferior fronto-occipital fasciculus and ↑ post-acute average MD within L cingulum cingulate @ ≤10 days P-INJ associated with ↑ parent HBI symptom score @ 3 months P-INJ ↑ MD within L cingulum cingulate, L uncinate fasciculus, and L cingulum hippocampus @ ≤10 days P-INJ associated with ↑ parent HBI symptom score @ 6 months P-INJ
Wu et al. (2020)	DTI	TBSS analysis of FA, MD, AD, RD maps	≤2 days P-INJ, asymptomatic, 7 days post-RTP, 6 months P-INJ Controls completed 4 timepoints @ same intervals	SCAT and BSI symptom scores, days until asymptomatic	↑ BSI symptom scores (r^2(s) = 0.50 to 0.59) and ↑ SCAT symptom severity score (r^2(s) = 0.49 to 0.56) @ 2 days post-injury associated with ↑ MD and ↑ RD in persistently affected white matter BSI symptom scores @ 2 days P-INJ predictive of MD changes @ 6 months P-INJ MD @ 2 days P-INJ predictive of the number of days until asymptomatic
Fleck et al. (2021)	DTI	Machine learning methods applied to ROI-based FA, MD, AD, and RD maps	≤4 days P-INJ Single timepoint for orthopaedic injury controls	PCSS scores, symptomatic status @ 1 week P-INJ	Features of DTI data predict symptom resolution status @ 1 week P-INJ with 62.3% accuracy (sensitivity: 59.4%; specificity: 65.1%) using a genetic fuzzy trees machine learning algorithm Specific DTI features contributing to this performance not reported
Chung et al. (2022)	DTI	TBSS analysis of FA, MD, RD, AD, MK, KAX, KRAD, axonal water fraction, intra-	≤2 days P-INJ, asymptomatic, 7 days post-RTP, 6 months P-INJ	SCAT3 symptom scores, symptomatic status	↓ % of significantly different voxels for KAX mTBI vs control @ asymptomatic (24.1%), 7 days post-RTP (22%), and 6 months P-INJ (0.2%) compared to 2 days P-INJ (35.3%)

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		axonal diffusivity, extra-axonal axial diffusivity, and extra-axonal radial diffusivity maps	Controls completed 4 timepoints @ same intervals		ND MK or extra-axonal axial diffusivity mTBI vs control @ asymptomatic, 7 days post-RTP, or 6 months P-INJ
Mayer et al. (2022)	DTI	Voxel-wise analysis of FA, MD, ODI, V_{ISO} and V_{IC} maps	7 days P-INJ, 4 months P-INJ Controls completed 2 timepoints @ same intervals	PCSI symptom scores and 5P risk score	Negative association between 5P risk score and FA and positive association between 5P risk score and ODI, V_{IC}, and white matter V_{ISO} for mTBI group No association between PCSI symptom score and DTI/NODDI metrics for mTBI group A random forest model using 5P risk score, clinical symptom data, FA, ODI, V_{IC}, white matter V_{ISO}, and gray matter V_{ISO} classified mTBI vs control more accurately than a model using only 5P risk score and clinical symptom data (AUC = 0.883 vs 0.744; balance accuracy = 0.802 vs 0.710, sensitivity = 0.820 vs 0.734, specificity = 0.784 vs 0.686)
Ware et al. (2022)	DTI	Automated deterministic tractography to generate average tract FA and MD values for the corpus callosum and 8 major tracts per hemisphere	11 days P-INJ, 3 Months P-INJ, 6 months P-INJ Orthopaedic injury controls completed 3 timepoints at same intervals	Parent and child HBI symptom scores, persistent symptom status @ 1 month P-INJ	↑ FA mTBI without persistent symptoms based on child report and parent report vs orthopaedic injury controls within superior longitudinal fasciculus (Child: Cohen's D = 0.37; 95% CI: 0.06 to 0.68; Parent: Cohen's D = 0.31; 95% CI: 0.02 to 0.59) ↑ MD mTBI with persistent symptoms vs mTBI without persistent symptoms based on child report and orthopaedic injury controls within anterior thalamic radiation in younger participants (10th percentile; mTBI: Cohen's D = 1.43; 95% CI: 0.59 to 2.27; Controls: Cohen's D = 1.94; 95% CI: 1.07 to 2.81) but ND in any tracts for older participants (90th percentile) ↓ MD for mTBI without persistent symptoms based on parent report vs orthopaedic injury controls @ 6 months P-INJ within the arcuate fasciculus (Cohen's D = -0.58; 95% CI: -0.11 to -1.04) and superior longitudinal fasciculus (Cohen's D = -0.49; 95% CI: -0.09 to -0.90)
Brown et al. (2023)	DTI	TBSS analysis of FA, MD, AD, and RD maps	3 days P-INJ, 4 weeks P-INJ Orthopaedic injury controls completed 2	Connor-Davidson resilience scale scores	FA within forceps minor, MD within R anterior thalamic radiation, and MD/RD within R superior longitudinal fasciculus @ 3 days P-INJ all associated with resilience at 3 days P-INJ in mTBI group No group effect mTBI vs orthopaedic control for associations of FA, MD, AD, or RD and resilience at either timepoint

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			timepoints at same intervals		No group x time interaction for the association of FA, MD, AD, or RD and resilience
Ware et al. (2023)	DTI	Connectivity matrices using average FA of fibre connections among the nodes to generate global and local level metrics including: degree, clustering coefficient, characteristic path length, small worldness, betweenness and degree centrality, and efficiency	~11 days P-INJ, 3 Months P-INJ, 6 months P-INJ Orthopaedic injury controls completed 3 timepoints at same intervals	Total premorbid symptoms were rated by parents during post-acute timepoint, persistent symptom status @ 1 month P-INJ	↓ clustering coefficient within Rolandic operculum for females with persistent mTBI symptoms vs mTBI without persistent symptoms based on child reported symptoms (Cohen's D = -0.89; 95% CI: -0.28 to -1.49), while males with persistent symptoms exhibited ↑ clustering coefficient within the same ROI (Cohen's D = 0.80; 95% CI: 0.19 to 1.42) @ all timepoints ↓ betweenness centrality within supramarginal gyrus and ↓ efficiency within the putamen for younger (10^{th} percentile) children with persistent mTBI symptoms based on child reported symptoms vs orthopaedic controls (Supramarginal gyrus: Cohen's D = -0.66; 95% CI: -0.16 to -1.17; Putamen: Cohen's D = -1.08; 95% CI: -0.33 to -1.83), while older children (90^{th} percentile) with persistent symptoms exhibited ↑ betweenness centrality and ↑ efficiency within the same ROIs (Supramarginal gyrus: Cohen's D = 0.89; 95% CI: 0.38 to 1.40; Putamen: Cohen's D = 1.30; 95% CI: 0.49 to 2.11) @ 3 months P-INJ, respectively ↓ clustering coefficient within putamen for females with persistent mTBI symptoms based on child symptom report vs orthopaedic controls (Cohen's D = -1.82; 95% CI: -0.90 to -2.74), while males with persistent symptoms exhibited ↑ clustering coefficient within the same ROI (Cohen's D = 0.98; 95% CI: 0.20 to 1.76) @ 6 months P-INJ Results based on parent reported symptoms demonstrate similar general patterns in clustering coefficient between males and females
Berto et al. (2024)	DTI	ROI-based analysis of FA and MD maps and tract-based profilometry	≤2 days P-INJ No control group	Days until RTP and early vs late recovery based on RTP <28 days	↓ mean voxel-wise and tract-based FA within white matter @ 2 days P-INJ associated with ↑ RTP (r(s) = -0.25 to -0.42) ↑ mean tract-based FA for mTBI with early recovery vs mTBI with late recovery across 47 tracts (Cohen's D_{mean} = 0.80, SD = 0.35) with the largest effect seen in the L inferior fronto-occipital fasciculus (Cohens D = 1.52) Tract-based mean FA @ 2 days P-INJ accurately discriminated between early vs late recovery mTBI using all 47 tracts (AUC = 0.86, balanced accuracy = 0.89, sensitivity = 1.0, specificity = 0.79) and a subset of 16 tracts (AUC = 0.90, balanced accuracy = 0.89, sensitivity = 1.0, specificity = 0.79)

