A systematic review of the benefits of Mindfulness-Based Interventions following transient ischaemic attack and stroke.

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A systematic review: mindfulness and TIA/stroke

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Introduction

Worldwide, stroke is the second most common cause of death (1) and a leading cause of long-term adult disability (2). In 2005, the global prevalence of living stroke survivors was estimated at 62 million; it is expected to rise to 77 million by 2030 (3). The absolute number of strokes is predicted to rise in response to demographic changes in the population and increased numbers of very old people. People experiencing first stroke or transient ischaemic attack (TIA) are at significant risk of subsequent stroke; 30-40% of people will have a further event within 5 years (4), which highlights the potentially wide window of opportunity for secondary prevention. As with all vascular disease, a person’s risk of stroke following TIA can be reduced using a range and variety of approaches, which include lifestyle interventions and behavioural changes (5,6). Traditionally acknowledged vascular risk factors only explain half of cerebrovascular disease risk (7) and there is a lack of attention paid to the potential role of psychosocial factors including perceived stress in the development of stroke disease (8). A growing body of scientific evidence confirms the association between psychological stress and the development of acute myocardial infarction (9-11) however such research is minimal in the area of stroke and TIA. Yet public perception highlights psychological stress as a key risk factor for stroke (12,13). The few studies that relate to stroke have reported severe self-perceived stress, stressful life events and poor adaptation to stress to be independently associated with increased risk of stroke (8,14-16), in particular fatal stroke (9,17).
Recent research in Scotland on multimorbidity using primary care data has found that in a nationally representative sample of 1.8 million people, only 6% of patients with stroke had no other long-term condition (18) and 64% had 3 or more other long-term conditions. Although one would expect comorbidity of stroke with other vascular conditions, 22% of stroke patients in the above study also had chronic pain, and 21% depression. Following stroke, systematic review evidence indicates that 33% of stroke survivors experience depression (19); rates for anxiety are 20% - 25% (20). Both depression and anxiety remain common several years after the initial stroke event (19,20).

**Mindfulness-based Interventions**

Mindfulness Based Interventions (MBIs) i.e. Mindfulness-Based Stress Reduction (MBSR) and Mindfulness-Based Cognitive Therapy (MBCT), which derive from ancient, eastern philosophies, are increasingly being offered as therapeutic interventions in contemporary clinical psychotherapeutic settings (20). MBSR is a structured, group-based self-management programme with potential to help people with long-term conditions to cope better with physical and psychological or emotional distress. Reviews across a range of physical and mental health problems suggest significant benefits of MBSR (21-24). A meta-analysis of 39 studies (25) reported large effect sizes (0.97, 0.95) for anxiety and depression. A systematic review (26) of MBSR specifically for people with long-term conditions found benefits in all 15 included studies including: enhanced ability to cope with symptoms; improved well-being; quality of life; and better health outcomes. The review suggested that MBSR has the potential for much wider application in primary care. Although the precise mechanism of action of mindfulness-based interventions is not known, increased
mindfulness appears to mediate improvement in functioning by reducing rumination and emotional avoidance and improving behavioural self-regulation (27). The standard format for MBSR is a sequence of eight weekly 2.5 hour classes with a 6 hour all-day class in week 6 (total of 26 hours class time). However, there is no theoretical or empirical basis for this time-intensive format, and a recent review found effect size to be unrelated to number of in-class hours (28). MBCT is a form of psychological therapy which aims to aid the prevention of relapse of depression. It blends features of cognitive therapy with the mindfulness techniques described above (29). A study of recovered recurrently depressed patients found that relapse rates were reduced by 50% (29).

