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A Meta-Analysis on the Differences in Neuroplasticity Between Women and Men after Traumatic Brain Injuries

Victoria A. Martin
Ouachita Baptist University

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Abstract

The current meta-analysis investigates the differences in neuroplasticity between women and men after a traumatic brain injury (TBI). Research on the differences in neuroplasticity between women and men is relatively new and few studies have reported outcome variables by gender after TBIs. Neuroplasticity is the brain's ability to adapt and change particularly because of learning or brain injuries. TBI is a leading cause of death and disability worldwide; because of this, learning more about these differences can give scientists and clinicians more information on how to better treat people with brain injuries. Current research is inconsistent on whether there is a difference in outcome between women and men after a TBI; therefore, a meta-analysis was performed with eight studies. The outcome variables in this study included the Glasgow Coma Scale (GCS) which measures the level of consciousness, Grooved Pegboard which measures motor functioning, Trails A and Trails B which measure attention and cognitive flexibility, and the Wisconsin Card Sorting Test (WCST) perseverative error scores which measure executive functioning. The means, standard deviations, and sample sizes were recorded. There was a significant difference in attention, cognitive flexibility, and executive functioning with men scoring worse. There was no significant difference in level of consciousness or motor functioning. Differences in neuroplasticity could be due to differences in behavior rather than biological differences in sex which could help explain the inconsistencies in results between previous studies.

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Traumatic Brain Injuries

A traumatic brain injury (TBI) is usually from a blow or a forceful jolt that is inflicted on the head or skull and affects typical brain function (Giordano et al., 2010). When a person gets hit in the head with a hard blow or from a forceful jolt their brain may shake inside their skull leading to bruising, nerve damage, or the breaking of blood vessels in the brain (Ratini, 2022). Common causes of TBI are from sports, motor vehicle accidents, physical violence, and other activities (Gamboa et al., 2006). The outcome of a TBI can vary depending on how severe the injury is, a person's genetics, and factors in the environment (Giordano et al., 2010). TBIs can have significant cognitive effects on a person and these effects can persist throughout a person's life without proper treatment. Some of the effects of a TBI include changes in personality, the ability to do activities independently, and the ability to maintain stable emotions, (Schretlen & Shapiro, 2003).

One famous example of how a TBI can change a person's life is the story of Phineas Gage. Phineas Gage was a construction foreman that worked on railroads (Ratiu et al., 2004). One day at work he got into an accident and an iron bar was shot through his cheek and skull (Ratiu et al., 2004). Gage miraculously survived the experience, but he was not the same person he was before the accident (Ratiu et al., 2004). Before the accident he was respectable, kind, and a leader however after the accident he became impulsive, constantly angry, and aggressive (Ratiu et al., 2004). Gage's accident has taught scientists a lot about the localization of brain functions, but this also tells us about how different types of head injuries can seriously change a person's life sometimes without them even realizing it (Ratiu et al., 2004).

The story of Phineas Gage is a rather extreme example of how TBIs can affect a person; there are many other more common examples that sometimes go unnoticed. There is currently a decrease in the number of men participating in American football due to the effects of chronic traumatic encephalopathy (CTE). CTE is a type of brain trauma that occurs due to multiple concussions and head injuries over time without proper recovery periods after injury (Tharmaratnam et al., 2018). A previous study found that out of 202 deceased former professional football players 87% of them had CTE (Tharmaratnam et al., 2018). On average, symptoms tend to not be noticeable until the athletes are 43 years old (Tharmaratnam et al., 2018). Some of the symptoms are irritability, aggression, memory impairment, suicidal thoughts, rapid changes in mood, and depression (Tharmaratnam et al., 2018).

Having a brain injury can also affect how others perceive you. Linden and Crothers (2006) compare brain injuries to having a mental illness. Neither are obvious to others who do not know about the injury or illness, and outward signs of injury or illness are not usually present. The illness or injury only becomes obvious when something seems different about them when people interact with them more frequently (Linden & Crothers, 2006). Women who were unemployed before they had a TBI were less likely to be employed after their injury and they also had a lower economic quality of life after their injury compared to men who had a TBI (Portiz et al., 2019).

