Management of behavioral and psychological symptoms of dementia (BPSD) by an aroma-massage with acupressure treatment protocol: a randomized clinical trial

ABSTRACT

Aims and objectives: This study evaluates the clinical effectiveness of a multi-component aroma-massage with an acupressure treatment protocol and compared it to cognitive training for the management of BPSD.

Background: Pharmacological interventions have been unsatisfactory in managing BPSD; thus, complementary and alternative medicine has been extensively researched to identify an adjunct safe and cost-effective intervention.

Design: This RCT utilized a three-arm parallel group design. Cognitive training was used as a conventional intervention to manage BPSD, whereas exercise was considered "treatment as usual" in this study; both were used as comparisons with the experimental protocol. There were three treatment groups: Group 1: aroma-massage with acupressure + exercise; Group 2: cognitive training + exercise; and Group 3: aroma-massage with acupressure + cognitive training.

Method: Sixty older adults were recruited and randomly assigned to the three groups (20 each). Using the 29-item Chinese Version of the Cohen-Mansfield Agitation Inventory, Neuropsychiatric Inventory, Mini-mental State Examination, and Barthel Index-20, the outcome measures were assessed at pre-intervention, post-intervention, and the 3-month follow-up to assess behaviour, ADL, cognition, and BPSD severity and distress. Multiple comparisons performed through repeated measures were analysed to detect between-group differences and within-subject differences, as well as the interaction effects between groups and times.

Results: The Group 1 and 3 participants showed a significant reduction in the severity and

distress caused by BPSD, whereas group 2 did not demonstrate similar effects.

Conclusions: This clinical study suggests that aroma massage with acupressure is as effective as cognitive training and can enhance cognitive training in reducing the severity and distress of BPSD.

Relevance to clinical practice: Aroma-massage with acupressure may serve as an adjunct therapy to reduce BPSD. This therapy is safe, cost-effective and can be implemented by caregivers and family members who are not professionally trained.

Keywords: essential oil, acupressure, therapeutic massage, agitation, dementia

WHAT DOES THIS PAPER CONTRIBUTE TO THE WIDER GLOBAL CLINICAL COMMUNITY?

- A multi-component intervention (aroma massage with acupressure) combining acupressure, aromatherapy, and therapeutic massage was developed. The intervention was observed to be safe and easily administered by non-professionals, including caregivers and family members with minimal training, as a long-term adjunct home intervention.
- Aroma massage with acupressure was found to significantly reduce the severity and distress of behavioural and psychological symptoms of dementia.
- Aroma-massage with acupressure has the potential to serve as an adjunct therapy in managing BPSD.

INTRODUCTION

Behavioural and psychological symptoms of dementia (BPSD) are defined by the International Psychogeriatric Association as "signs and symptoms of disturbed perception, thought content, mood, or behaviour that frequently occur in patients with dementia" (Finkel *et al.* 1997 p.1060). BPSD are commonly found in people with dementia (Cerejeira *et al.* 2012, Azermai 2015). These heterogeneous symptoms are distressing and difficult to manage for carers and health care professionals, thus placing a tremendous burden on family members, and often leading to institutional care (Herrmann *et al.* 2006).

The use of antipsychotics is the conventional approach for BPSD management (Greve & O'Connor 2005). However, the effects remain doubtful, as antipsychotics may increase the risk of falls, cerebrovascular accidents (Liperoti *et al.* 2009), and fatalities (Schneider *et al.* 2006). Therefore, there has been an interest in exploring non-pharmacological interventions, such as cognitive behavioural techniques (Fung *et al.* 2012) to treat individuals with BPSD.

Cognitive training aims to overcome age-related cognitive decline and has been extensively studied in people with dementia (Clare *et al.* 2010). It refers to interventions that provide structured practice on tasks relevant to different aspects of cognitive functioning, with a view to addressing cognitive function and/or cognitive impairment directly (Martin *et al.*, 2011). Several review and meta-analytical studies have reported the positive effects of cognitive training (Mayer *et al.* 2012, Alves *et al.* 2013, Bahar-Fuchs *et al.* 2013). Some researchers (Kraft 2012, Schneider & Yvon 2013) have reported that cognitive training would have a better effect in conjunction with physical activity. However, exercise on its own has been extensively reported to have positive effects on cognitive functioning and functional

mobility in healthy older adults (Colcombe & Kramer 2003, Forte *et al.* 2013).

Complementary and alternative medicine (CAM) is another option that has recently received much worldwide attention (Akhondzadeh & Moroozian 2002). Nurses and allied health professionals have increasingly used aromatherapy, acupuncture, and herbal medicine to reduce BPSD. As a result, there is a need for nurses and other allied health professionals to familiarize themselves with complementary and alternative medicine (Watson, 2008).