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Churchill et al. (2025)	DTI	ROI-based analysis of FA and MD maps	Pre-injury baseline, ≤7 days P-INJ, RTP, 1-3 months post-RTP, 1-year post-RTP No control group	Days until RTP	↑ MD within L corona radiata and internal capsule @ early symptomatic (≤7 days P-INJ), RTP, 1-3 months post-RTP, and 1-year post-RTP relative to pre-injury baseline ↓ FA within genu of corpus callosum @ early symptomatic relative to pre-injury baseline ↓ FA within L corona radiata and internal capsule @ RTP and 1-3 months post-RTP relative to pre-injury baseline No association between post-injury differences in FA or MD relative to pre-injury baseline and number of days to RTP
Adult cohort studies					
Yuh et al. (2014)	DTI	Whole brain voxel-wise analysis and ROI-based analysis of FA, MD, AD, RD maps	11 days P-INJ No control group	GOS-E score and RPQ symptom scores @ 3- and 6-months P-INJ	ND in 3-month or 6-month GOS-E or RPQ score between CT/MRI-negative and CT/MRI-positive mTBI ↓ FA in ≥1 ROIs compared to control mean associated with ↓ 3-month GOS-E (Spearman's correlation = -0.34), ↓ 6-month GOS-E (Spearman's correlation = -0.25), and ↑ 6-month RPQ scores (Spearman's correlation = 0.29) ↓ FA in ≥1 ROIs compared to control mean associated with increased odds of lower GOS-E score at 3-months P-INJ (univariable odds ratio per unit decrease in GOS-E: OR 3.9 [95% CI: 1.5, 10.0]) and 6-months P-INJ (univariable odds ratio per unit decrease in GOS-E: OR 2.7 [95% CI: 1.01, 7.1])
Strauss et al. (2016)	DTI	Whole brain voxel-wise analysis of FA maps and ROI-based analysis of FA, MD, AD and RD maps	~7 days P-INJ Single timepoint for controls	RPQ symptom scores and health-related QOL scores	No association between whole brain FA @ ~7 days P-INJ and RPQ symptom scores @ 1 year P-INJ ↑ mean MD and RD and mean ↓ FA within areas with abnormally low FA @ ~7 days P-INJ associated with ↓ health-related QOL (Spearman's correlations = -0.596 to 0.514) @ 1 year P-INJ ↑ FA within the R thalamus and R cerebellar hemisphere @ ~7 days P-INJ associated with ↓ emotional and somatic symptoms @ 1 year P-INJ
Dall'Acqua et al. (2017)	DTI	Streamline-based connectivity analysis	≤7 days P-INJ, 1 year P-INJ Controls completed 2 timepoints at same interval	RPQ symptom scores, persistent symptom status @ 6-months P-INJ	ND structural connectivity mTBI without persistent symptoms (n = 43) vs mTBI with persistent symptoms (n=6) @ both timepoints No association between RPQ symptom score change and change in structural connectivity across timepoints

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Yin et al. (2019)	DTI	Voxel-wise analysis of FA maps and TBSS of FA, MD, AD, RD maps	≤7 days P-INJ, 1 month P-INJ, 3 months P-INJ Controls completed 3 timepoints at same intervals	RPQ symptom scores, PTSD Checklist – Civilian Version scores, and Beck Depression Inventory scores	No association between FA @ any timepoint and RPQ symptom scores, PTSD scores, or Beck Depression Inventory Scores @ the corresponding timepoint ↑ RPQ symptoms scores and ↑ Beck Depression Inventory Scores @ 7 days P-INJ associated with ↓ FA within the forceps major @ 3 months P-INJ (RPQ: r = -0.5; Beck: r = -0.57)
Stenberg et al. (2021)	DTI, DKI	Voxel-wise analysis of FA, MD, AD, RD, KFA, MK, KAX, and KRAD maps	~3 days P-INJ Single timepoint for controls	Persistent symptom status @ 3 months P-INJ	↓ FA, KFA and ↑ RD @ ~3 days P-INJ in mTBI with persistent symptoms vs mTBI without persistent symptoms @ 3 months P-INJ ↓ FA, KFA, MK, KRAD, KAX and ↑ MD, AD, RD @ ~3 days P-INJ in mTBI with persistent symptoms @ 3 months P-INJ vs control ↓ MK, KRAD, KAX @ ~3 days P-INJ in mTBI without persistent symptoms @ 3 months P-INJ vs control
Palacios et al. (2022)	DTI	TBSS analysis of FA, MD, AD, and RD maps	2 weeks P-INJ, 6 months P-INJ Single timepoint for controls	GOS-E @ 6 months P-INJ	↑ global AD and MD @ 2 weeks P-INJ for mTBI with GOS-E = 8 (n = 173) vs mTBI with GOS-E <8 (n = 194) ↑ global AD @ 2 weeks P-INJ associated with ↓ odds[‡] (OR = 0.75; 95% CI: 0.61 to 0.92) of GOS-E <8 @ 6 months P-INJ ↑ AD @ 2 weeks P-INJ within 8/14 white matter tracts associated with ↓ odds[‡] of GOS-E <8 @ 6 months P-INJ with strongest associations observed for the superior longitudinal fasciculus (OR = 0.69; 95% CI: 0.56 to 0.85) and superior fronto-occipital fasciculus (OR = 0.73; 95% CI: 0.59 to 0.90)
Cai et al. (2023)	DTI	TBSS analysis of FA, MD, AD, and RD maps	14 days P-INJ, 6 months P-INJ Single timepoint for controls	Emotional resilience vs neuro-psychiatric distress phenotypes determined @ 2 weeks P-INJ	↓ global AD mTBI with neuropsychiatric distress (n = 78) vs mTBI with emotional resilience (n = 94) @ both timepoints ↓ AD within fornix (Cohen's D = 0.48) and superior cerebellar peduncle (Cohen's D = 0.5) mTBI with neuropsychiatric distress vs mTBI with emotional resilience @ 2 weeks P-INJ ↓ AD within external capsule, fornix stria terminalis, superior fronto-occipital fasciculus, sagittal stratum, uncinate fasciculus, internal capsule, cerebral peduncle, and medial

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					lemniscus mTBI with neuropsychiatric distress vs mTBI with emotional resilience @ 6 months P-INJ (Range of Cohen's D = 0.36 to 0.62)
Gugger et al. (2023)	DTI	Structural network deviations assessed via node deviation index and network deviation index generated from a structural brain network	14 days P-INJ, 6 months P-INJ Single timepoint for controls	RPQ symptoms scores, BSI symptom scores, and GOS-E score @ 6 months P-INJ	↑ proportional change in network deviation from 14 days P-INJ to 6 months P-INJ associated with ↑ proportional change in RPQ and BSI symptom scores between timepoints (r = 0.46) ↑ proportional change in network deviation from 14 days to 6 months P-INJ associated with ↓ GOS-E scores @ 6 months P-INJ (r = -0.51) Predicted global recovery score @ 6 months P-INJ (determined as the first component of a PCA analysis on RPQ, BSI, and GOS-E scores @ 6 months P-INJ) based on node deviation index @ 14 days P-INJ demonstrated a strong correlation with actual recovery score (r = -0.59; 95% CI: -0.77 to -0.31; r^2 = 0.23)
Li et al. (2023)	DTI	Voxel-wise analysis of FA, RD, and track density maps	7 days P-INJ, 1 year P-INJ, 2 years P-INJ Single timepoint for controls	RPQ symptom scores, Beck Depression Inventory, Beck Anxiety Inventory, and Pittsburgh Sleep Quality Index scores, persistent symptom status @ 1 year & 2 years P-INJ	↓ FA within peri-thalamic thalamic reticular nucleus @ 7 days P-INJ for mTBI with persistent symptoms (1 year P-INJ: n = 19; 2 years P-INJ: n = 10) vs mTBI with resolved symptoms (1 year P-INJ: n = 11; 2 years P-INJ: n = 7) @ 1- & 2-years P-INJ ↑ RD within peri-thalamic thalamic reticular nucleus @ 7 days P-INJ for mTBI with persistent symptoms vs mTBI with resolved symptoms @ 1- & 2-years P-INJ
Pinto et al. (2023)	DTI	Voxel-wise analysis of FA and MD maps	7-10 days P-INJ Single timepoint for controls	Recovery status based on GOS-E <8 score @ 6 months P-INJ	Support vector machine trained on voxel-wise FA and MD @ ~7-10 days P-INJ combined with age and sex correctly classified mTBI vs control with mean AUC = 0.88 ± 0.04 Support vector machine trained on voxel-wise FA and MD @ ~7-10 days P-INJ combined with age and sex correctly classified mTBI with incomplete recovery (n = 87) vs mTBI with complete recovery (n = 92) with mean AUC = 0.71 ± 0.12