Approximately 1.4 million people every year are diagnosed with a TBI and approximately 5.3 million people in the United States have a disability because of a TBI (Gamboa et al., 2006). TBIs are still a leading cause of death and disability worldwide (Brown et al., 2012; Giordano et al., 2020). Unfortunately, TBIs are often not reported or not diagnosed (Giordano et al., 2010). There is also currently a misconception in the general public that TBIs are only an issue that young men deal with. Men do have more TBIs than women; however, women still make up about one fourth to one third of the number of incidences (Farace & Alves, 2000). This is only true; however, from puberty to middle age and the number of incidences is approximately the same for women and men throughout childhood and in older adults (Farace & Alves, 2000).

Neuroplasticity

Neuroplasticity is the brain's ability to adapt and change primarily through learning or after a brain injury (Demarin et al, 2014). Neuroplasticity can be adaptive when function is gained but it can also be maladaptive when there is loss of function (Cramer et al., 2011). Neuroplasticity can be observed in a wide variety of brain diseases as well as normal aging and health (Cramer et al., 2011).

Originally it was believed that the brain was stagnant and did not change. What you were born with is what you would live with and die with. In 1923, Karl Lashley found that the motor area of the brain in monkeys had considerable changes after a month due to the different types of motor tasks the monkeys had to perform (Kaczmarek, 2020). However, these findings were ignored as well as any other findings that pointed to the brain being able to change. Later in 1983, Merzenich and colleagues observed changes in cortical somatosensory fields (Kaczmarek, 2020). This finding was also met with opposition however in 1984 Merzenich conducted a study by amputating a monkey's finger and then recorded the electrical activity in the monkey's somatosensory area (Kaczmarek, 2020). He found that cortical representation of the amputated finger was redirected to the remaining digits (Kaczmarek, 2020). Since this study, many studies have investigated neuroplasticity and how the brain can adapt and change.

Neuroplasticity can not only be observed in brain injuries but also in a person's behavior. A person's brain can be affected by what they do and their environment. A study by Maguire et al. (2000) found that there was a difference between the hippocampi of taxi drivers and non-taxi drivers. The taxi drivers had larger posterior hippocampi and there was a positive correlation with the size of the hippocampus and the length of time they were a taxi driver (Maguire et al., 2000). This suggests that taxi drivers have better navigation related structures in their brains and that they do improve and change as they work longer as a taxi driver.

Very little research has investigated individual differences in neuroplasticity. It is widely observed that the brain is most plastic during childhood and then the plasticity decreases with age. However, very little is known if people have higher plasticity compared to others due to gender, the environment they grew up in, genetics, or the activities they participate in.

Difference Between Women and Men

There is a substantial amount of research that points to neural differences between the sexes; however, a conclusive answer based on the structure and function of the brain has not been found for these differences (Eliot, 2013). Other research suggests the outcomes are not very different between women and men and that sex-difference research has a history of studies having weak statistical power and a misinterpretation of the results as well as other errors that lead to a deceptive understanding of sex-differences (Eliot, 2019). There is also publication bias because many studies that did not find a significant difference between women and men are not published leading to the idea that there is a difference when there may not be (Eliot, 2019).The term *neurosexism* has become popular to explain this idea that there are strict differences between the female and male brain, and this leads to a bias in how studies are conducted, and how results are interpreted. This information is then absorbed by the media and can have detrimental effects on our understanding of the complexity of gender differences (Fine, 2013). Fine (2013) did an analysis of functional magnetic resonance imaging (fMRI) research that investigated sex differences and found that the current literature is biased to show that there are sex differences in the brain that are fixed and unchanging because of false-positive claims, interpretations based on stereotypes, and lack of attention to the possibility of plasticity in the brain and mind.

There is a large-scale debate about the extent of neural differences between men and women and previous studies are divided on which sex has the worst outcome after TBI (Giordano et al., 2020). Farace and Alves (2000) found that in 85% of their measures, women scored worse than men after a TBI; however, the clinical opinion at the time was that men tend to have a worse outcome than women.

Current Study

The current study is a meta-analysis of the differences in neuroplasticity between women and men after a TBI. Research on the differences in neuroplasticity between men and women is relatively new and few studies have reported outcome variables by gender after TBIs (Farace & Alves, 2000). Based on the findings from a meta-analysis done by Farace and Alves (2000) we hypothesized that women would have a worse outcome than men after a TBI. Learning more about these differences can give scientists and clinicians more information on how to better treat people with brain injuries as well as a better idea of whether there are sex-differences in how plastic the brain is.

