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Exploring Traumatic Brain Injuries in Rats: A Comprehensive Systematic Review

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Abstract

A significant percentage of instances of Traumatic Brain Injuries (TBIs) are mild TBIs, such as concussions and constitute a serious public health problem. It is necessary to study the processes and pathological consequences of mild traumatic brain injuries in animals to assess treatment options. The purpose of this review is to investigate existing research on mild TBI in rats, with an emphasis on concussion and closed head injury. We performed a review search using keywords including closed head injury, concussion along with mild TBI, as well as rat on PubMed, Web of Science and Google Scholar. A total of 200 publications from PubMed, 300 from Web of Science and 400 from Google Scholar were found during the search. We thoroughly reviewed and chose 40 papers for analysis, according to the PRISMA recommendations. The authors' classification of closed head injuries in rats or mice as moderate satisfies the inclusion requirements for the article. Our findings demonstrate the great diversity of approaches to modelling MTBIs. Furthermore, we found that experimental MTBI research had a low representation of female rats as well as young and old animals. The findings can be used to compare the injury models in context and serve as a basis for choosing the best MTBI model to test a certain assumption. We ensure that this assessment will serve as a helpful beginning point for figuring out what has been accomplished and what information is lacking in the effort to mitigate the impact of MTBIs.

Keywords: Rats, Brain Injuries, Concussion, Closed Head Injury

INTRODUCTION

The electroencephalography (EEG) monitoring of human subjects in the critical care unit indicates that no convulsive seizures, known as Non-Convulsive Status Epilepticus (NCSE), occur in around 20% of patients with severe traumatic brain injury (TBI) (1). In the first three days following an accident, 33% of persons experience these kinds of seizures. The frequency of seizures had a bimodal distribution. (2) Given that NCSE is associated with neural shrinkage, elevated pressure inside the skull, brain chemical disruption and an elevated risk of death, measures are needed to prevent NCSE (3). Interestingly there is no published animal model for post-TBI NCSE (4). This paradigm is used to study TBI processes and create post-TBI recovery therapies (5). It has been demonstrated that antiepileptic medication treatment, including topiramate and levetiracetam, improves recovery following Fluid Percussion Injury (FPI). There hasn't been much research done on post-impact electrographic abnormalities, even though the majority in the lateral FPI model. They started to monitor rats following the induction of severe lateral FPI using video-EEG (6). Every year, a staggering 10 million individuals worldwide experience TBI resulting in hospitalization or fatality. Survivors of TBI exhibit cognitive, physical and psychological impairments (7). The VCS and the amount of water in the brain are measured 24 hours after the injury and the effect of prior treadmill activity on cerebral edema and neurological outcomes are measured to achieve this (8). A major global health and well-being concern, TBI persists in its ramifications. Reduced consciousness, forgetfulness and anomalies of the nervous system are some of the symptoms of TBI, which is defined by the centres for disease control as a head injury of any kind (9). Although TBI was thought to be transient, it has links to an elevated risk of Parkinson's disease and the onset of chronic traumatic encephalopathy (CTE). 52,000 TBI-related deaths and 275,000 hospital admissions occur in the US

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each year and some disabilities from TBI are severe and permanent (10). This significant TBI burden has prompted extensive attempts to understand and treat the disorder. The complex interactions between physics and biology that lead to morbidity following head traumas are becoming understood due to recent studies. Rat models are essential to our investigation since they are used in pre-clinical research on traumatic brain injury because of their importance in helping to comprehend the intricate systems at play.