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Table 5 (*continued*)

					Support vector machine trained with ROI-wise FA and MD performed worse for mTBI vs control (AUC = 0.69 ± 0.06) and similar for incomplete vs complete recovery (AUC = 0.68 ± 0.09)
Richter et al. (2024)	DTI	TBSS of FA and MD maps	~13 days P-INJ No control group	Recovery status based on GOS-E <8 score @ 3 months P-INJ	21 of 48 white matter tracts were prognostically relevant for discrimination of incomplete versus complete mTBI recovery @ 3 months P-INJ (AUC = 0.80, 95% CI: 0.77-0.84; R^2 = 0.70, 95% CI: 53-86; sensitivity = 0.69, 95% CI: 0.60-0.78; specificity = 0.71, 95% CI: 0.62-0.81) The top three prognostic tracts were the L superior cerebellar peduncle, R uncinate fasciculus, and L posterior thalamic radiation Inclusion of DTI significantly improved prognostic performance of clinical prediction models
Zhuo et al. (2024)	DTI	DTI along the perivascular spaces (DTI-ALPS) index	~14 days P-INJ, 6-12 months P-INJ Single timepoint for controls	RPQ symptom scores and PSQI scores	No association between DTI-ALPS index and RPQ scores @ any timepoint ↑ DTI-ALPS index from 14 days P-INJ to 6-12 months P-INJ associated (r = -0.42) with ↓ PSQI scores over same interval Multivariable model including DTI-ALPS index @ 14 days P-INJ predictive (AUC = 0.84) of mTBI with memory problems @ 6-12 months P-INJ

‡ – reduced odds per standard deviation higher global AD; AD – axial diffusivity; AUC – area under the curve; BSI – Brief Symptom Inventory; DKI – Diffusion Kurtosis Imaging; DTI – Diffusion Tensor Imaging; FA – fractional anisotropy; GOS-E – Glasgow Outcome Scale Extended; HAM-A – Hamilton Anxiety Rating Scale; HAM-D – Hamilton Depression Rating Scale; HBI – Health and Behaviour Inventory; KAX – axial kurtosis; KFA – kurtosis fractional anisotropy; KRAD – radial kurtosis; MD – mean diffusivity; MK – mean kurtosis; mTBI – mild traumatic brain injury; ND – no difference; NODDI – neurite orientation dispersion and density imaging; ODI – orientation dispersion index; PCSI – Post Concussion Symptom Inventory; PCSS – Post Concussion Symptom Scale; P-INJ – post-injury; RD – radial diffusivity; RPQ – Rivermead Post Concussion Symptoms Questionnaire; RTP – return to play; ROI – region-of-interest; SCAT – Sport Concussion Assessment Tool; TBSS – tract based spatial statistics; V_{IC} – intracellular volume; V_{ISO} – isotropic volume.

Table 6
Results from studies using blood-oxygenation level dependent imaging grouped by cohort age.

Authors	MRI sequence(s)	Imaging analysis	Imaging timepoints	Measure of symptoms or functional recovery	What does imaging tell us about symptoms and/or functional recovery?
Paediatric and young adult cohort studies					
Churchill et al. (2017)	rs-fMRI	Global functional connectivity analysis	≤7 days P-INJ, RTP Single timepoint for controls	SCAT3 symptom scores, days until RTP	Difference in global functional connectivity between mTBI timepoints (≤7 days P-INJ – RTP) within supplementary motor area, paracentral lobule, middle cingulum, L precentral gyri and bilateral precentral gyri associated with number of days to RTP (R^2 = 0.282; 95% CI: 0.027-0.631) Decreased global functional connectivity @ RTP associated with shorter recovery times
Manning et al. (2017)	rs-fMRI	ICA network analysis	≤3 days P-INJ, 3 months P-INJ Single timepoint for controls	SCAT3 and PCSS symptom scores, days until RTP	No association between functional connectivity @ ≤3 days or 3 months P-INJ and symptom scores @ same timepoint ↓ intra-cerebellar functional connectivity @ 3 months P-INJ strongly associated with ↑ PCSS symptom scores @ ≤3 days P-INJ (*r(s)* = -0.767 to -0.941) ↓ functional connectivity between occipital pole and superior lateral occipital cortex @ 3 months P-INJ strongly associated with ↑ days until RTP (*r* = -0.668)
Meier et al. (2017)	rs-fMRI	Voxel-wise global brain connectivity and ReHo analysis	≤2 days P-INJ, 1 week P-INJ, 1 month P-INJ Single timepoint for controls	HAM-D and HAM-A scores, days until RTP	No association between ReHo and HAM-D, HAM-A or days until RTP @ any timepoint
McCuddy et al. (2018)	rs-fMRI	Network-level functional connectivity analysis	≤2 days P-INJ, 1 week P-INJ, 1 month P-INJ	HAM-D scores	↓ connectivity between default mode, ventral attention, dorsal attention, and fronto-parietal networks associated with higher HAM-D scores @ 2 days P-INJ ↑ connectivity between R amygdala to R caudate and L thalamus associated with ↑ HAM-D scores @ 2 days P-INJ

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Table 6 (*continued*)

			Single timepoint for controls		Similar relationships observed between functional connectivity of emotion processing ROI and HAM-D @ 1 week P-INJ Several individual HAM-D items were significantly related to functional connectivity of emotion processing ROI (*r*(s) = -0.58 to -0.69)
Churchill et al. (2019b)	rs-fMRI	Global functional connectivity analysis	≤6 days P-INJ, RTP, 1 year P-INJ Single timepoint for controls	Clinical severity composite score combining SCAT3 symptom scores and days until RTP	↓ global functional connectivity within the thalamus and frontal, temporal, and occipital gyri @ ≤7 days P-INJ strongly associated with ↑ clinical severity score (Spearman's correlations = -0.64 to -0.79) ↓ global functional connectivity within the middle temporal gyrus @ RTP moderately associated with ↑ clinical severity score (Spearman's correlation = -0.57) ↓ global functional connectivity within the Rolandic operculum and frontal gyri @ 1 year P-INJ strongly associated with ↑ clinical severity score (Spearman's correlations = -0.62 to -0.77)
Murdaugh et al. (2018)	rs-fMRI	ICA network analysis	≤7 days P-INJ, 3-4 weeks P-INJ Controls completed 2 timepoints at same intervals	PCSS symptom scores	No association between functional connectivity changes and PCSS symptom score @ ≤7 days P-INJ or @ 3-4 weeks P-INJ
Meier et al. (2020)	rs-fMRI	fALFF and ReHo analysis	≤2 days P-INJ, asymptomatic, 7 days post-RTP Controls completed 3 timepoints at same intervals	SCAT and BSI symptom scores, days until asymptomatic	ReHo within the middle and superior frontal gyri @ ≤2 days P-INJ associated with BSI psychological symptoms @ asymptomatic No association between ReHo and SCAT symptom scores @ ≤2 days P-INJ No association between ReHo @ ≤2 days P-INJ and number of days until asymptomatic