Method

Literature Search

A literature search was conducted by using PsycINFO and manual search. Search terms were combinations of *Human Sex Differences, Traumatic Brain Injury, Human Females,* and *Health Outcomes.* There were 382 hits for the search after duplicates were removed. Because of a lack of time, a search for unpublished data was not conducted, nor was a search through conference programs, but ideally, this data would also have been included. The sample size, mean, standard deviation, outcome variable, outcome measure, sex of the participants, and sample characteristics were recorded for each article. See Table 1 for further details on each article.

Inclusion and Exclusion Criteria

To be included in the current study, the studies would have to specify the sex of the participants, include an outcome variable, and the participants will have to have had a traumatic brain injury. Studies also had to separately report the means and standard deviations for both the female and male participants. There were no restrictions on the severity of the injury. The outcome variables had to be measured after the TBI and have at least three different samples of participants in order to be included in the current study. There were no criteria on when the dates of the studies were published. Studies did not have to include both female and male participants however all of the studies that were included did happen to do this.

Outcome Measures

Trails A and B and the WCST have been found not to have a difference in scores based on gender (Tombaugh, 2004; Shan et al., 2008). Some studies have found gender differences in performance on the grooved pegboard; however, other studies have found that differences in gender did not affect the participants' performance (Lafayette Instrument Company, 2015).

Trails A and B

The Trail Making Test (TMT) was originally part of an individual test battery for the army in 1944 and was later added into the Halstead-Reitan Battery (Tombaugh, 2003). The TMT is split into two parts (A and B). Both parts have 25 circles separated on the paper. In trails A, the circles are labeled 1-25 and the participants have to draw a line to connect the numbers in order from 1 to 25. In trails B, the circles are labeled with numbers (1-13) and letters (A-L) and the participants have to draw a line that alternates between numbers and letters (1-A-2-B-3-C, etc.). The participants are timed during these tasks and any errors are pointed out and the patients must correct the error before moving on. Higher times indicate scoring worse. On average, trails A takes 29 seconds with anything over 78 seconds indicating impairment and trails B takes generally 75 seconds with anything over 273 seconds indicating impairment. Trails A measures attention and Trails B measures mental flexibility as it requires the ability to alternate between different types of stimuli (Salthouse, 2011; Salthouse et al., 2000).

Wisconsin Card Sorting Test

The Wisconsin Card Sorting Test (WCST; Grant & Berg, 1948) is used as a measure for executive functioning. The participants are given four reference cards with differing stimuli color (red, blue, green, or yellow), shape (triangle, circle, square, cross), and number (1, 2, 3, or 4). Participants then have to match cards to the reference cards and are not given instructions on how they need to be matched and are only told if they are correct or incorrect. In this study the preservative responses were used. Preservative error is when participants continue to use the same response strategy after there is a rule switch. This is due to the error in inhibiting a dominant response. The greater the score the more errors were performed and thus a worse outcome.

Glasgow Coma Scale

The Glasgow Coma Scale (GCS) was first published by Teasdale and Jennett in 1974 in order to have a way to measure TBI severity (Savitsky et al., 2016). The GCS measures responsiveness of motor functioning, eye movement, and verbal response or the level of consciousness of a patient (Savitsky et al., 2016). See Table 2 for the criterion and the points given based on the response. The more responsive the patient the higher the GCS score will be and the less severe the injury is classified. The GCS then categorizes the patient by severity with mild scoring between 14-15, moderate between 9-13, and severe 3-8 (Savitsky et al., 2016). The GCS has a high level of inter-observer reliability for trauma patients (Savitsky et al., 2016).

Grooved Pegboard

The Grooved Pegboard (GPB; Lafayette Instrument Company, 2015) measures motor functioning. The pegboard has multiple holes with different shapes and the participants are instructed to move pegs into the holes that match their shape. Only one peg can be picked up at a time and the test starts by just using the participant's dominant hand and is completed again with their non-dominant hand. The length of time it takes the participant to place all of the pegs is recorded and the longer the time the worse the score.

Results

The current study used a random-effects model because it is assumed that the true effect is different across studies. This is due to the fact that there are different populations of people, and it is extremely unlikely that the true effect would be the same for all of the studies included. See Table 3 for further information regarding the results of the meta-analysis.