Recent economic trends mean that health providers are looking for innovative ways of delivering clinically effective services that are cost effective or cost-neutral. MBIs i.e. MBSR and MBCT use minimal resources and therefore are inexpensive to deliver, they can be delivered in a range of settings, including community-based locations, and following the initial eight week course, individuals can practice mindfulness independently, without support from rehabilitation services. Potential benefits are wide-ranging. Physical and psychological health benefits include improved glycaemic control in individuals with type 2 diabetes mellitus (30), alleviation of emotional distress in diabetes (31), alleviation of depression in individuals with cardiac disease (32) and diabetes (33), alleviation of anxiety and reduction in levels of perceived stress in a range of conditions including heart disease, cancer, anxiety and depression (25,34). Thus, given the high prevalence of comorbidity, in particular depression and anxiety disorder (18-20), amongst stroke patients, mindfulness-based interventions are potentially relevant therapeutic
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interventions, offering a range of health benefits including alleviation of perceived psychosocial stress.

**Why it was important to do this review**

Emerging evidence, demonstrates an association between self-perceived psychological stress and ischaemic stroke (35). A recent large scale epidemiological study found evidence of stress as an independent risk factor for stroke (36). As described above, a feature of stroke is recurrence, and people experiencing first stroke or TIA are at significant risk of subsequent stroke (4). Therefore, equipping patients with skills and coping strategies to help reduce or manage perceived psychological stress, may represent an important secondary prevention intervention. Scoping searches undertaken in Mindfulness Research Monthly (www.mindfulexperience.org), the Database of Abstracts of Reviews of Effectiveness (DARE), the Cochrane Database of Systematic reviews and the JBI (Joanna Briggs Institute) Library of Systematic Reviews failed to identify a relevant systematic review. Therefore we conducted a systematic review that aimed to evaluate the benefits of mindfulness-based interventions as therapeutic interventions following stroke/TIA.

**Methods**

**Selection criteria**

To enable the identification and selection of the best available evidence regarding the therapeutic benefits of MBIs following stroke/TIA, we determined inclusion criteria relating to Study design, Participants, Interventions and Outcomes (SPIO) (Box 1). SPIO is an adaptation of the PICO (Population, Interventions, Comparison,
Outcomes) framework which is commonly used to define the parameters of systematic reviews where designs other than randomised controlled trials (RCTs) are also considered (37).

A broad definition of stroke was adopted, to include ischaemic stroke, haemorrhagic stroke, subarachnoid haemorrhage and TIA (38). As with many other mind-body interventions, mindfulness as a therapeutic intervention is inherently varied and heterogeneous, therefore different forms, duration and frequency of mindfulness-based interventions were included (28).

**Search strategy**

In April 2012 a systematic search for published and unpublished studies was conducted in six major electronic bibliographic databases: Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, CINAHL, AMED (Allied and Complementary Medicine Database) and PsycInfo. To identify any additional published and/or unpublished trials, we also searched ProQuest Dissertations & Theses Database and contacted stroke/mindfulness researchers. Selected medical subject headings (MeSH) were combined with keywords relating to stroke and mindfulness to create a search strategy which was finalised for use in MEDLINE (appendix 1) and amended for use in the other databases, using appropriate controlled vocabulary, Boolean operators and search symbols. Delimiters were: dates searched (1980 – 2012); research subjects (human); and language (English). RefWorks was used to store and manage the results of the database searches.
Selection of papers for inclusion

The bibliographic records identified by the searches were screened for relevance using broad inclusion criteria i.e. ‘stroke’ and ‘mindfulness’. All relevant papers were then screened, using the SPIO inclusion criteria (Box 1), to select eligible papers. All selected papers were subject to methodological appraisal. To reflect the range of study designs permissible within the inclusion criteria, a range of standardised critical appraisal checklists were selected for use in this review. The Scottish Intercollegiate Guidelines Network (SIGN) checklist for randomised controlled trials grades evidence as: ++ where All or most of the criteria have been fulfilled. Where they have not been fulfilled the conclusions of the study or review are thought very unlikely to alter; + Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought unlikely to alter the conclusions; and - Few or no criteria fulfilled. The conclusions of the study are thought likely or very likely to alter (39). The Joanna Briggs Institute’s (JBI) Comparable cohort/case control studies checklist (40) scores studies using nine methodological criteria; the Newcastle-Ottawa Quality Assessment scale uses ten methodological criteria to assess cohort studies (41).

