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The effectiveness of physical exercise as an intervention to reduce depressive symptoms following traumatic brain injury: A meta-analysis and systematic review.

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The effectiveness of physical exercise as an intervention to reduce depressive symptoms following traumatic brain injury: A meta-analysis and systematic review.

Alongside the obvious health benefits, physical exercise has been shown to have a modest anti-depressant effect for people in the general population. To the authors' knowledge, there are no current literature reviews or meta-analyses available exploring this effect for people with a traumatic brain injury (TBI). A systematic review of intervention studies utilizing physical exercise and mood outcome measures for a TBI population was performed in November 2016. Baseline and outcome data were extracted for the nine studies which met the inclusion criteria. Effect sizes were calculated for the three controlled trials and six uncontrolled trials and entered into the meta-analysis. Consistent with research in non-brain injury populations, the current meta-analysis identified a small to medium effect size of physical exercise on reducing depressive symptoms in people with a TBI. This would support further rigorous trials to provide additional evidence for the efficacy of physical exercise interventions for people with TBI. Limitations of the current meta-analysis and clinical implications are discussed.

Keywords: traumatic brain injury; depression; exercise; intervention; rehabilitation

Introduction

The National Institute of Neurological Disorders and Stroke define traumatic brain injury (TBI) as a type of acquired brain injury which is the result of sudden trauma, which causes damage to the brain (NINDS, 2015). It is estimated that there are approaching 1.3 million people across the UK living with a disability, as a direct result of a traumatic brain injury (TBI), at a cost of about £15 billion per year (Parsonage, 2012). TBI is associated with short and longer term disability, which is often a complex interaction between cognitive, physical and psychosocial impairment (Driver, Ede, Dodd, Stevens & Warren, 2012).

Depression and TBI

Depression is reportedly the most common psychiatric disorder to emerge following TBI (Koponen et al., 2002; Alderfer, Arciniegas & Silver, 2005; Bryant et al., 2010) with rates ranging between10% and 77% (Varney, Martzke & Roberts, 1987; O'Donnell, Creamer, Pattison & Atkin, 2004). The variability in reported prevalence rates is likely to be due to the variability in the criteria used to identify the presence of depressive symptoms. Kreutzer, Seel & Gourley (2001) attempted to combat the significant variability by examining 722 outpatients with TBI utilizing the DSM-IV criteria for depression. They found that 42% of outpatients in fact met the criteria for a Major Depressive Disorder (DSM-IV; American Psychiatric Association, 1994).

Despite heterogeneity in reported rates of depressive symptoms and diagnoses of depression following TBI, it is clear that depressive symptoms are elevated a year following injury (Jorge, et al., 1993) and appear to remain elevated for up to a decade

later (Holsinger et al., 2002). The emergence of depressive symptoms following TBI is likely to be due to a combination of factors including neuro-biological changes, psychological adjustment and the social context in which the individual resides (Alderfer, Arcinniegas & Silver, 2005).

Depressive symptoms following TBI can hinder the recovery process (Rosenthal, Christensen & Ross, 1998; Seel & Kreutzer, 2003; Mooney, Speed & Sheppard, 2005). Studies have shown that patients reporting depressive symptoms following TBI have a lower quality of life, poorer health status and poorer psychosocial functioning than non-depressed individuals with TBI (Hibbard et al., 2004; Rapoport, Kiss, & Feinstein, 2006; Chamelian & Feinstein, 2006). Depressive symptoms have also been associated with worse global outcomes (measured by the Glasgow Outcome Scale) five to seven years following TBI (Whitnall et al., 2006).

Treatment of Depression Following TBI

There is some evidence that antidepressant medication can help to alleviate depressive symptoms following TBI (see Fann, Hart & Schomer, 2009 for a systematic review). Selective Serotonin Reuptake Inhibitors are often recommended as a first line medication following TBI due to their favourable profile of side-effects (see Warden et al., 2006). There appears to be some limited data available supporting the use of Electro Convulsive Therapy to reduce depressive symptoms following TBI but sample sizes are small and narrowly selected (Fann, Hart & Schoner, 2009).