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Stephenson et al. (2020)	rs-fMRI	fALFF and ReHo analysis	1 week P-INJ, 4 months P-INJ Controls completed 2 timepoints at same interval	PCSI symptom scores, PedsQL™ scores, or PROMIS outcome scores, persistent symptom status @ 4 months P-INJ	No association between fALFF and PCSI symptom scores, PedsQL™ scores, or PROMIS outcome scores ND for fALFF or ReHo between control vs recovered mTBI @ 4 months vs persistent mTBI @ 4 months for whole-brain or subject-specific analysis
Onicas et al. (2023)	rs-fMRI	Global and local level functional connectivity analysis of efficiency, clustering coefficient, small worldness, betweenness and degree centrality	11 days P-INJ, 3 Months P-INJ, 6 months P-INJ Orthopaedic injury controls completed 3 timepoints at same intervals	Total premorbid symptoms were rated by parents, persistent symptom status @ 1 month P-INJ	↓ global clustering coefficient for females with persistent mTBI symptoms based on parent reported symptoms vs orthopaedic controls @ 3 months P-INJ (Cohen's D = -1.09; 95% CI: -0.39 to -1.79) ↓ clustering coefficient within postcentral gyrus for females with persistent mTBI symptoms based on parent reported symptoms vs orthopaedic controls @ 3 months P-INJ (Cohen's D = -0.97; 95% CI: -0.45 to -1.50) ↓ nodal efficiency within inferior occipital gyrus was observed in for females with persistent mTBI symptoms vs orthopaedic controls (Cohen’s D = -0.74; 95% CI: -0.09 to -1.39), while males with persistent symptoms exhibited ↑ nodal efficiency within the same ROI (Cohen's D = 0.65; 95% CI: 0.07 to 1.23) @ 3 months P-INJ ↑ nodal efficiency within the calcarine fissure for females with persistent mTBI symptoms vs orthopaedic controls (Cohen's D = 0.82; 95% CI: 0.07 to 1.57), while males with persistent symptoms exhibited ↓ nodal efficiency within the same ROI (Cohen's D = -0.78; 95% CI: -0.14 to -1.42) @ 6 months P-INJ
van der Horn et al. (2024)	rs-fMRI	Dynamic and static functional	1 week P-INJ, 4 months P-INJ	PCSI symptom scores, PedsQL™,	No association between dynamic brain states and clinical measures within the mTBI groups

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Table 6 (*continued*)

		connectivity analysis	Controls completed 2 timepoints at same interval	scores, or PROMIS scores, GOS-E score @ 4 months P-INJ, persistent symptom status @ 4 months P-INJ	No association between dynamic brain states and persistent symptom status within the mTBI groups No association between static functional connectivity and clinical measures within mTBI groups
Onicas et al. (2025)	rs-fMRI	Network-based functional connectivity analysis	11 days P-INJ, 3 Months P-INJ, 6 months P-INJ Orthopaedic injury controls completed 3 timepoints at same intervals	Total premorbid symptoms were rated by parents, persistent symptom status @ 1 month P-INJ	↑ connectivity between dorsal attention and ventral attention networks for females without persistent mTBI symptoms vs orthopaedic controls (Cohens D = 0.94; 95% CI: 0.31 to 1.57) and females with persistent mTBI symptoms (Cohens D = 1.32; 95% CI = 0.53-2.12) @ 3 months P-INJ ND between-network connectivity for males with/without persistent mTBI symptoms @ any timepoint ND within-network connectivity for any group comparison @ any timepoint
Adult cohort studies					
Sours et al. (2015a)	rs-fMRI	Wavelet analysis of default mode network ROIs by decomposing BOLD timeseries into 4 frequency ranges: 0.125-0.250 Hz, 0.060-0.125 Hz, 0.030-0.060 Hz, 0.015-0.030 Hz	11 days P-INJ, 6 months P-INJ Single timepoint for controls	RPQ symptom scores collected, persistent symptom status @ 6-months P-INJ	↑ average strength within global default mode network in the 0.125-0.250 Hz frequency range @ 11 days P-INJ for mTBI without persistent symptoms @ 6 months P-INJ vs mTBI with persistent symptoms @ 6 months P-INJ and controls ↑ average strength within global default mode network in the 0.125-0.250 frequency range from 11 days P-INJ to chronic 6 months P-INJ within both the mTBI without persistent symptoms and mTBI with persistent symptoms but ND between groups for the amount of change ↑ average strength within the L/R lateral parietal, posterior cingulate cortex, and R parahippocampal gyrus nodes of the default mode network @ 11 days P-INJ for mTBI without persistent symptoms @ 6 months P-INJ vs mTBI with persistent symptoms @ 6 months P-INJ and controls

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					↑ average strength within the medial prefrontal cortex and R inferior temporal gyrus nodes of the default mode network in the 0.125-0.250 Hz frequency range @ 6 months P-INJ for mTBI without persistent symptoms vs mTBI with persistent symptoms and controls
Dall'Acqua et al. (2017)	rs-fMRI	ROI-based functional connectivity analyses	≤7 days P-INJ, 1 year P-INJ Controls completed 2 timepoints at same interval	RPQ symptom scores, persistent symptom status @ 6-months P-INJ	↑ functional connectivity within the 15-edge subnetwork in mTBI without persistent symptoms (n = 43) from acute to chronic timepoint ND functional connectivity within the 15-edge subnetwork in mTBI with persistent symptoms (n=6) from acute to chronic timepoint No association between RPQ symptom score change and change in functional connectivity across timepoints
Palacios et al. (2017)	rs-fMRI	Probabilistic ICA analysis followed by network-based modelling	≤2 weeks P-INJ Single timepoint for controls	GOS-E score and RPQ symptom scores @ 6 months P-INJ	No association between functional connectivity measured ≤2 weeks P-INJ and RPQ scores @ 6 months P-INJ in CT/MRI positive mTBI ↓ functional connectivity measured within 2 weeks P-INJ in visual network, occipito-cerebellar network, dorsal visual stream, and posterior default mode network associated with ↑ RPQ scores @ 6 months P-INJ in CT/MRI negative mTBI
Madhavan et al. (2019)	rs-fMRI	Whole brain and network-based fALFF analysis and seed-based functional connectivity analysis	≤3 days P-INJ, 10 days P-INJ, 2-4 weeks P-INJ, 3-4 months P-INJ Controls completed 2 timepoints 10-21 days apart	SCAT2 symptom scores	↓ whole brain fALFF within gray matter associated with concurrent ↑ symptom severity scores (r = -0.28) ↓ whole brain fALFF mTBI with concurrent symptom severity scores >30 vs controls >fALFF observed within motor, visual, language and salience networks for mTBI with symptom severity <5 vs symptom severity >30 Seed-based connectivity within default mode, dorsal attention, motor, salience and visual networks at early encounter predictive of late encounter symptom severity
D'Souza et al. (2020)	rs-fMRI	Voxel-wise between-group	≤1 week P-INJ, 6 months P-INJ	RPQ symptom scores	↓ functional connectivity within sensorimotor (r = -0.37) and anterior default mode (r = -0.33) networks associated with ↑ RPQ score in mTBI @ ≤1 week P-INJ

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		comparison of resting-state functional connectivity	Single timepoint for controls		↓ functional connectivity within sensorimotor network associated with ↑ RPQ score in mTBI @ 6 months P-INJ (*r* = -0.61)
Ekdahl et al. (2023)	rs-fMRI	ICA network analysis	7 days P-INJ, 4 months P-INJ Single timepoint for orthopaedic injury controls	RPQ symptom scores, Fatigue Severity Scale scores, Hospital Anxiety and Depression Scale scores	No association between ICA-derived functional connectivity networks and RPQ symptom scores, fatigue scores, or anxiety/depression scores
Li et al. (2023)	rs-fMRI	Within-thalamic and thalamo-cortical functional connectivity analysis	7 days P-INJ, 1 year P-INJ, 2 years P-INJ Single timepoint for controls	RPQ, Beck Depression Inventory, Beck Anxiety Inventory, and Pittsburgh Sleep Quality Index scores, persistent symptom status @ 1 year & 2 years P-INJ	↑average within-thalamic functional connectivity and ↑average low-frequency thalamo-cortical coherence associated with ↑RPQ symptom scores (*r*(s) = 0.288 to 0.336) and ↑ Beck Depression Inventory scores @ 7 days P-INJ (*r*(s) = 0.287 to 0.372) ↑ within-thalamic functional connectivity @ 7 days P-INJ for mTBI with persistent symptoms (1 year P-INJ: n = 19; 2 years P-INJ: n = 10) vs mTBI with resolved symptoms (1 year P-INJ: n = 11; 2 years P-INJ: n = 7) @ 1- & 2-years P-INJ A GLM including within-thalamic functional connectivity and thalamo-cortical coherence @ 7 days P-INJ (controlling for age and sex) associated with RPQ symptom scores @ 1 year (r^2=0.453) and 2 years (r^2=0.667) P-INJ
Woodrow et al. (2023)	rs-fMRI	Thalamo-cortical functional connectivity	2 weeks P-INJ, 6 months P-INJ, 1 year P-INJ Single timepoint for controls	RPQ symptom scores, persistent symptom status @ 6 months P-INJ	↑ connectivity between ventral anterior and ventrolateral dorsal nuclei of thalamus and cortical regions @ 2 weeks P-INJ for mTBI with persistent symptoms vs mTBI without persistent symptoms and controls ND thalamo-cortical connectivity @ 2 weeks P-INJ for mTBI with GOS-E=8 vs mTBI with GOS-E<8
					Significant time x group interaction of L/R ventral anterior and R ventrolateral nuclei connectivity between mTBI with persistent symptoms and mTBI without persistent symptoms between 2 weeks and 12 months P-INJ