Due to the paucity of available evidence, no papers were excluded on the grounds of quality. However, methodological issues are discussed below and reported in the evidence table.

Data extraction

Data, including details of study design and methods, interventions (delivery and content), populations, and primary and secondary outcomes, were extracted from
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papers using a data extraction tool developed by the authors. All screening and assessment processes were conducted by two reviewers (ML and JB) who worked independently and then met to discuss and agree the outcomes; any disagreements were resolved consensually.

**Data synthesis**

Due to the heterogeneous nature of the papers included in the review, meta-analyses were not possible; therefore the review findings are presented in narrative form.

**Results**

The database searches retrieved 1,509 unique bibliographic records. Using the screening methods described above, three papers were found to be eligible for inclusion in the review (see figure 1). One additional paper (42), which reported an MSBR intervention evaluated with a mixed population i.e. stroke and traumatic brain injury was identified from a subsequent eTOC (electronic Table of Contents) alert. We contacted the author who conducted additional analyses and provided us with ‘stroke only’ data; therefore 4 papers were included in the final stage of the review: Johansson *et al.* (42), Magnusson *et al.* (43), Joo *et al.* (44) and Moustgaard *et al.* (45). To enable comprehensive completion of data extraction forms, we requested additional information from the authors. No response was received from two authors; however we were provided with a full-text copy of Moustgaard’s thesis (46) which enabled us to complete the data extraction for the associated paper.

*[Insert figure 1 about here]*
Study characteristics

Johansson et al. (42) reported a wait-list RCT, Magnusson et al. (43) reported a case-control study, and Joo et al. (44) and Moustgaard et al. (45) reported case series. The key characteristics of the studies, including study design, aim, setting, population, intervention design and delivery, and primary and secondary outcomes, are presented in the evidence table (table 1). The studies were conducted in four different countries i.e. Sweden (42), Korea (44), Denmark (43) and Canada (45). Johansson et al. (42) and Moustgaard et al. (45) recruited participants who had had a stroke from the general population. Joo et al. (44) recruited participants who were more than six months post-surgery for cerebral aneurysm rupture; it is not clear where they were recruited from, but it is likely that they were recruited from a clinical setting. Magnusson et al. (43) recruited participants who had had a stroke; it is not clear where they were recruited from, but it is likely that they were identified from a clinical database.

[Insert table 1 about here]

Methodological quality of included papers

In terms of methodological quality, the study by Johansson et al. (42) was graded as being of mid-level (+) quality i.e. Some of the criteria have been fulfilled. Those criteria that have not been fulfilled or not adequately described are thought unlikely to alter the conclusions (39). However, the quality of the other three studies was poor. Moustgaard et al. (45) and Joo et al. (44) both scored 3 out of a possible 9 on the JBI Comparable cohort/case control studies checklist. Magnusson et al. (43) scored only 2 stars (out of a possible 10) on the Newcastle-Ottawa assessment
scale. Particular methodological issues were small sample sizes, attrition rates and issues of generalisability. Attrition rates were 24% (n=7) in the study by Johansson et al. (2012), 23% (n=7) in Moustgaard et al.’s study (45), and 61% (n=17) in the study by Joo et al. (44). However, intention to treat analysis was not conducted in these three studies. In terms of generalisability, Joo et al.’s (44) intervention was delivered only to participants who had had an aneurysmal subarachnoid haemorrhage (SAH); SAH accounts for < 5% of all strokes (47).

**Outcomes**

None of the studies reported perceived stress, our primary outcome of interest. In one study (Johansson et al 42), sensitivity to stress was a single item in the 13 item Mental Fatigue Scale and no change in individual scores was reported. However all studies did report secondary outcomes of interest, including other psychological outcomes i.e. anxiety, depression and mental fatigue, as well as physiological outcomes i.e. blood pressure, and psychosocial outcomes i.e. perceived general health and quality of life.