The use of psychological interventions to alleviate depressive symptoms following TBI has been well-researched. Initial systematic reviews were limited to just a few

randomized controlled trials (Comper, Bisschop, Carnide, & Tricco, 2005; Soo & Tate, 2007) but two comprehensive meta-analyses were carried out more recently specifically investigating the effectiveness of psychological interventions to reduce depressive symptoms following TBI. Stalder-Lüthy, Messerli-Bürgy, Hofer et al's (2013) systematic review included 13 studies, 10 of which utilized Cognitive Behavioural Therapy (CBT) in their treatment protocol. The subsequent meta-analysis included 7 of the 13 studies which met the inclusion criteria. Overall, the authors reported a significant medium effect (ES=.69; 95% CI= .29 - 1.09) for psychological intervention on reducing scores on depression questionnaires for participants with TBI. The results of the meta-analysis should be treated with caution due to the small number of studies included and the inclusion of a variety of psychological intervention limits the ability to make specific treatment recommendations based upon the analysis.

Waldron, Casserly and O'Sullivan (2013) also conducted a systematic review and meta-analysis to analyze more specifically the use of CBT to treat symptoms of depression and anxiety following TBI. 24 studies were indentified in the review; 12 out of the 24 studies were included in the meta-analysis and included depression related outcome measures. The studies specifically targeting symptoms of depression following TBI reportedly showed a large average effect size (ES = 1.15) but with a significant range from 0 to 2.39.

Qualitative research has explored the treatment preferences for people reporting symptoms of depression following TBI using telephone interviews with self-identified depressed and non-depressed individuals 12 months following TBI (Fann et al., 2009). 84% of the sample (n=145) rated physical exercise as their preferred treatment method

above all others (including talking therapy, antidepressant medication, group therapy, self-help and alternative medicine). Physical exercise intervention could be delivered in a group format and would thus benefit from the advantages of group based interventions. This could include the cost saving of having more than one individual receiving the intervention from each paid professional.

Exercise intervention for depression in non-TBI participants

There are a number of reasons why it is plausible that exercise would have an anti depressant effect. It has been proposed that exercise can act as a distraction from negative thoughts (Nolen-Hoeksema & Morrow, 1993) but also can result in positive feedback from others and an increase in self-esteem (Bosscher, 1993). Research has also suggested that physical exercise can lead to experiences of mastery which has been shown to be a reliable way to increase self-efficacy and subsequently improve symptoms of depression (Bandura, 1997; Craft, 2005; Peterson & Seligman, 1984). Animal studies have also demonstrated that exercise results in increased serotonogic drive (Gomez-Merino, Bequet, Berthelot, Chennaoui & Guezennec, 2001) and increased neurogenesis (Bjornebekk, Mathe & Brene, 2005) which can have an anti-depressant effect.

There are six systematic reviews and meta-analyses since 2001 available to the current author, reviewing the use of exercise to reduce depressive symptoms in non-TBI populations (Lawlor & Hopker, 2001; Sjosten & Kivela, 2006; Stathopoulou, Powers, Berry, Smits, & Otto, 2006; Mead et al., 2009; Rethorst, Wipfli & Landers, 2009; Krogh, Nordentoft, Sterne & Lawlor, 2011). Conclusions from these reviews vary from reporting methodological weakness from trials and therefore no conclusive effect

(Lawler & Hopker, 2001; Sjosten & Kivela, 2006) to a meta-analysis of 11 treatment outcome studies reporting a very large combined effect size for exercise as an intervention for symptoms of clinical depression (Statholoulou et al., 2006).

The Cochrane review reported a non significant moderate effect of exercise for reducing depressive symptoms when their analysis was limited to robust trials (Mead et al., 2008). Krogh and colleagues (2011) only included participants with a clinical diagnosis of depression whereas the other five reviews had much broader inclusion criteria. Krogh and colleagues (2011) concluded that exercise was shown to have a small effect on reducing depressive symptoms based on a standardized mean change of -.04, but follow-up data from five of the 13 studies suggested that this effect was no longer present after the intervention had finished.