BSI – Brief Symptom Inventory; fALFF – fractional amplitude of low frequency fluctuations; GOS-E – Glasgow Outcome Scale Extended; HAM-A – Hamilton Anxiety Rating Scale; HAM-D – Hamilton Depression Rating Scale; ICA – independent component analysis; mTBI – mild traumatic brain injury; PCSI – Post Concussion Symptom Inventory; PCSS – Post Concussion Symptom Scale; PedsQL™ – Paediatric Quality of Life Inventory; P-INJ – post-injury; PROMIS – Patient-Reported Outcomes Measurement Information System; RPQ – Rivermead Post Concussion Symptoms Questionnaire; RTP – return to play; ReHo – regional homogeneity; ROI – region-of-interest; rs-fMRI – resting-state functional magnetic resonance imaging; SCAT – Sport Concussion Assessment Tool

Table 7
Results from studies using Arterial Spin Labelling imaging grouped by cohort age.

Authors	MRI sequence(s)	Imaging analysis	Imaging timepoints	Measure of symptoms or functional recovery	What does imaging tell us about symptoms and/or functional recovery?
Paediatric and young adult cohorts					
Meier et al. (2015a)	ASL	Voxel-wise linear mixed-effects model to assess changes in CBF as a function of recovery in mTBI group	≤2 days P-INJ, 1 week P-INJ, 1 month P-INJ Single timepoint for controls	HAM-D and HAM-A, recovery outcome based on days to RTP: >14 days = poor outcome	↓ CBF mTBI with poor outcome vs mTBI with good outcome within R dorsal midinsular cortex @ 1 month P-INJ (Cohen's D = 1.92) CBF within R dorsal midinsular cortex @ 1 month P-INJ associated with T1 HAM-D total symptom score (r = -0.64)[†] and T1 HAM-A total symptom score (r = -0.56)[†]
Stephens et al. (2018)	PCASL	Whole-brain and ROI-based analysis of rCBF maps	≤2 weeks P-INJ, 6 weeks P-INJ Single timepoint for controls	PCSS symptom scores, high vs low symptom subgroups @ <2 weeks P-INJ, persistent symptom status @ 6 weeks P-INJ	ND in rCBF for high symptom vs low symptom mTBI (physical, emotional, cognitive, sleep-related categories) vs controls @ ≤2 weeks P-INJ ND rCBF within L dorsal anterior cingulate cortex for mTBI without presence of physical symptoms vs controls @ ~6 weeks P-INJ ↑ rCBF within L dorsal anterior cingulate cortex for mTBI with presence of physical symptoms vs controls @ ~6 weeks P-INJ
Churchill et al. (2019b)	ASL	Voxel-wise analysis of CBF maps	≤6 days P-INJ, RTP, 1 year P-INJ Single timepoint for controls	Clinical severity composite score combining SCAT3 symptom scores and days until RTP	↓ CBF within middle frontal, middle temporal, and superior parietal gyrus @ ≤7 days P-INJ strongly associated with ↑ clinical severity score (Spearman's correlations = -0.63 to -0.78) No association between CBF and clinical severity score @ RTP ↑ CBF within inferior frontal gyrus @ 1 year P-INJ strongly associated with ↑ clinical severity score (Spearman's correlations = 0.73 to 0.75)
	ASL		≤2 days P-INJ		

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Table 7 (*continued*)

Wang et al. (2019)		Voxel-wise analysis of CBF maps	Single timepoint for controls	SCAT3 symptom scores, days until asymptomatic	↓ rCBF within R inferior parietal lobule (*r* = -0.47) and R supramarginal gyrus (*r* = -0.44) @ ≤2 days P-INJ associated with ↑ number of days until asymptomatic
Sicard et al. (2024)	PASL	Z-score perfusion maps were used to identify voxels of abnormal hyperperfusion or hypoperfusion	≤4 days P-INJ, 1 month P-INJ Single timepoint for orthopaedic injury controls	HBI symptom scores, symptomatic status	↑ adjusted perfusion within L precuneus and ↓ adjusted perfusion within L superior frontal gyrus associated with ↑ HBI symptom scores in mTBI @ both timepoints ↓ adjusted perfusion within R cerebellum and R lingual gyrus symptomatic mTBI (n = 10) vs orthopaedic control @ 1 month P-INJ ↑ adjusted perfusion within L medial orbitofrontal cortex, R middle frontal gyrus and bilateral caudate and ↓ adjusted perfusion within bilateral calcarine asymptomatic mTBI (n = 59) vs orthopaedic control @ 1 month P-INJ
Churchill et al. (2025)	ASL	ROI-based analysis of CBF maps	Pre-injury baseline, ≤7 days P-INJ, RTP, 1-3 months post-RTP, 1-year post-RTP No control group	Days until RTP	ND in CBF @ early symptomatic (≤7 days P-INJ) mTBI relative to pre-injury baseline ↓ CBF within bilateral insular, orbitofrontal, temporal, and parietal regions @ RTP relative to pre-injury baseline ↑ CBF within medial temporal ROIs @ early symptomatic, RTP, and 1-year P-INJ, relative to pre-injury baseline, associated with ↑ days until RTP
Adult cohorts					
Sours et al. (2015b)	PASL	CBF ratio between CBF maps extracted from default mode and task positive networks	1 week P-INJ, 1 month P-INJ, 6 months P-INJ Single timepoint for controls	RPQ symptom scores, persistent symptom status	↑ CBF in the default mode network vs task positive network for mTBI without persistent symptoms @ all timepoints ND CBF in the default mode network vs task positive network for mTBI with persistent symptoms @ all timepoints

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Table 7 (*continued*)

						ND CBF in default mode network, task positive network or CBF ratio for mTBI with persistent symptoms and/or mTBI without persistent symptoms vs controls @ any timepoint
Li et al. (2024)	PCASL	Perfusion-based functional connectivity analysis of insula ROIs	≤7 days P-INJ	No control group	Post-traumatic headache intensity, frequency, and status	↑ perfusion-based functional connectivity between insular subdivisions and L middle cingulate cortex, L supplementary motor area, R thalamus, and R Rolandic operculum @ ≤7 days P-INJ in mTBI with post-traumatic headache vs mTBI without post-traumatic headache @ 3 months P-INJ ↑ perfusion-based functional connectivity between L posterior insula and R thalamus associated with ↑ headache frequency (r = 0.357) and ↓ perfusion-based functional connectivity L dorsal anterior insula and L thalamus associated with ↑ headache intensity (r = -0.388) Perfusion-based functional connectivity of insular subdivisions @ 7 days P-INJ discriminated between mTBI with post-traumatic headache vs mTBI without post-traumatic headache @ 3 months P-INJ with AUC estimates of 0.715-0.939

† – no multiple comparisons correction reported; ASL – Arterial Spin Labelling; AUC – area under the curve; CBF – cerebral blood flow; rCBF – relative cerebral blood flow; HAM-A – Hamilton Anxiety Rating Scale; HAM-D – Hamilton Depression Rating Scale; HBI – Health and Behaviour Inventory; mTBI – mild traumatic brain injury; PASL – Pulsed Arterial Spin Labelling; PCASL – Pseudo-Continuous Arterial Spin Labelling; PCSS – Post Concussion Symptom Scale; P-INJ – post-injury; RPQ – Rivermead Post Concussion Symptoms Questionnaire; ROI – region-of-interest; SCAT – Sport Concussion Assessment Tool.

concurrent symptom measures (McCuddy et al., 2018, Churchill et al., 2019b, Li et al., 2023).