Executive Functioning

Two studies (k) were used for the WCST with 5 different samples. The total $N = 1,333$ with 341 being females. Between women and men there was a $MD = 2.11$ with a 95% confidence interval of -3.90 to -.32. There was a significant difference between women and men (*p* = .021) with men (*M* = 41.01) scoring higher than women (*M* = 35.20). A chi-squared test of independence was conducted to examine heterogeneity. *Q(*df) = 3.037 (4) with *p* = .55 indicating that there is not a significant difference in heterogeneity therefore there is little variation in the study outcomes between the studies. The level of heterogeneity was low (I^2 = 0.00) meaning <1% of the total variation across the studies was due to real heterogeneity and not due to chance. This indicates that there is potentially a common effect size that is representative of the true effect found in the population.

Attention

Four studies (*k*) were used for Trails A with 7 different samples and the total *N* = 1,922 with 513 being females. Between women and men there was a *MD* = 1.01 with a 95% confidence interval of -1.70 to -.32. There was a significant difference between women and men (*p* = .004) with men (*M* = 58.03) scoring higher than women (*M* = 52.42). A chi-squared test of independence was conducted to examine heterogeneity. *Q(*df) = 9.246 (6) with *p* = .16 indicating that there is not a significant difference in heterogeneity therefore there is little variation in the study outcomes between the studies. The level of heterogeneity was moderate (I^2 = 35.107) meaning 35.107% of the total variation across the studies was due to real heterogeneity and not due to chance. This indicates that there is potentially a common effect size that is representative of the true effect found in the population.

Motor Functioning

Three studies (*k*) were used for GPB with 6 different samples and the total *N* = 1,671 with 406 being females. Between women and men there was a *MD* = .56 with a 95% confidence interval of -1.39 to .27. There was not a significant difference between women and men (*p* = .185). A chi-squared test of independence was conducted to examine heterogeneity. *Q(*df) = 5.133 (5) with *p* = .40 indicating that there is not a significant difference in heterogeneity therefore there is little variation in the study outcomes between the studies. The level of heterogeneity was low (I^2 = 2.586) meaning 2.586% of the total variation across the studies was due to real heterogeneity and not due to chance. This indicates that there is potentially a common effect size that is representative of the true effect found in the population.

Level of Consciousness

Four studies (*k*) were used for GCS with 4 different samples and the total *N* = 4,237. Between women and men there was a *MD* = .09 with a 95% confidence interval of -.28 to .11. There was not a significant difference between women and men (*p* = .379). A chi-squared test of independence was conducted to examine heterogeneity. *Q(*df) = 2.257 (3) with *p* = .52 indicating there is not a significant difference in heterogeneity therefore there is little variation in the study outcomes between the studies. The level of heterogeneity was low (I^2 = 0.00) meaning <1% of the total variation across the studies was due to real heterogeneity and not due to chance. This indicates that there is potentially a common effect size that is representative of the true effect found in the population.

Cognitive Flexibility

Five studies (*k*) were used for Trails B with 8 different samples and the total *N* = 1,835. Between women and men there was a *MD* = .98 with a 95% confidence interval of -1.96 to -.003. There was a significant difference between women and men (*p* = .049) with men (*M* = 129.16) scoring higher than women (*M* = 115.38 A chi-squared test of independence was conducted to examine heterogeneity. *Q(*df) = 7.535 (7) with *p* = .38 indicating there is not a significant difference in heterogeneity therefore there is little variation in the study outcomes between the studies. The level of heterogeneity was low ($I^2 = 7.097$) meaning 7.097% of the total variation across the studies was due to real heterogeneity and not due to chance. This indicates that there is potentially a common effect size that is representative of the true effect found in the population.

Publication Bias

Due to the small number of studies, the funnel plots may not be a reliable way to test for publication bias. Publication bias did show up in the funnel plots for any of the relationships however it is hard to determine if this is due to the small number of studies or because there is a lack of publication bias. See Figures 1-5 for the publication bias funnel plots.

Discussion

I expected that women would have scored worse on the outcome measures and would therefore have less neuroplasticity than men. However, men actually scored worse than women on the Wisconsin Card Sorting Test, Trails A, and Trails B reflecting less neuroplasticity for executive functioning, attention, and cognitive flexibility. There was not a significant difference in scores on the Grooved Pegboard and the Glasgow Coma Scale which measured motor functioning and level of consciousness. My findings did contradict the findings of Farace and Alves (2000) however the research investigating gender difference in TBI outcome is very contradictory and there are no large-scale conclusive studies that have been completed thus far due to the lack of research and specifications of gender. The lack of congruency between studies and meta-analyses could be because of the poor research that has been done previously relating to gender differences or due to a lack of research and understanding towards individual differences and neuroplasticity. There is the potential that individual differences in neuroplasticity are due to differences in behavior rather than due to biological differences.