To the authors' knowledge, at the time of writing there were no systematic literature reviews or meta-analyses reviewing the use of exercise as an intervention to alleviate depressive symptoms following TBI. The present meta-analysis aims to answer the following question: *Is physical exercise an effective intervention to reduce depressive symptoms following TBI?*

Method

Identification and selection of studies

Three electronic databases (PubMed, PsychInfo and Web of Science) were searched in November 2016. The following Boolean search terms were used: "brain injur*" AND "exercise" AND ("mood" OR "depress*"). An ancestral search of identified published

articles was also conducted. The search was limited to articles published in English. Initially, articles were screened via examination of abstracts and then full articles were assessed according to the following inclusion criteria:

- Participants must be aged 18 or older and have sustained a TBI.

- Interventions must utilize physical exercise.

- Research papers must be clinical trials.

- Study data must be quantitative.

- Studies must have a depression related outcome measure.

- Control group data must be from a comparable population, if not the study will be analyzed as a non-controlled trial.

Where data was missing in the published papers, authors were contacted by email and via Research Gate (three reminders were sent to non-responders).

Assessment of study quality

Study quality or methodological rigour of each study included in the analysis was assessed utilizing the criteria proposed by Reichow, Volkmar and Cicchetti (2008). This method was selected as it has been shown to have sound psychometric properties (Reichow et al., 2008) and is deemed to be superior to alternative methods (Wendt & Miller, 2012). Each study in the current meta-analysis was evaluated according to Reichow's (2011) primary and secondary indicators for research design. Each indicator (for example, participant characteristics, independent variable etc.) was rated as high, acceptable or unacceptable. Based on the number of ratings for each indicator, a strength rating can be determined by Reichow and colleagues' (2008) original

classification. This results in a rating of strong, adequate or weak methodological

rigour. See Table 1 for individual ratings of studies included in the meta-analysis.

Data analysis

Data for standardized measures related to mood or depression were extracted from

each paper by the principal author, where multiple measures were available, only those

relating to depression were extracted. All statistical analyses were conducted via the

Metafor package (Viechtbauer, 2010) for the statistical software environment, R (R

Core Team, 2016). The effect sizes for each study were calculated using the mean

change in scores divided by the baseline standard deviation (Jansen, Viechtbauerm

Lenssen, Hendriks & A de Bie, 2011). This calculation is commonly referred to as

Glass's Δ in the literature (Becker, 2000). For controlled trials, the difference between

effect sizes for the two arms of the trial were used, for uncontrolled trials, the effect size

from baseline to post intervention was calculated relative to zero (Viechtbauer, 2010).

Positive values represent an average improvement in scores from baseline to post-

intervention measures. An effect size of 0.2 to 0.5 can be interpreted as a small effect,

0.5 to 0.8 as a medium effect and >0.8 as a large effect (Cohen, 1988). To estimate the

standard error of the calculated effect sizes, the pre and post-test correlations were

extracted from the literature for each of the standardized measures included in the meta-

analysis (Aben, Verhey, Lousberg, Lodder & Honig, 2002; Beck, Steer & Brown, 1996;

Curran, Andrykowski & Studts, 1995; Radloff, 1977).

A meta-analysis to establish the average effect of exercise intervention across the

selected studies was conducted. There are two largely accepted models used to

compute a meta-analysis, a fixed effect model and a random effects model (Hunter &

Schmidt, 2000). A fixed effect model works on the assumption that the true effect within each study is essentially the same and that any difference in observed effect size represents random error. A random effects model allows the meta-analysis to predict an overall Standardised Mean Change (SMC) based on the distribution of true effect sizes. This distribution represents random error as in the fixed effects model but also true difference in effect size due to variance between studies (Borenstein, Hedges & Rothstein, 2007). It was hypothesized that there would be systematic differences between the studies (heterogeneity) due to variation within the interventions used and anticipated variability in methodological rigour. A random effects model was therefore the most appropriate method for the present meta-analysis. The random effects meta-analysis was run using Metafor for R (Viechtbauer, 2010) and calculated the SMC which represents the average of a distribution of values.