ASL perfusion: Region-specific links between CBF and symptom burden obtained during the same-visit exist but demonstrate variable directionality. Lower perfusion in middle frontal, middle temporal, and superior parietal gyri at acute visits align with higher clinical severity (Churchill et al., 2019b). Lower dorsal mid-insular CBF at 1 month P-INJ relates to higher anxiety/depression symptoms at the same timepoint (Meier et al., 2015a). Perfusion within the precuneus and superior frontal lobe associates with greater symptom burden at four days and one month P-INJ (Sicard et al., 2024).

3.4.2. Longitudinal coupling of imaging and clinical change

Structural and SWI: Longitudinal volume loss within subcortical structures (thalamus, hippocampus, amygdala, and putamen) from 10 days to six months P-INJ relates to worse symptoms and GOS-E scores at 6 months (Zhuo et al., 2021). Greater change within the anterior cingulate cortex and insula from seven days to one month P-INJ was associated with greater symptom scores over the same interval (Xu et al., 2023).

Diffusion MRI: Relationships between changes in diffusion indices and clinical changes are selective. Reduced FA and increased AD/radial diffusivity (RD) from seven days to RTP relate to greater acute symptom severity and longer RTP (Churchill et al., 2017, Churchill et al., 2019a). At the network level, greater rise in deviation from 14 days to six months P-INJ correlates with increases in symptom scores and lower GOS-E scores at 6 months (Gugger et al., 2023). No longitudinal coupling between changes in structural connectivity and symptom scores were observed elsewhere (Dall'Acqua et al., 2017).

Resting-state fMRI: Connectivity trajectories relate to measures of recovery more than changes in symptom scores. Changes in global connectivity from acute timepoint to RTP associated with days until RTP (Churchill et al., 2017). Subnetwork connectivity appears to increase over time in those who recover relative to those who do not (Dall'Acqua et al., 2017). Significant time x group effects were reported for thalamo-cortical connectivity between two weeks and 12 months P-INJ in mTBI patients with persistent symptoms compared to those without persistent symptoms (Woodrow et al., 2023).

ASL perfusion: There were no explicit analyses evaluating longitudinal changes in ASL and relationship with clinical changes. In athletes with pre-injury baseline imaging, regional CBF shifted, relative to baseline, from no differences in the symptomatic phase to reduced regional CBF at RTP (Churchill et al., 2025).

3.4.3. Prognostic value of acute imaging for follow-up outcomes

Structural and SWI: The predictive value of acute structural/SWI features and follow-up clinical outcomes are mixed. A pair of large studies report no prognostic value (Mayer et al., 2020a, Moen et al., 2024). In contrast, a pair of studies report measurement of enlarged perivascular spaces at 14 days P-INJ is predictive of incomplete recovery and memory-related symptoms at 6–12 months P-INJ (Walter et al., 2024, Zhuo et al., 2024). Higher susceptibility within the superior longitudinal fasciculus (SLF) and other association tracts at 24 h P-INJ relates to delays in RTP (Koch et al., 2018). Extra-axial lesions at two weeks P-INJ predict lower cognitive symptoms at three months P-INJ (Evans et al., 2018). Microbleeds at three days P-INJ predicts higher symptom burden at three months and one year P-INJ (Studerus-Germann et al., 2018), and acute complicated mTBI predicts greater symptom severity and delayed RTW (Huovinen et al., 2022).

Diffusion MRI: Early assessment of diffusion provides the most consistent prognostic signal. Measurement of FA and MD within 48 h P-INJ are indicative of the number of days required to RTP or become asymptomatic (Meier et al., 2016, Wu et al., 2020). Acute FA and MD also relate to symptom scores measured at 3–6 months P-INJ (Ware et al., 2020, Stenberg et al., 2021). Acute diffusion features may assist prediction of early versus late recovery (Fleck et al., 2021, Gugger et al.,

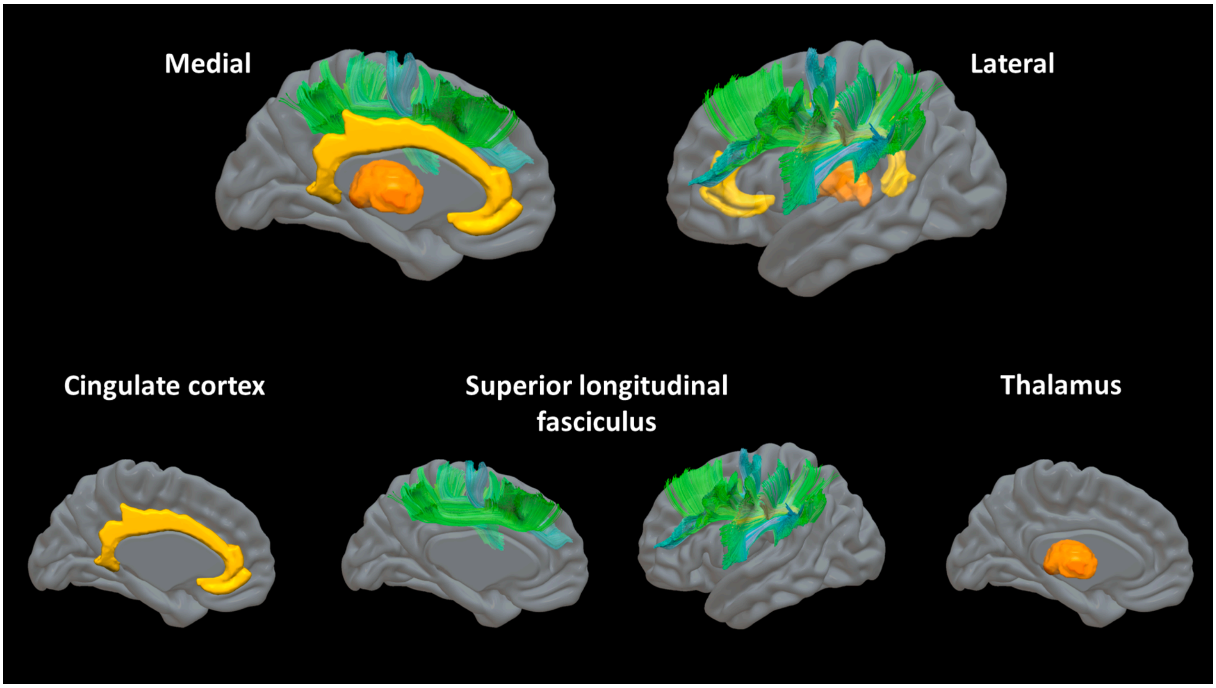

Fig. 3. Structures-of-interest associated with mTBI recovery outcomes with the cingulate cortex shown in yellow, the thalamus shown in orange, and the superior longitudinal fasciculus (SLF) shown in blue-green. Visualization of the cingulate cortex and thalamus are based on the Harvard-Oxford Cortical and Subcortical Structural Atlas (Desikan et al., 2006); while visualization of the SLF is based on the HCP1065 Population-Averaged Tractography Atlas (Yeh 2022). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

2023, Bertò et al., 2024). Lower FA in ≥ 1 ROI at 11 days P-INJ predicts worse GOS-E and symptom scores at 3–6 months P-INJ (Yuh et al., 2014). Patterns in FA, MD, and AD at 7–14 days P-INJ are predictive of incomplete vs complete recovery at 3–6 months P-INJ (Palacios et al., 2022, Pinto et al., 2023, Richter et al., 2024). Abnormal MD/RD and low FA at one week P-INJ predict lower quality of life at one year P-INJ while higher acute FA in the thalamus/cerebellum predicts fewer symptoms at one year (Strauss et al., 2016). Peri-thalamic FA/RD at seven days P-INJ separates persistent versus resolved symptoms at 1–2 years (Li et al., 2023).