The study (11) introduced rats that underwent isoflurane anaesthesia and they were randomized to be part of the experimental control group that was sham-operated or the group that had lateral FPI-induced severe Traumatic Brain Injury. After the impact of the fictitious procedure, electrodes were inserted and "video-electroencephalogram (EEG)" surveillance has initiated. The article (12) aimed at damaged rats that experienced seizures in the first 72 hours after TBI. The research (13) proposed traumatic brain injury was when most rats' epileptiform EEG patterns started to decline. The study (14) explored interesting to note that some naïve and sham rats had post-operation seizures, but they did not show the same EEG backdrop textures that are particular to the non-convulsive SE that TBI animal's exhibit. The article (15) provided insight into escaped diagnosis up until this point by showing that moderate psychological symptoms and non-convulsive SE occur by left FPI-induced TBI. The research (16) addressed Immunosenescence, or the deregulation of the immune system brought by age, is thought to have a significant impact on the results of traumatic brain injury. The study (17) illustrated that rats were put to death either 24 hours or 1 week after the injury so that immune cell populations in the brain and peripheral were analyzed using flow cytometry. The article (18) described that telomere length was measured as an indicator of neurological health. When compared to their younger counterparts, middle-aged rats showed more noticeable sensors after traumatic brain injury, motor deficits and smaller telomeres. The research (19) evaluated that age and TBI reduced cortical volume as well as cognitive performance separately. The study (20) explored middle-aged rats that had TBI and shorter telomeres along with more sensory impairments than younger rats.

METHODS

Search Parameters

PRISMA criteria were used to study closed-head trauma models of mild TBI. We searched PubMed, Web of Science and Google Scholar for mild TBI, concussion, closed head injury and rat. The analysis omitted reviews, fluid percussion and controlled cortical impact, which is intriguing. We performed a sophisticated Boolean search on platforms to find titles and abstracts. Rats with mild TBI, A head wound, or brain trauma. These searches generated 200 PubMed, 300 Web of Science and 200 Google Scholar items. After integrating these lists and deleting superfluous references, Figure (1) displays 700 relevant publications.

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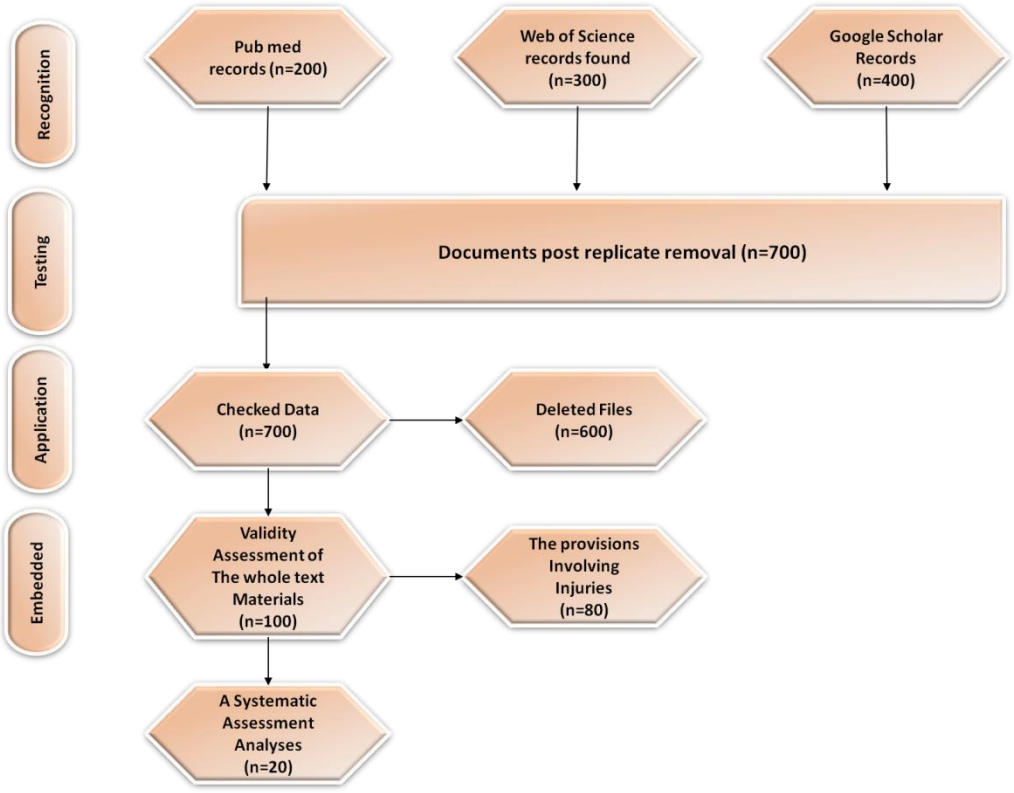