Results

Of the 204 articles screened via examination of abstracts, 137 were deemed not to be relevant to the topic of interest and were excluded. This left 67 articles to be assessed in full according to the inclusion criteria described above. Of the 67 full-text articles assessed, 10 were identified as satisfactorily meeting the inclusion criteria above, however unfortunately one author did not respond to requests for data; therefore 9 final studies were included in the meta-analysis. Figure 1 (Moher et al., 2009) illustrates the flow of studies through the meta-analysis. The designs of the final studies included randomized controlled trials, non-randomized controlled trials and non-controlled trials.

Characteristics of studies included

Quality: The methodological quality of the studies included in the analysis were all rated to be of 'Adequate' (Chin, Keyser, Dsurney & Chan, 2015; Damiano, Zampieri, Acevedo & Dsurney, 2016; Driver & Ede, 2009; Lee, Ashman, Shang, & Suzuki, 2014; Schwandt et al., 2012; Weinstein et al., 2017; Wise, Hoffman, Powell, Bombadier & Bell, 2012) or 'Strong' quality (Bellon et al., 2015; Rzezak et al., 2015).

Participants: All participants were recruited from the community, were over the age of 18 and provided informed consent to participate in the individual studies. Seven out of the nine studies relied on a diagnosis of a TBI from a physician, whereas two of the studies relied on self reported TBI (Bellon et al., 2015 & Wise et al., 2012). All participants had experienced a brain injury at least six months previous to participating in the study. Severity of TBI was only reported in three of the nine studies and was reported as mild-moderate (Chin et al., 2015 & Rzezak et al., 2015) and moderate-severe (Schwandt et al., 2012). Two studies had healthy volunteer control groups which were not included in the analysis and were treated as uncontrolled trials (Damiano et al., 2016 & Rzezak et al., 2015). One study used a wait list control group (Lee et al., 2014) and two had control groups participating in alternative interventions including nutrition education (Bellon et al., 2015) and vocational rehabilitation training (Driver & Ede, 2009). Both of the control groups included in the analysis were from a brain injury population with randomization of participants to either group (Bellon et al., 2015; Driver & Ede, 2009).

Figure 1. Flow diagram showing study selection process (PRISMA; Moher et al., 2009)

Intervention type: Eight out of the nine studies had an aerobic intervention including treadmill, exercise bike and swimming, one study used a walking

intervention. The intervention length was between eight and 12 weeks apart from one study which had just two sessions, one week apart (Rzezak et al., 2015). All interventions had a supervised element with home practice being set in between supervised sessions.

Outcome measures: All of the studies in the meta-analysis used a mood related outcome measure including the Beck Depression Inventory (BDI-II; Beck, Steer & Brown, 1996), The Hamilton Depression Inventory (HAM-D; Hamilton, 1960), The Profile of Mood States – Short Form (POMS-SF; Curran, Andrykowski & Studts, 1995), The Brunel Mood Scale (BRUMS; Terry & Lane, 2003), Centre for Epidemiological Studies-Depression Scale (CES-D; Radloff, 1977) and the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983). See Table 1 for a summary of studies included in the meta-analysis.

Table 1. Summary of included studies (n=9)

Effect of exercise intervention

See Figure 2 for a forest plot illustrating the meta-analysis of all 9 studies with the main outcome measure following the completion of the exercise intervention. The pooled SMC was 0.48 (95% CI 0.16 to 0.81). This represents a statistically significant positive small to medium overall effect size of physical exercise to reduce depressive symptoms in people following TBI.

Figure 2. Meta-analysis of exercise intervention studies using exercise intervention to reduce depressive symptoms in people following TBI.