Resting-state fMRI: Acute connectivity predicts later symptom and functional outcomes in multiple cohorts. Reduced network-based connectivity at two weeks P-INJ predicts higher symptom burden at six months P-INJ in uncomplicated mTBI (Palacios et al., 2017). Within-thalamic and thalamo-cortical connectivity at 7–14 days P-INJ relate to higher symptom scores and incomplete recovery at 1–2 years P-INJ (Li et al., 2023, Woodrow et al., 2023). Acute global and seed-based connectivity predicts longer RTP times and later symptom severity (Churchill et al., 2019b, Madhavan et al., 2019).

ASL perfusion: Early perfusion demonstrates preliminary prognostic value. Acute hyperperfusion within medial temporal ROI is associated with longer RTP times (Churchill et al., 2025). Lower relative CBF within 48 h P-INJ in inferior parietal/supramarginal gyri predicts more days until asymptomatic (Wang et al., 2019). Insula-centred perfusion connectivity at seven days P-INJ distinguishes post-traumatic headache at three months and relates to later burden (Li et al., 2024).

4. Discussion

This review synthesises acute and longitudinal MRI evidence linking neuroimaging features to symptom burden and functional recovery after mTBI. Same-visit associations were modest and inconsistent for conventional structural/SWI and morphometry, while diffusion and resting-state metrics demonstrated stronger correlations. Longitudinal analyses appeared to convey more signal than cross-sectional observations with subcortical atrophy and selected diffusion/connectivity indices aligning with clinical changes. Prognostically, early diffusion and within-thalamic/thalamo-cortical connectivity most consistently predicted persistent symptoms and incomplete recovery at follow-up. Due to heterogeneity of study designs and reporting, *meta*-analysis was not possible. Instead, qualitative synthesis of key findings is discussed, emphasising results replicated in multiple studies. In cases of conflicting results, greater weight is given to findings from large multi-site studies and/or those with lower risk of bias.

4.1. Neuroimaging insights into recovery

Appraisal of the neuroimaging literature has provided valuable insights into mTBI recovery outcomes and underlying neural mechanisms. Notably, three anatomical structures – the thalamus, cingulate cortex, and superior SLF – were each associated with poor recovery outcomes in five or more studies (Fig. 3). Reduced thalamic volume, intra-thalamic functional connectivity, thalamo-cortical functional connectivity, decreased global functional connectivity within the thalamus, diffusion changes within anterior thalamic radiation, and changes in clustering coefficient within the thalamus corresponded with persistent symptom status (Strauss et al., 2016, McCuddy et al., 2018, Churchill et al., 2019b, Zhuo et al., 2021, Ware et al., 2022, Li et al., 2023, Ware et al., 2023, Woodrow et al., 2023, Richter et al., 2024). Greater susceptibility and diffusion changes within the SLF were related to persistent symptom status, symptom severity, and increased RTP time (Meier et al., 2016, Manning et al., 2017, Evans et al., 2018, Churchill et al., 2019a, Palacios et al., 2022, Ware et al., 2022, Brown et al., 2023). Changes in functional connectivity, fALFF, and CBF within the anterior, middle, and/or posterior cingulate cortex were also associated with symptom burden and persistent symptom status (Sours et al., 2015a, Sours et al., 2015b, Churchill et al., 2017, Palacios et al., 2017, McCuddy et al., 2018, Stephens et al., 2018, Madhavan et al., 2019, Xu et al., 2023, Li et al., 2024). These observations highlight two impactful trends. First, these structures are crucial to the integration and relay of cognitive, sensory, and emotional stimuli throughout the brain. The current literature suggests that greater mTBI-related disruption to these key integrative regions and tracts indicates a higher likelihood of more severe symptoms and longer recovery outcomes. Second, disruptions related to mTBI in each of these structures were observed using multiple imaging modalities, indicating the multi-scale impact of injury on these structures and its implications for recovery. These findings suggest that multiscale disruptions to integrative structures such as the thalamus, SLF, or cingulate cortex may underpin the heterogeneity of mTBI symptoms and recovery outcomes. Collectively, variability in recovery outcomes appears more closely linked to disruption of integrative regions and tracts than to focal injury to localised, function-specific areas.

Several studies used follow-up clinical data to stratify mTBI patients based on persistent symptom and/or recovery status. They assessed acute imaging findings to identify initial differences in recovery trajectories. These studies suggest divergent trends in acute neuroimaging markers between patients who develop persistent symptoms and those who recover fully (Yuh et al., 2014, Sours et al., 2015a, Palacios et al., 2022, Ware et al., 2022, Gugger et al., 2023, Li et al., 2023, Pinto et al., 2023, Ware et al., 2023, Woodrow et al., 2023, Bertò et al., 2024, Richter et al., 2024, Walter et al., 2024, Zhuo et al., 2024). For instance, acute increases in FA were reported in paediatric mTBI patients who did not develop persistent symptoms, whereas reduced FA was associated with persistent symptoms (Ware et al., 2022, Li et al., 2023). Additionally, acute differences in structural and functional connectivity were frequently observed in patients with persistent symptoms compared to controls. At the same time, those asymptomatic at the follow-up showed no acute differences (Sours et al., 2015a, Ware et al., 2022, Li et al., 2023, Ware et al., 2023, Woodrow et al., 2023). Whether these differences are attributable to individual and/or injury-related factors remains unclear. Overall, the available data indicate that neuroimaging acquired within two weeks of injury yields measurable signatures associated with divergent recovery trajectories after mTBI.

4.2. Considerations for future studies

This review has identified five recommendations that should be considered in future studies to strengthen the mTBI neuroimaging literature. First, it is *strongly* recommended that all future mTBI neuroimaging studies collect and report a measure of symptom burden and/or functional recovery. The primary reason for excluding 135 studies during the screening phase of this review was the absence of a functional recovery outcome measure (Fig. 1). An additional 17 studies were excluded because, although they included a recovery measure, they did not report any findings relating the recovery measure to neuroimaging results. Considering the expense and effort of neuroimaging research, failing to simultaneously acquire data that elucidate the clinical significance of neuroimaging findings represents a missed opportunity. There are few barriers to the inclusion of these measures (i.e. GOS-E or PCSS) as they are easy, fast ($\leq$10 min), and free to administer. The current understanding of the heterogeneity of mTBI symptomology and recovery, as well as the neuroimaging methods best equipped to explain these complexities, could be significantly advanced if these measures were consistently included and analysed.

Second, investigators should use clinical data to identify meaningful subgroups/phenotypes of mTBI patients to guide neuroimaging analysis. This review highlights the value of this approach through the insights gained by analysing acute imaging data stratified by persistent symptom status at follow-up. However, this methodology can be extended to explore neurobiological correlates of different symptom-driven phenotypes within mTBI patients. For example, Cai et al., reported reduced global and tract-based AD in mTBI patients with neuropsychiatric distress compared to those with emotional resilience at both acute and follow-up timepoints (Cai et al., 2023). A subset of studies used RPQ, HBI, or PCSS symptom subscales to specifically analyse cognitive, emotional, somatic, and/or sleep disturbance phenotypes and their relation to neuroimaging findings (Evans et al., 2018, Stephens et al., 2018, Studerus-Germann et al., 2018, Baker et al., 2020, Ware et al., 2020, Zhuo et al., 2021, Ware et al., 2022, Woodrow et al., 2023). Aggregating these findings is challenging at this stage due to differences in the modalities of neuroimaging acquired and analyses performed. Nonetheless, this method should be explored in further detail to understand whether specific regions-, networks-, or tracts-of-interest underpin the various symptom reporting patterns and patient phenotypes observed in clinical practice.