Figure (1). Study selection (Using PRISMA)
(Source: Author)

The methods flow chart shows the steps involved in our investigation. 700 items were retrieved during the identification phase, which involved searches on two different web-based platforms. A comprehensive review of the complete texts was conducted to determine the eligibility of these publications after an initial screening based on abstracts resulting in the elimination of 500 articles (21). They next excluded papers about mild TBI associated with recurrent injuries, leaving 20 articles about TBI alone for our thorough analysis. However, piston-driven models became common in 2002. From 1941 to 1987, 'other' models produced unorthodox minor brain injury.

PERFORMANCE ANALYSIS

A detailed systematic evaluation of rat TBI employing closed-head trauma models focused on the piston-driven models. The researchers found 700 relevant publications using PRISMA criteria and a sophisticated Boolean search across Pub Med, Web of Science and Google Scholar. In the 1990s, piston-driven types ruled. The investigation covered search parameters, model evolution and piston-driven models. Methodological differences, common data items and motor skills, affective behaviour and histopathological outcomes were examined.

Models of closed head injuries powered by pistons

Piston injuries mainly originate from piston alignment with the scalp or skull and impact force, depth, or velocity power piston devices with pneumatics, electricity, or nitrogen (22). This group has animal location and damage site variations. CHIMERA's face-up creature's blow bends its head. After a piston hits its head, the "Hit & Run" animal hangs by its pair and moves freely (23). While lying flat and moving laterally, some models hit injured animals at an angle. Animal signal data covers gender, species and age. Figures (2) (A) and 2 (B) were. Anesthesia and surgical indication are common piston-driven model injury data points.

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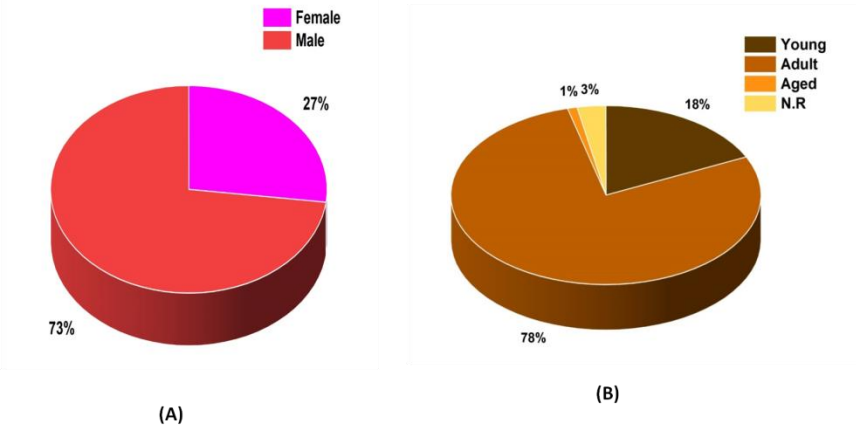

Figure (2). Animal-specific piston-driven closed head injury models (A) Sex and (B) Age
(Source: Author)

Standardized animal-specific data for closed head injury models using piston-driven devices

In head injury models, animal-specific data is emphasized (24). The majority of piston-driven injury articles used rats (26%; SA 2.1). In situations where animal gender was disclosed, 72% were male, SA 2.2. If women were included, 94% of the publications featured men as well and gender-specific data separation was seen in half of the cases, preventing a thorough sex analysis (SA 2.3) (25). The majority of research used adult animals (78%), followed by pups (19%; SA 2.4).

Closed-head a harm model with piston: damage-induced functional changes

According to the examination of the piston-driven model, 23 percent of the articles documented fatality (26). 90% of death rates ranged from 0% to 5% (SA 2.19) (26). A study indicated that none of the deaths were high; only moderate (SA 2.19) (27). In 32% of models of Closed Head Injuries (CHI) powered by pistons, the righting reflex was detected and 78% of the models exhibited a duration of delay of 1-11 minutes (SA 2.21).