Tests of heterogeneity were significant ($p<0.01$), confirming that heterogeneity was present amongst the studies included in the analysis. A funnel plot of the studies included in the meta-analysis (see Figure 3) revealed a couple of smaller studies with large effect sizes (Driver & Ede, 2009; Schwandt et al., 2012), it is possible that this represents a slight positive publication bias in the literature and a wider distribution of effect sizes amongst smaller studies would be expected. It is unlikely that small studies with small or non-significant results are published, thus it is common to find publication bias in the literature.

Figure 3. Funnel plot of all studies included in the meta-analysis

As a conservative method to assess whether or not the smaller studies were unduly skewing the results of the meta-analysis, the analysis was re-run excluding the two smaller studies. The results showed an overall SMC of 0.35 (95% CI 0.17 to 0.52) which falls within the statistically significant small to medium effect size range, suggesting that there is a small but positive effect of exercise in reducing depressive symptoms in people with a TBI, despite heterogeneity between the studies used in the analysis.

As a conservative assessment of difference between the randomized controlled trials and uncontrolled studies; the analysis was also re-run including only the randomized controlled trials and only the uncontrolled trials separately. The overall SMC was 0.95 (95% CI -0.70 to 2.61) when only the randomized controlled trials were included in the analysis however there was significant heterogeneity between the two studies. The overall SMC when the analysis was re-run for only the uncontrolled trials was 0.40 (CI 0.23 to 0.57).to 0.57).

Discussion

The small to medium main effect of exercise on reducing depressive symptoms in the current meta-analysis appears comparable to previous meta-analyses investigating the effectiveness of exercise on symptoms of depression in non-TBI populations (Krogh, Nordentoft, Sterne & Lawlor, 2011; Mead et al., 2008).

The current meta-analysis provides tentative support for the use of exercise to reduce depressive symptoms whilst the individual is engaged in the exercise intervention, but only one study included in the meta-analysis provided six month follow up data to assess change over time (Wise et al., 2012). Scores on the BDI reduced on average by five points (scores range from zero – 63 with scores above 29 indicating clinically significant levels of depression), from baseline to 10 week measures, there was no further reduction in BDI scores at six month follow up but the reduced scores were maintained and participants reported continuing to exercise for an average of 146.6 minutes. Unfortunately the authors did not collect data from the control group at six month follow-up. It will be important for future exercise intervention studies to collect follow-up data for intervention and control groups to further understand the effect of change over time. Initial results from Wise and colleagues (2012) are however promising.

Study Quality

It was not possible to conduct a meta-analysis solely including randomized controlled trials due to the relative lack of published research which met the inclusion criteria described above. Only two randomized controlled trials were available in the

literature (Bellon et al., 2015; Driver & Ede, 2009). Driver and Ede (2009) randomly allocated participants who met the inclusion criteria to either a vocational rehabilitation control group or the physical exercise group, but assessors were not blinded to the randomization. Similarly Bellon et al. (2015) randomly allocated participants to control (nutrition education) or a walking (exercise) group but the arms of the study were not blinded.

Interestingly there was a large discrepancy in the SMC between the RCTs. Driver and Ede (2009) finding a SMC for exercise on depressive symptoms as compared to a control group of 1.87, meaning that the participants in the exercise group were averagely scoring 1.87 standard deviations lower (representing an improvement) on depression related measures relative to the control participants. Bellon et al. (2015) found a more modest improvement in depression related outcome measures for the exercise group compared to the control group (0.18).

The RCTs differed in the delivery of the intervention, whereby Driver and Ede (2009) delivered a group aquatic programme and Bellon et al. (2015) delivered one to one training. To understand whether group delivered exercise intervention is more efficacious, vastly more research is needed using methodologically sound RCTs to be able to utilize a meta-regression, to explore the potential differences in efficacy due to intervention delivery method. It should also be noted that the two control groups undertook different interventions which included a vocational rehabilitation group (Driver & Ede, 2009) and a nutrition educational programme (Bellon et al., 2015). Therefore the SMC was ultimately detecting differences in change between exercise

interventions and differing control conditions, which will likely differ in their own effect on depression measure scores.