This leads into the nature versus nurture debate. How much of the differences in who we are as a person are predetermined by our biology and how much of these differences are because of our environment? Current research investigating individual differences in TBI outcome has a focus on differences in "nature" such as strict biological sex differences however individual differences in outcome may be better understood looking through a lens of "nurture" and how behavior and environment effect the brain.

We change how we behave based on the environment that we are in and the people we are with. This can be seen in the phenomenon called code switching. Code switching is when a person changes how they speak (for example, they may speak formally at work but when they are hanging out with friends, they will use slang and speak informally) when they are around certain people or in a certain environment. This also is reflected in behavior. People will change their behavior based on what situation they are in in order to "fit in with the crowd". This can be seen in the experiment done by Tanner Kent in 2011 where they had confederates stand in an elevator with a participant (Blogspot.com, 2016). In one part of the study, they had the confederates all stand facing the sides of the elevator rather than standing facing the door of the elevator as is typical. The participants would appear confused at first but would change to stand the way the confederates were standing. This study was a replication of a prank that aired on a popular hidden camera show called Candid Camera in 1962 (Blogspot.com, 2016). This prank was based on conformity research done by Asch in the 1950s (Blogspot.com, 2016).

We change how we behave based on what type of person we believe we are and what type of person we need to act like in the given situation. Therefore, stereotypes and preconceived notions about how a man or a woman should behave can impact how we act in certain situations. Our behavior can change our brains like with taxi drivers' brains mentioned previously being different from the average driver's brains. This has also been investigated in learning a second language. Studies investigating the effects of bilingualism and learning another language on neuroplasticity have found results pointing to increasing plasticity in areas of the brain related to language while participants were learning another language (Bubbico et al., 2019). There are differences in our brains because of the regular behaviors we do, and this could ultimately play a factor in how our brains operate and change to accommodate for head injuries.

Limitations

One limitation of the current study was the small number of articles that were included. Due to time constraints, unpublished data was not included as it would have been difficult to acquire, but ideally unpublished data would have been included to give a more realistic idea of the differences in outcome after TBIs between women and men. Studies in other languages were also not included because of the difficulty in translating. There was also a lack of different databases used to find articles. Because of this some articles could have been missed that would have met the inclusion criteria. Finding more studies through various databases and unpublished data should help combat any potential issues with publication bias as well.

Another limitation to consider is that this study separates gender as women and men, but many people do not identify as women and men. This is a limitation in most gender differences research and could potentially have an effect on what kinds of people are participating in these types of studies and how people are responding to the demographic information related to gender. Future studies looking into gender differences may want to consider investigating the effects of masculinity versus femininity to combat this issue.

Future Directions

A large-scale meta-analysis is necessary to get a better idea on if there is a difference in neuroplasticity between women and men. More research is also necessary to investigate this idea further, and researchers need to report the gender of their participants to help in this endeavor. For future studies, it would be beneficial to include unpublished articles and articles that are in different languages. Searching through conferences programs and more databases will also help in finding more studies that investigate the differences in neuroplasticity between women and men after a TBI. Investigating this relationship through a non-dichotomous lens related to gender could also offer interesting results. Investigating femininity versus masculinity may offer a different perspective on individual differences in neuroplasticity.

Future studies should also investigate differences in what kinds of people are getting TBIs and how what they do could potentially affect how well they recover afterwards. For example, is the difference really between football players and soccer players rather than female athletes and male athletes? The inconsistencies in previous studies could be due to this rather than there actually being differences between women and men. A more diverse and larger meta-analysis addressing the limitations in the current study would allow for a better understanding of differences in neuroplasticity between women and men after a TBI. Future studies should also consider the impact differences in behavior may have on neuroplasticity over biological individual differences like gender.