Motor skill testing: closed-head piston drive harm models

Two articles indicated a considerable shift from sham following injury, but one exhibited no deficit, suggesting the piston-driven CHI model did not exhibit NSS deficits (28). SA 2.21 had no balance beam test losses after piston-driven damage, unlike five articles. Nine of 10 rotarod-tested publications failed, however SA 2.22 did not change after injury (29). After TBI, five of six open field tests showed issues, whereas SA 2.23 did not (30). Figure (3) and Table (1), SA 2.24, showed piston-driven CHI motor testing deficits after pedal spinning and wiring suspension.

Table (1). Using pistons to model closed head injury motor skills
(Source: Author)

Motor Function	Deficit	No deficit
Other Behavior	3	1
Open field	6	2
Rotarod	10	2
Balance Beam	6	2

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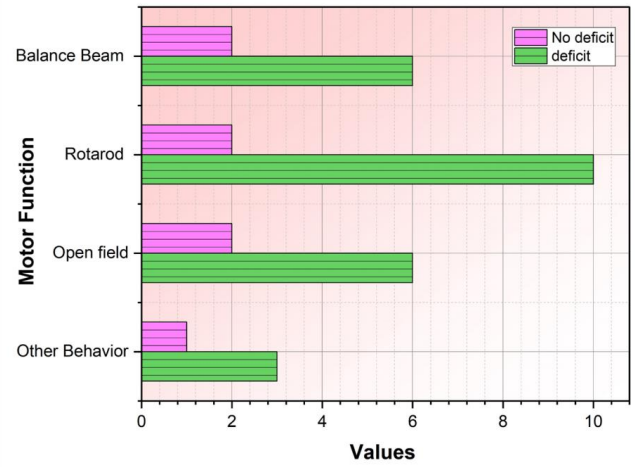

Figure (3). Modelling motor skills after closed head injury with pistons
(Source: Author)

Histopathology of a sealed injury to the head pushed by a piston model

Piston-driven CHI articles had 74% histopathological results (31). Modifications in cells or organs were nine of ten, damage by thirteen of fourteen (SA 2.30). SA 2.31 covered gliosis in 19 publications (32). Damaged myelin was described in three articles (SA 2.32) (33). Among other histological endpoints, the blood–brain barrier (1/1), pain (2/0), cleaved induction (1/0) and increased enrolment n = (deficit/no deficit). Figure (4) and Table (2), SA

Table (2). Piston-driven closed head histopathology
(Source: Author)

Histopathology	**deficit**	**No deficit**
Other	9	1
Edema	1	1
Myeliu	4	1
Gliosis	20	1
Blood Brain Barrier	2	2
Axonal Injury	14	2
Cell or Tissue Changes	10	1

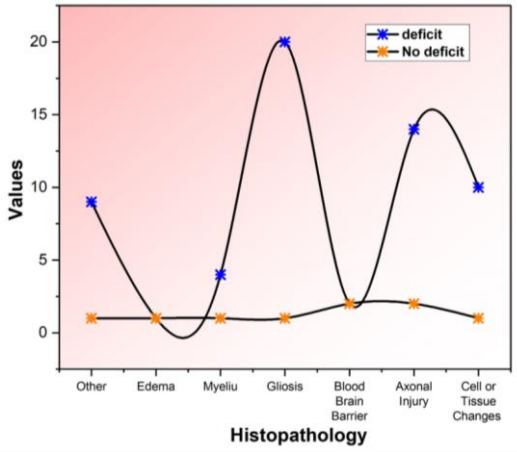

Figure (4). Histopathology of piston-driven closed head harm
(Source: Author)

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Other models

The last group of TBI models, "Other" models, is divided by the device used to cause the damage or the biomechanical process used of such items (34). Examples of turning harms (SA 3.1) are the most common, while the Crusher model with reaction is the least used (35). These earlier models provide valuable insight into the history of modelling mild traumatic brain injuries. Our next section will explore these models from most to least used (36). These two rotation-inducing TBI models are the most published "Other" models and involve a rotating biomechanical process.