One non-randomized controlled trial (Lee et al., 2014) was included in the analysis. The study utilized a waiting list control group design whereby participants were allocated to either group dependent on their personal circumstances and availability. Potentially this could indicate that participants who were available for the intervention group were more motivated to participate in an exercise intervention, thus it is important to consider the effect of non-randomization when interpreting the results.

The remaining six studies included in the analysis were non-controlled trials (Chin et al., 2015; Schwandt et al., 2012; Weinstein et al., 2017; Wise et al., 2012) or were controlled trials with healthy volunteer data which was not included in the analysis (Damiano et al., 2016; Rzezak et al., 2015). Due to the lack of controlled trials utilizing an exercise intervention to reduce depressive symptoms following TBI, it was important to include the uncontrolled trials in the meta-analysis. This does however highlight important issues with the analysis. The SMC for the controlled trials were calculated relative to the change in the control group whereby the uncontrolled trials were calculated relative to zero. As expected, the overall effect size for the uncontrolled trials was larger than that for the controlled trials but both still fell within the small to medium effect size range.

Limitations

There were several limitations to the current meta-analysis. Due to the small number of controlled intervention studies, the analysis included uncontrolled trials and

controlled trials which likely contributed to the heterogeneity between studies in the analysis but equally reflects the current state of the literature on this important subject. Also, due to the small number of studies that met the inclusion criteria, it was not possible to run further regression analyses to understand the effects of different specific exercise interventions, group versus one to one, duration of intervention etc. It will be important to investigate these potential predictive variables when more research becomes available in the literature.

As with all meta-analyses, there is the risk of inflated type I publication bias towards research published with significant positive findings. As discussed above, this is likely the case for the current meta-analysis but when controlling for this using the conservative method of re-running the meta-analysis, there remained a small but positive overall effect of exercise on reducing depressive symptoms. Ultimately the current results should be interpreted with caution and the literature would greatly benefit from more research into this important potential intervention.

Conclusion

In conclusion, exercise may be efficacious in reducing depressive symptoms in individuals who have sustained a TBI. The heterogeneous sample of studies available to the current meta-analysis has made it difficult to draw comprehensive conclusions but is representative of the current literature available. It will be imperative for future research to include properly controlled trials to further understand the effect of physical exercise on reducing depressive symptoms in people who have sustained a TBI. The potential cost effectiveness of group exercise intervention programmes and feedback

from patients' preferences (Fann et al., 2009) would support further research into the area.

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Table 1. Summary of included studies (n=10)

Author/ Year	Design	N (pre)	N (post)	Control group	Mean Age (SD)	Time since injury	Sex M:F	Outcome Measure	Summary of Intervention	Findings	Setting	Quality rating (Reichow et al., 2008)
Damiano et al. (2016)	Non-Controlled Trial	12	12	Healthy Volunteers not included in analysis	31.3 (9.4)	TBI >6 Months	7:5	HAM-D	Elliptical training at home over 8 weeks, 5 days per week at 30 minutes per session	Improvement in sleep and scores on the HAM-D compared to non-TBI control	Home-based	A
Weinstein et al. (2017)	Non-Controlled Trial	10	10	No	32.9 (6.5)	TBI >6 Months	4:6	POMS-SF	Aerobic treadmill exercise supervised, 12 weeks, 3 per week, 30 minute sessions, heart rate maintained at 70-80% of reserve.	Improvement in short-term mood responses	Community	A
Bellon et al. (2015)	Randomized Controlled Trial	69	69	Yes Nutrition education program	43.7 (15.8)	TBI >6 Months	41:28	CES-D	Home-based walking program measured via pedometer aim 5% increase per week until goal of 40% increase in weeks 8-12. Coaching contact 3 times per week tapered off at end	Improvement in depression symptoms following the program	Home-based	S
Chin et al. (2015)	Non-Controlled trial	7	7	No	33.3 (7.9)	TBI >6 Months	2:5	BDI-II	Aerobic treadmill exercise supervised, 12 weeks, 3 per week, 30 minute sessions, heart rate maintained at 70-80% of reserve.	Improvement in cardiovascular fitness no changes in BDI-II	Medical Research Center	A