Third, authors should accompany their tests of statistical significance with standardised measures of effect. Less than half of studies in this review reported the magnitude of the observed difference/association reported in their results. Twenty-two studies provided a correlation coefficient or coefficient of determination (Yuh et al., 2014, Meier et al., 2015a, Meier et al., 2016, Strauss et al., 2016, Churchill et al., 2017, Manning et al., 2017, Koch et al., 2018, McCuddy et al., 2018, Churchill et al., 2019b, Madhavan et al., 2019, Wang et al., 2019, Yin et al., 2019, D'Souza et al., 2020, Wu et al., 2020, Zhuo et al., 2021, Gugger et al., 2023, Li et al., 2023, Xu et al., 2023, Bertò et al., 2024, Li et al., 2024, Richter et al., 2024, Zhuo et al., 2024), seven studies stated Cohen's D effect estimates (Meier et al., 2015a, Ware et al., 2022, Cai et al., 2023, Onicas et al., 2023, Ware et al., 2023, Bertò et al., 2024, Onicas et al., 2025), and only four studies reported odds ratios (Yuh et al., 2014, Palacios et al., 2022, Moen et al., 2024, Walter et al., 2024). Understanding the magnitude of difference/association of statistically significant findings is essential to advancing our understanding of mTBI symptom burden and recovery. Additionally, authors are encouraged to clearly report effect sizes, standard error/confidence intervals, and number of observations to enable future *meta*-analysis of study findings.

Fourth, future efforts are encouraged to extend beyond simply testing for group differences by exploring the predictive capability of their observed findings. For instance, can we use neuroimaging data to accurately *predict* who is likely to have persistent symptoms versus those who are not, or can we *classify* individuals with a cognitive symptom phenotype versus emotional or somatic? By incorporating additional analyses to explore these questions, we can advance our understanding of major clinical issues in mTBI, such as identifying individuals needing targeted treatment and determining the specific treatments required to address their underlying issues. We recommend interested readers refer to Gugger et al. (2023), Mayer et al. (2022), Palacios et al. (2022), Pinto et al. (2023), Bertò et al. (2024) and Richter et al. (2024) as good examples of incorporating these analytical frameworks.

Finally, research groups may consider adopting integrative analytical methods to understand how multiple neuroimaging modalities jointly explain or predict differences/associations in mTBI symptom burden and recovery. In this review, several studies reported results for multiple imaging modalities in the same article, but analysed each modality in isolation, which is consistent with a reductionist approach (Churchill et al., 2017, Dall'Acqua et al., 2017, Murdaugh et al., 2018, Churchill et al., 2019b, Li et al., 2023, Zhuo et al., 2024, Churchill et al., 2025). Here, we challenge the community to embrace a biological systems approach to understanding the heterogeneity of mTBI (Ahn et al., 2006). Rather than viewing each imaging modality as an independent aspect of the brain's response to injury, consider each modality a partial representation of multi-component covariation across the entire brain (Stone et al., 2020, Avants et al., 2021). This review has demonstrated how qualitatively integrating findings across multiple modalities helped identify the thalamus, SLF, and cingulate cortex as structures-of-interest related to mTBI recovery outcomes. Given the volume and complexity of these datasets, quantitative integrative analysis may be well suited for thoughtful applications of machine learning, such as featureless neural networks. This approach would be particularly fitting for research questions interested in exploring the accuracy of multi-modality neuroimaging datasets to predict mTBI symptomology and recovery trajectories at the expense of interpretability of features contributing to predictive performance. In contrast, integrative statistical designs enable dimensionality reduction of joint relationships within the data into interpretable components that can be used in standard null-hypothesis testing or machine learning algorithms (Stone et al., 2020, Avants et al., 2021). Application of this approach has yielded novel insights into the multimodal effects of low-level blast-exposure on brain health in military members (Stone et al., 2020, Stone et al., 2023). In a recent study, the authors applied linked independent component analysis to structural and diffusion-weighted images to identify regions that co-vary across participants with a history of TBI (Waters et al., 2025). This technique identified an interpretable imaging feature that correlated with levels of UCH-1, cognitive function, and TBI burden (Waters et al., 2025), further highlighting the potential of integrative analytical frameworks. Overall, migration towards methodological and analytical frameworks that embrace the complexity of mTBI may unlock our understanding of the variability in patient experience and outcomes.

4.3. Limitations

A limitation of this review is that included studies were not constrained by specific MRI acquisition parameters or post-processing software. During the screening process, it became clear that there were considerable inconsistencies, particularly in diffusion tensor imaging (DTI) studies, which used different spatial resolutions, b-values, single- versus multi-shell data, and varied approaches to tractography. Previous research has demonstrated that differences in such aspects can impact study findings. Whilst this has been the motivation behind efforts to harmonize acquisitions and processing across multiple MRI sites in large scale studies, this is not a trivial task and requires advanced deep learning techniques which are beyond the scope of the current review (Liu and Yap 2024, Marzi et al., 2024). It is worth noting that many of the multi-site studies included in this review controlled for imaging site in their statistical models or deployed *ComBat* harmonization to account for these challenges (Fortin et al., 2018).

Another limitation of the review is the lack of explicit separation of findings by participant age. This is a challenging issue as several studies have cohorts with overlapping age status categories (children, adolescence, adulthood). In our review, a total 18/62 studies included samples with a mean age < 18 years and we observed that some studies highlighted differences in the relationship between imaging findings and recovery outcomes based on maturation status (Ware et al., 2022). To distinguish between life stages, we present our results into two age bands: i) paediatric/young adult and i) adult. However, we acknowledge that further research is needed to clarify age-specific outcome measures in MRI studies, particularly in relation to distinct periods of brain maturation. To highlight this point, Ware et al., and Onicas et al., used data from the A-CAP initiative to explore whether sex and age influence differential injury responses, measured by neuroimaging in paediatric mTBI patients who developed persistent symptoms. The authors reported reduced structural and functional connectivity in females who developed persistent symptoms compared to controls (i.e. reduced clustering coefficient within the putamen and reduced nodal efficiency within the inferior occipital gyrus). In contrast, males with persistent symptoms showed the opposite effect within the same brain regions (Onicas et al., 2023, Ware et al., 2023). Furthermore, Ware et al., also observed reduced betweenness centrality associated with the supramarginal gyrus and putamen in younger children with persistent symptoms compared to controls (Ware et al., 2023). In contrast, the opposite effect was seen in older children who developed persistent symptoms (Ware et al., 2023).

A further limitation is that several studies stratified participants based on clinical outcome (e.g. recovery status) and then compared acute imaging features between groups. This approach introduces potential for reverse causality or circular inference since outcome measures are used to define imaging comparison groups. Such strategies are common in early biomarker discovery and therefore were not penalised during risk of bias assessment. These studies remain informative for hypothesis generation and may guide future prospective designs aiming to validate prognostic imaging markers.

Nevertheless, a key strength of this review is the consistency of trends observed across studies, despite differences in acquisition methods, processing techniques, clinical assessments, and participant characteristics. For example, the relationship between mTBI-related changes in thalamic structure and function and recovery outcomes was identified in children, young adults, and adults, whether the sample consisted of athletic populations or patients from emergency departments. These trends emerged despite substantial variability in imaging acquisition and analysis methods. This consistency suggests that certain common effects of mTBI may influence recovery outcomes across a range of factors, including injury mechanism, age, and other methodological differences.

5. Conclusions

In conclusion, longitudinal studies reveal that acute neuroimaging markers differ between mTBI patients who develop persistent symptoms versus those who recover, with age and sex potentially influencing neuroimaging findings. Although structural MRI findings show limited correlation with mTBI clinical outcomes, acute changes in white matter and functional connectivity are more strongly associated with symptom burden and functional recovery outcomes. Across multiple imaging modalities, disruptions to integrative structures such as the thalamus, cingulate cortex, and SLF were associated with increased symptom burden and worse recovery outcomes. Finally, this review stresses the need to include measures of symptom burden and functional recovery as standard practice within mTBI focused neuroimaging investigations.

CRediT authorship contribution statement

Joshua P. McGeown: Visualization, Writing – original draft, Investigation, Methodology, Data curation, Formal analysis, Conceptualization. **Mangor Pedersen:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Remika Mito:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Alice Theadom:** Writing – review & editing. **Jerome J. Maller:** Writing – review & editing. **Paul Condron:** Writing – review & editing. **Samantha J. Holdsworth:** Writing – review & editing, Project administration, Conceptualization.

Ethics approval

Not applicable.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

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