Alternative model: Model-animal data components

The present group used anaesthesia in 81% of investigations Figure (5), SA 3.3 and head immobilization in 83% (SA 3.3) (33). The helmeted scalp was hit at 24%, the helmeted skull at 12%, the intact scalp at 43% and the skull at 19%. Rats dominated 87% of papers (37). Most research (75%), regardless of species, used male subjects (38). One of the female-subject papers examined sex disparities in outcomes. These experiments used adult animals.

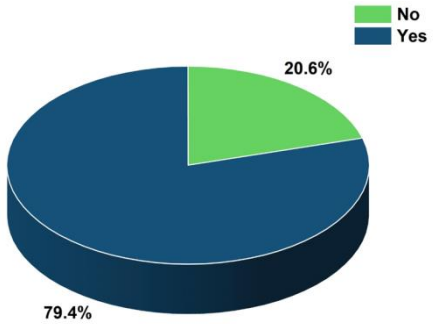

Figure (5). Using anesthesia
(Source: Author)

Function and histopathological changes after injury in "Alternative" model

This publishing section compares behavioural testing and histological analysis frequency. This field uses histology more than behavioural testing (39). Figure (6) and Table (3) show that 52% of studies mentioned histology. One histology research showed no deficits and six found cell coupled with tissue abnormalities (40). Two trials showed no axonal injury histological evidence, while five indicated deficiencies (SA 3.16). This data shows the broad use of histology, the cellular and axonal modification effects stated in the papers.

Table (3). Histological changes in the 'other' model
(Source: Author)

Histopathology	No deficit	deficit
Other	1	5
Edema	1	1
Myeliu	1	1
Gliosis	2	5
Blood Brain Barrier	1	1
Axonal Injury	3	6
Cell or Tissue Changes	2	7

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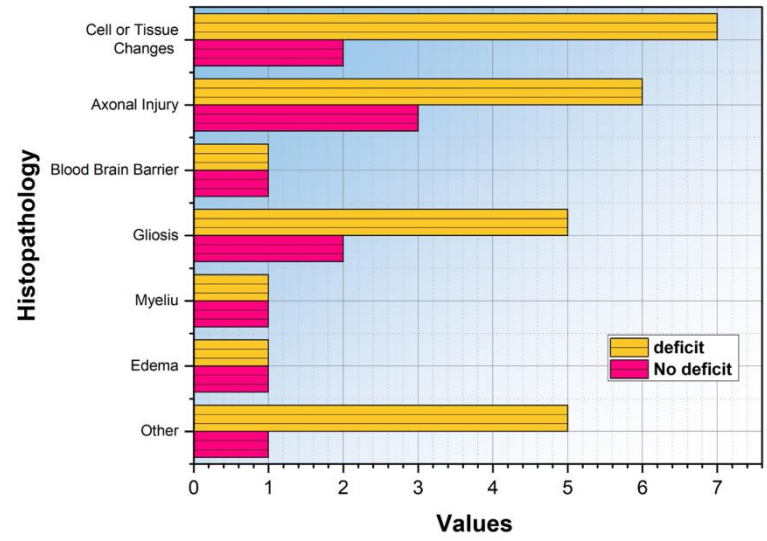

Figure (6). 'Other' model injury histological
(Source: Author)

CONCLUSION

A PRISMA search using PubMed, Web of Science and Google Scholar produced seven hundred relevant publications. Twenty publications were left for in-depth analysis after 500 publications underwent a rigorous review process. Combining these papers into a summary shows a trend in the modelling of TBI, highlighting the use of piston-driven models in most recent studies. Examining emotional behaviours and physical skills is made possible by this growth in modelling. The evaluation of closed head injuries using a piston-driven system not only revealed histological abnormalities but also highlighted the importance of gathering data particular to individual animals. The systematic review looked at "alternative" TBI models that included rotational aspects, highlighting the need for a variety of modelling approaches. Our review highlight the progress made in the field, but it also emphasizes its diversity with its thorough examination of rat TBI study methodologies and their conclusions. This systematic review highlights the diverse methods and discoveries made, which advances our knowledge of traumatic brain injury and highlights the complexity of this important field of study.

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