Study	Design			Control	Age	TBI	Ratio	Measure	Intervention	Outcome	Setting	
Rzezak et al. (2015)	Non-Controlled Trial	12	12	Yes Healthy Volunteers not included in analysis	31.83 (9.5)	TBI >6 Months	12:0	BRUMS	2 sessions between 1-2 weeks apart. 1st session cycling at high intensity until voluntary exhaustion. 2nd session 30 minutes cycling of moderate intensity exercise.	Reductions in depression and anxiety symptoms compared to controls	Laboratory	S
Lee et al (2014)	Non-Randomized Controlled Trial	21	21	Yes Waiting list control group	46.1 (15.2)	TBI >12 Months	9:12	BDI-II	Group exercise instructor led 60 minutes twice per week for 8 weeks. Physical exercises accompanied by verbal affirmations (IntenSati)	Less depressive symptoms and more positive affect after completion of the program	Rehabilitation Outpatient Department	A
Schwandt et al. (2012)	Non-Controlled Trial	4	4	No	29 Range 19-48	TBI >11 Months	3:1	HAM-D	Supervised aerobic either cycle, treadmill or step machine 3 times per week over 12 weeks. 30 minutes exercise plus warm up and cool down	Reduction in depressive symptoms and increase in self-esteem	Hospital	A
Wise et al. (2012)	Non-Controlled Trial	40	37	No	39.7 (12.6)	TBI >6 Months	15:25	BDI	Supervised once per week 30mins aerobic exercise and education with further 4X 30 min sessions unsupervised. Telephone follow-up	Exercise was maintained and depressive symptoms reduced	Community	A
Driver & Ede (2009)	Randomized Controlled Trial	16	16	Yes Vocational Rehabilitation Class	37.65 (2.34)	TBI >12 Months	Missing data	POMS	8 Week aquatic exercise class (24 sessions, aerobic and resistance) 1hour per session. Control was 8 week reading and writing skills class	Increase in positive mood in aquatic group reduction in negative – anxiety and depression.	Community	A

TBI = Traumatic Brain Injury, HAM-D = Hamilton Depression Inventory, POMS-SF = Profile of Mood States – Short Form, CES-D = Centre for Epidemiological Studies-Depression Scale, BDI-II = Beck Depression Inventory second edition, BRUMS = Brunel Mood Scale, BDI = Beck Depression Inventory, POMS = Profile of Mood States.

Figure 1. Flow diagram showing study selection process (PRISMA; Moher et al., 2009)

Figure 2. Meta-analysis of exercise intervention studies using exercise intervention to reduce depressive symptoms in people following TBI.

Figure 3. Funnel plot of all studies included in the meta-analysis

Identification

Records identified through
PUBMED, PsycINFO and
Web of Science
(n = 195)

Additional records
identified through other
sources: ancestral search
and review papers.
(n = 9)

Screening

Records screened
(n = 204)

Records excluded based
on abstract as topic not
relevant to meta-analysis
or review papers.
(n = 137)

Eligibility

Full text articles assessed
for eligibility.
(n = 67)

Full-text articles excluded.
(n = 58)

Mood outcomes not
reported: 17

Non-exercise based
intervention: 22

Duplicates: 17

Retrospective study: 1

Insufficient data: 1

Included

Studies included in meta-
analysis
(n = 9)

Damiano et al 2016	0.26 [-0.10, 0.62]
Weinstein et al 2016	0.81 [0.34, 1.29]
Chin et al 2015	0.37 [0.02, 0.72]
Rzezak et al 2015	0.34 [0.12, 0.57]
Lee et al 2014	-0.63 [-1.48, 0.22]
Bellon et al 2015	0.18 [0.08, 0.27]
Schwandt et al 2012	2.62 [0.72, 4.52]
Wise et al 2012	0.55 [0.38, 0.73]
Driver & Ede 2009	1.87 [0.93, 2.80]
RE Model	0.48 [0.16, 0.81]

Standardized Mean Change

Standard Error (y-axis); Standardized Mean Change (x-axis)