**Intervention characteristics**

Johansson et al. (42), Joo et al. (44) and Moustgaard et al. (45) delivered ‘typical’ MBSR interventions (as described above). Moustgaard et al. (2007 Moustgaard et al. 45), who used a cognitive behavioural therapy approach (MBCT), described their intervention as being adapted to suit the ‘physical and emotional’ needs of people who have had stroke. Magnusson et al. (43) delivered an Integrated Rehabilitation Program, which incorporated key elements of MBSR e.g. meditation, relaxation and
awareness exercises; it is not clear how this was delivered; however is likely that this was delivered on a one-to-one basis. All four interventions were of short duration. Both Johansson et al. (42) and Joo et al. (44) delivered their interventions weekly for eight weeks in 2½ hour sessions, and collected follow-up data directly after the intervention. Moustgaard et al. (45) delivered their intervention weekly over nine weeks, in 1¾ hour sessions; follow-up data were collected at 10 days post-intervention and again three months post-intervention. Magnusson et al. (43) delivered their intervention in 15 sessions (mean). They aimed to deliver the first 10 sessions within the first month of the intervention and collected observational data at a single but unspecified time point.

**Participant characteristics**

Review data were extracted from four papers, which included four completed studies with 160 participants (baseline). Johansson et al. (42), Joo et al. (44) and Moustgaard et al. (45) reported participant characteristics for completers only (table 1). The age and gender of participants is presented in table 2. Notably, participants were young if compared with the general stroke population; the mean age for acute stroke in Western countries is approximately 75 years (48).

[Insert table 2 about here]
Psychological outcomes

Depression

Moustgaard *et al.* (45) measured depression using the Beck Depression Inventory, Revised (BDI-II) and HADS, and Johansson *et al.* (42) used the Comprehensive Psychopathological Rating Scale (CPRS). Moustgaard *et al.* (45) reported that all BDI-II scales demonstrated a reduction in the number of depressive symptoms endorsed at post-test and follow up, than at pre-test. The HADS depression score demonstrated an overall improvement between pre-test and post-test, which was maintained at three-month follow up and was statistically significant (table 3). Johansson *et al.* (42) reported no significant differences in CPRS for depression outcomes between the MBSR groups and control or on repeated measures testing in the intervention group (table 4), however as was the case for anxiety the sample size was very small and the study underpowered, which the authors felt explained the results.

[Insert tables 3 and 4 about here]

Anxiety

Joo *et al.* (44) measured anxiety using the State-Trait Anxiety Inventory (SAI) and the Trait Anxiety Inventory (TAI); Moustgaard *et al.* (45) measured anxiety using the Hospital Anxiety and Depression Scale (HADS) and the Beck Anxiety Inventory (BAI). Johansson *et al.* (42) measured anxiety using the Comprehensive Psychopathological Rating Scale (CPRS).
Joo et al. (44) reported a reduction in state anxiety and trait anxiety, the latter having borderline significance, thus demonstrating a trend towards a reduction in anxiety following the eight-week MBSR course (table 5). Moustgaard et al. (45) reported a significant reduction in the BAI total score between pre-test and three-month follow-up, but not between post-test and three-month follow-up. The HADS anxiety score demonstrated an overall improvement between pre-test and post-test, which was maintained at three-month follow-up and was statistically significant. Johansson et al. (42) reported no significant differences in CPRS for anxiety outcomes between the MBSR groups (n=2) and (waitlist) control, or on repeated measures testing in the intervention groups (table 6), however the sample size was small and the authors felt the results were due to a type II error.

Mental fatigue

Johansson et al. (42) measured mental fatigue using the Self-assessment of Mental Fatigue (SMF). They reported reduced self-reported mental fatigue in both intervention groups following the MBI, one of which was significant (table 7).