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Table 1
Summary of studies included in meta-analysis

Study	N	Outcome variables	Outcome measure	Sample characteristics
Bounds et al. (2003)	F =23 M=55	Attn, Cog Fl, MF	Tr A, Tr B, GPB	Missouri residents who were provided services by the Missouri Division of Vocational Rehabilitation
Johnson et al. (1996)	F=66 M=31	LoC	GCS	From the TBI research program at a Level I trauma center (LDS Hospital, Salt Lake City, Utah)
Kokkinou et al. (2020)	F=40 M=163	LoC	GCS	Adult patients who spoke Greek or English with moderate-to-severe TBI admitted int eh ICU during the target period
Liossi & Wood (2009)	F=75 M=75	LoC, Attn, Cog Fl	GCS, Tr A, Tr B	Patients referred between Jan. 2001 and Dec. 2004 to Swansea University Head Injury Clinic
Niemeier et al. (2007)	F=1023 M=2764	LoC	GCS	Rehabilitation inpatients between the ages of 18 and 49 with TBI admitted to level I trauma centers between 1989 and 2002
Niemeier et al. (2013)	F=315 M=1054	Attn, Cog Fl, MF, Exec Func	Tr A, Tr B, GPB, WCST	Rehabilitation inpatients between the ages of 18 and 49 with TBI admitted to level I trauma centers between 1989 and 2002
Ratcliff et al. (2007)	F=100 M=225	Attn, Cog Fl, MF, Exec Func	Tr A, Tr B, GPB, WCST	Patients from the TBI Model Systems of Care National Database (TIBMS) between 1990 and 2002
Rigon et al. (2016)	F=25 M=28	Cog Fl	Tr B	Patients were recruited through ads and brain injury units in Iowa City, IA and Madison, WI

Note. F = Females, M = Males, LoC = Level of Consciousness, MF = Motor Functioning, Attn = Attention, Cog Fl = Cognitive Flexibility, Exec Func = Executive Functioning, Tr A = Trails A, Tr B = Trails B, GCS = Glasgow Coma Scale, GPB = Grooved Pegboard, WCST = Wisconsin Card Sorting Test

Table 2
GCS Criterion and Points Given

Criterion	Points Given
Eye-Opening	
Eye-opening spontaneously	4
Eye-opening to sound	3
Eye-opening to pain	2
No response	1
Verbal Response	
Orientated	5
Confused conversation	4
Inappropriate words	3
Incomprehensible sounds	2
No response	1
Motor Response	
Obeys command	6
Localizes to pain	5
Withdraws to pain	4
Flexion decorticate posture	3
Abnormal extension decerebrate posture	2
No response	1

Note. Information collected from Yousuf (2021); Points are totaled from each Criterion to make to final score; Scores range from 3 to 15

Table 3
Meta-analytic results for each outcome variable

	k	Total *N*	*MD* (95% CI)	*Q* (*df*)	I^2
Level of Consciousness					
Females	4	1,204	.09 (-.28, .11)	2.26 (3)	0.00
Males	4	3,033			
Motor Functioning					
Females	3	406	.56 (-1.39, .27)	5.13 (5)	2.59
Males	3	1,265			
Attention					
Females	4	513	1.01* (-1.70, -.32)	9.25 (6)	35.11
Males	4	1,409			
Cognitive Flexibility					
Females	5	509	.98* (-1.96, -.003)	7.56 (7)	7.10
Males	5	1,326			
Executive Functioning					
Females	2	341	2.11* (-3.90, -.32)	3.04 (4)	0.00
Males	2	992			

Note. * $p < .05$; Q = Cochran's Q statistic for heterogeneity; I^2 = the amount of the observed variance that is due to true differences in effect size

Figure 1. Funnel plot for GCS

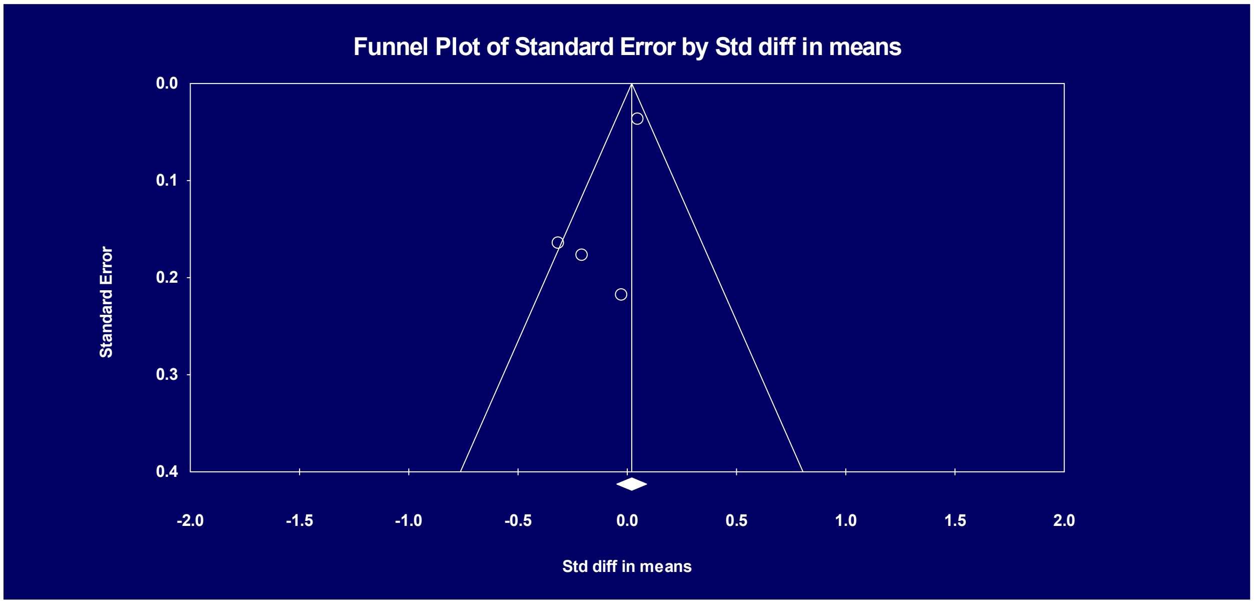

Figure 2. Funnel plot for GPB

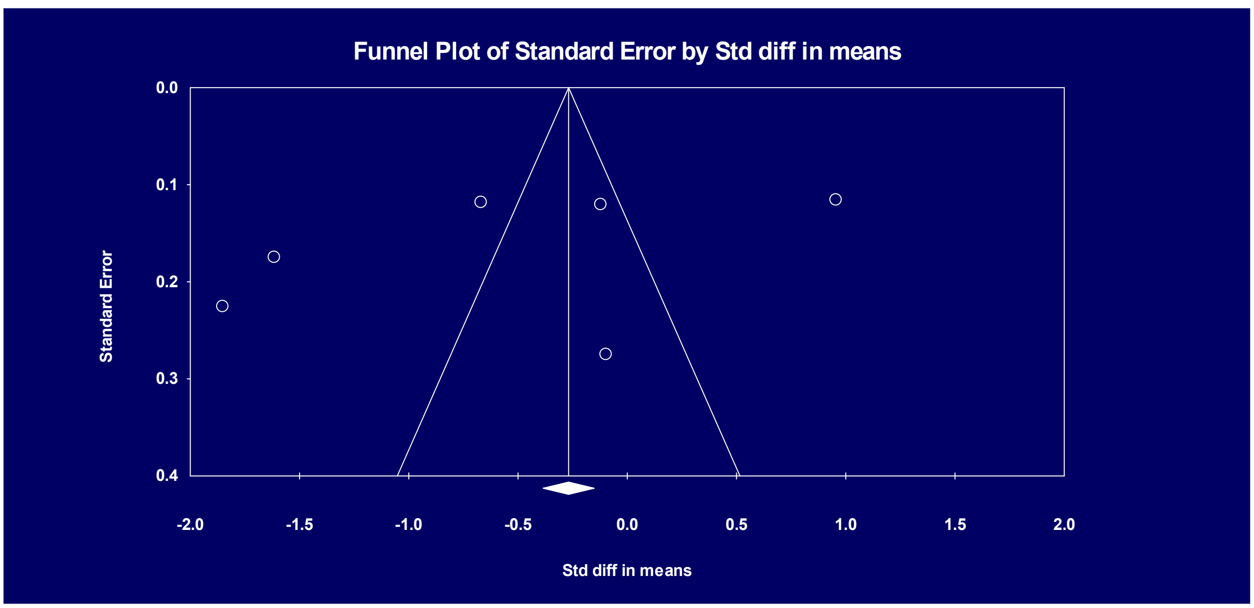

Figure 3. Funnel plot for Trails A