Physiological outcomes

Blood pressure

Only Joo et al. (44) measured change in blood pressure. They reported a reduction in systolic and diastolic blood pressure following the eight-week intervention; neither result was statistically significant (table 8).
Psychosocial outcomes

Perceived general health and quality of life

Only Moustgaard et al. (45) measured perceived general health, using the Short-Form General Health Survey (SF-36) and quality of life, using the Stroke Specific Quality of Life Scale (SS-QoL). In general, the authors reported improvements in perceived general health and in quality of life which were maintained (table 9); however, there were some exceptions. Both subscales (physical component score (PCS) and mental component score (MCS)) of the SF-36 revealed improvement between pre-test and post-test which was maintained at three-month follow-up. In addition, the SSQoL total score, and most subscales, showed improvement at follow-up. Unexpectedly, the mobility scale and upper extremity scale scores revealed improvement between pre-test and three-month follow-up.

Discussion

To our knowledge, this is the first systematic review of Mindfulness-Based Interventions for TIA/stroke. A comprehensive search and subsequent screening identified only four eligible papers. Study designs were varied and participant numbers were small. Interventions tested included mindfulness-based stress reduction, mindfulness-based cognitive therapy and an integrated rehabilitation programme which incorporated elements of MBSR. The structured interventions were delivered to groups or in one-to-one sessions. None of the studies evaluated the effectiveness of mindfulness-based interventions on perceived psychosocial
stress, although one underpowered study found no change in sensitivity to stress on a single item score in a composite Mental Fatigue Scale. However, a range of psychological, physiological and psychosocial outcomes including anxiety, depression, mental fatigue, blood pressure, perceived health and quality of life were measured and, overall, the results demonstrate a positive trend in favour of the therapeutic benefits of mindfulness-based interventions. And, in addition to the psychosocial benefits of MBIs, perceived physical improvement, sustained over three months, was also noted in one, small study (45). Importantly, no evidence of harm was found, and no adverse events were reported.

As described above, there is a growing body of evidence which suggests an association between perceived psychological stress and TIA/ischaemic stroke although the explanatory mechanisms have yet to be fully identified. ‘Stress’ is widely perceived by members of the public to be a precursor to the onset of TIA/stroke (12,13) and furthermore is seen as a risk factor which is modifiable by the individual experiencing it (49). Therefore, incorporating education and training about how to cope with and manage psychosocial stress into multimodal interventions for the secondary prevention of stroke is likely to be of benefit and will do no harm.

Increasingly, the imperative to address psychological care needs of stroke survivors and their families is accepted as an essential aspect of acute stroke care and longer term rehabilitation (50). And while clinical guidelines recommend implementation of assessment processes and interventions designed to help people cope with and manage psychological problems following TIA/stroke (e.g. 51-53), the widespread lack of adequate resourcing of contemporary psychological care after stroke has been highlighted (54). Resourcing issues and sustainability are increasingly
important considerations, particularly in light of current economic austerity measures in the developed world and ongoing financial constraints in the developing world.

Mindfulness-based interventions are inexpensive to deliver, require little equipment or other resources, and are flexible in terms of delivery location (a space large enough to accommodate a group of ten people is all that is required). Following completion of the 8-week course, groups may become self-sustaining thus enabling participants to gain psychosocial benefits associated with peer support, and/or to continue to practise on their own.

**Strengths of this review**

To ensure that we had indentified all potentially revenant studies, our search strategy was broad and comprehensive, and included grey literature resources. And, acknowledging the paucity of evidence in the field, we extended our review inclusion criteria to include a range of experimental and non-experimental study designs, thus enabling us to draw on a wider evidence-base.