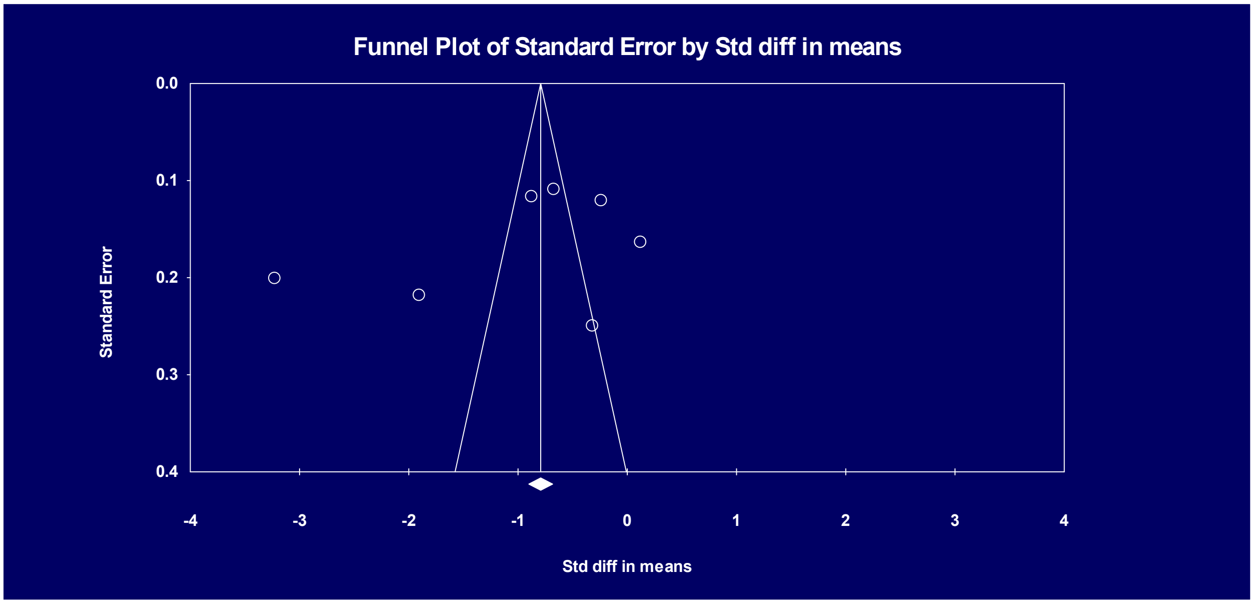

Figure 4. Funnel plot for Trails B

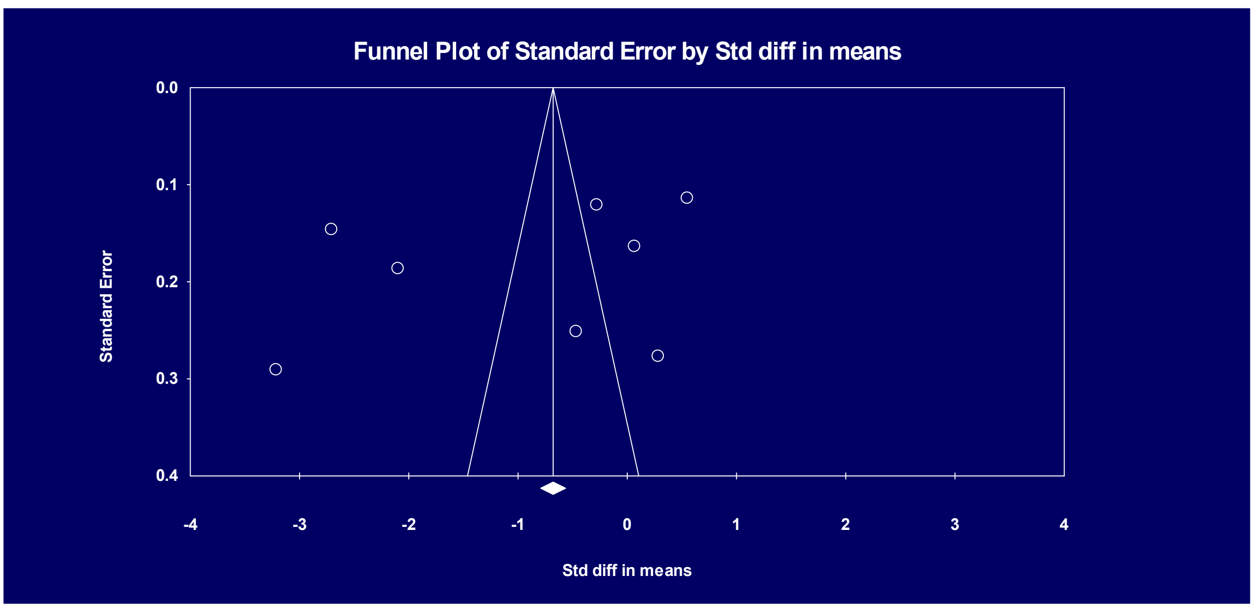

Figure 5. Funnel plot for WCST