**Limitations of this review**

In terms of the search strategy, there is no subject heading for Mindfulness, however, we were able to compensate for this by using associated subject headings and appropriate key words. Also, due to resource constraints, we limited our review to studies published in the English language and therefore may have excluded other potentially relevant studies. In terms of the quality of the evidence generated by our review, we included all relevant studies, irrespective of methodological quality; however, this is common practice in reviews such as this, in which the included papers used a range of research designs, and measuring quality across
heterogeneous study designs remains an unresolved and contentious issue for reviewers and the subject of continuing debate

**Limitations of the included papers**
The studies included in the review were small and of poor methodological quality. We found only one trial and that had small numbers and a mixed neurological population. There was no evidence of sample size calculation, and the study was underpowered for stroke. Across the four studies, there was considerable heterogeneity relating to characteristics of the populations studied, outcomes measured, outcome measures, and intervention design and delivery, and therefore meta-analysis was not possible. Three studies used MBSR and one used MBCT, therefore we are unable to make distinction between these two forms of mindfulness-based interventions in relation to stress management following TIA/stroke. None of the studies had a longitudinal perspective so we are unable to determine the effectiveness of MBIs in the long-term. In light of these methodological limitations, the review findings should be viewed with caution.

**Implications for practice**
This systematic review demonstrates that MBIs may be beneficial in practice across a range of psychological, psychosocial and physical limitations induced by TIA/stroke and are unlikely to cause any harm. However, the paucity of evidence prevents an overt recommendation to incorporate MBIs into current practice.
Implications for research

Mindfulness-based interventions are amenable to standardisation. Large scale, methodologically robust, longitudinal trials of standardised interventions are required to determine the effectiveness of MBIs in relation to coping with and managing perceived psychosocial stress following TIA/stroke. To gain understanding of participants’ perceptions of the acceptability and relevance of MBIs, qualitative explorations are required. However, generating good evidence of the efficacy and acceptability of MBIs will only be the first step towards implementation, and issues regarding practitioner training and governance need to be resolved.

Conclusions

The evidence generated by this review suggests that there may be therapeutic benefit to be derived from mindfulness-based interventions following TIA/stroke. The review paves the way for further, longitudinal investigation of feasibility, effectiveness and acceptability of mindfulness-based interventions amongst diverse stroke populations.

[Word count: 3,873]

DECLARATIONS OF INTEREST

None

SOURCES OF SUPPORT

None
REFERENCES


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**TABLES AND FIGURES**

Table 1: Study characteristics and key findings

Table 2: Participants by number age and gender

Table 3: Depression: BDI-II; HADS

Table 4: Paired t-test p values for change in depression using CPRS

Table 5: Anxiety: SAI; TAI; HADS

Table 6: Paired t-test p values for change in anxiety using CPRS

Table 7: Paired t-test p values for change in mental fatigue using SMF

Table 8: Systolic blood pressure

Table 9: Perceived general health and quality of life

Box 1. Inclusion criteria: Study design, Participants, Interventions and Outcomes

Figure 1. Flowchart of study selection

**APPENDICES**

Appendix 1: Search String: MEDLINE with Full Text (EBSCOhost)
Appendix 1

Search String: MEDLINE with Full Text (EBSCOhost)

S1. (MM "Stroke+")

S2. (MM "Cerebrovascular Disorders+")

S3. (MM "Ischemic Attack, Transient")

S4. stroke

S5. cerebrovascular accident

S6. cerebrovascular disord*

S7. transient ischemic attack

S8. transient ischaemic attack

S9. minor stroke

S10. S1 or S2 or S3 or S4 or S5 or S6 or S7 or S8 or S9

S11. (MH "Meditation")

S12. (MM "Relaxation Therapy+") OR (MM "Relaxation+")

S13. (MM "Breathing Exercises")

S14. mindfulness

S15. meditation
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S16. relaxation

S17. breathing technique*

S18. breathing exercise*

S19. S11 or S12 or S13 or S14 or S15 or S16 or S17 or S18

S20. S10 and S19

S21. S10 and S19

S22. S10 and S19 Limiters - Date of Publication from: 19800101-20121231; Age Related: All Adult: 19+ years; Languages: English; Human