BACKGROUND

Aromatherapy has a long history of clinical application referring to the use of essential oils, due to their sedative properties, for people with severe dementia to reduce agitation (Holmes *et al.* 2002, Fung *et al.* 2012). It is a non-pharmacological approach that has been widely used to manage insomnia (Wolfe & Herzberg 1996), reduce behavioural disturbances (Fujii *et al.* 2008), and improve social engagement (Kermode & MacMahon 1998) in people with dementia. Through pharmacokinetics, essential oils penetrate the body through the olfactory systems, external skin, or the lining of orifices (Jäger *et al.* 1992, Buchauer *et al.* 1993) and then enter into the bloodstream. Lavender essential oil, through inhalation alone (Lin *et al.* 2007), will reach the brain through the bloodstream and then bind on the receptor sites for serotonin, which is considered to resemble neuroleptics (Louis & Kowalski 2002, Tsang *et al.* 2013), resulting in the effect of mediating emotional disturbances.

Acupressure is another non-invasive and safe intervention, when it is properly administered. It may be performed by professionals or carers who have received brief training. Yang *et al.* (2007) have studied acupressure using five acu-points on 31 people with dementia, and they found a significant reduction in verbal and physical attacks. Lin *et al.* (2009) conducted a large-scale RCT with 133 subjects to study the treatment effect of acupressure on the same five acu-points, combined with Montessori-based activities, on the

agitation of people with dementia; they reported a significant reduction in aggressive behaviour and physical non-aggressive behaviour. A combination of these two interventions (i.e., essential oil + acupressure) has constituted a popular, harmless, and effective approach for the treatment and management of BPSD (Yang *et al.* 2015).

Essential oils and therapeutic massage are non-invasive and safe, with minimal side effects. Both interventions may be used by carers under the supervision of qualified therapists (Fung *et al.* 2012). Therapeutic massage works on the integumentary system to improve circulation, on the musculoskeletal system to reduce muscle fatigue and on the lymphatic system to facilitate the flow of lymph. It may reduce stress, agitation, and restlessness (Lee *et al.* 2011). Together with aromatherapy, therapeutic massage has an alleviation effect on depression (Yim *et al.* 2009) and is the only method for people with dementia who cannot communicate to connect with other people (Hansen *et al.* 2006).

Interestingly there is evidence to show the positive outcomes of aromatherapy, acupressure, and therapeutic massage, when each treatment is clinically applied alone to manage BPSD. However, there is limited evidence to show the outcomes of these three interventions when they are combined for treatment use.

To test if the combination of aromatherapy, acupressure, and therapeutic massage works effectively for BPSD, the “aroma massage with acupressure treatment protocol” was developed. It is expected that this protocol is easily administered and has minimal adverse side effects. If the protocol is shown to be effective, it can provide one more option in managing BPSD cases that are difficult to treat using conventional approaches.

This study aimed to evaluate the clinical outcomes of the newly developed “aroma massage with acupressure treatment protocol” through a clinical trial and compare it with cognitive training, which is regarded as the conventional approach to the management of BPSD. Two hypotheses derived from the aim of this study: (1) the newly developed protocol

would be as effective as cognitive training in reducing BPSD, and (2) the newly developed protocol would enhance the effect of cognitive training.

METHODS

Settings and Participants

Assuming a medium effect size (f=0.52737), based on the Cohen-Mansfield Agitation Inventory (CMAI; Cohen-Mansfield *et al.*1989) as an outcome measure of BPSD and previous studies (Ballard, O'Brien, Reichelt, & Perry, 2002; Fu, Moyle, & Cooke, 2013; Holmes *et al.*, 2002; Wells, Dawson, Sidani, Craig, & Pringle, 2000), at least 45 subjects in three groups (i.e., 15 in each group) were required to obtain a 95% power, with α equals to 0.05 for analysis using repeated measure ANOVA.

The clinical trial was conducted from September 2013 to March 2015. Sixty-eight older adults with BPSD were recruited from three long-term geriatric care facilities operated by a non-government organization in Hong Kong. The inclusion criteria were older adults who 1) were 60 years of age or older, had a CMMSE score below 18 if illiterate, 19 if they had 1-2 years of education, and 20 if they had more than 2 years of education, 2) were reported to have BPSD, and 3) were willing to participate in the research, with informed consent signed by their guardian or carer.

The exclusion criteria were older adults who 1) were allergic to essential oils, 2) refused to give consent, 3) suffered from musculoskeletal conditions that were contra-indicated to acupressure at the selected points, and 4) were over-sensitive to tactile stimulation.

Eight guardians refused to join the study, and 60 people were included in this study, with an acceptance rate of 88.2%.

This research was a three-arm parallel group design RCT with random sampling. After individual written consent was obtained from their guardians, the participants fitting the

above inclusion criteria were reported to the researcher by their case therapists at the time of inclusion and were then randomly assigned (using blocked randomization, block size 3) to the three treatment groups at a 20:20:20 ratio. The allocation results were only disclosed to the case therapists to arrange the interventions. This finding was not known to the guardians such that they were unaware of the differences among the three treatment groups. The participants received their treatments individually in a treatment room, thus, they were also unaware of the differences between the three treatment groups. The three treatment groups were Group 1: aroma-massage with acupressure + exercise; Group 2: cognitive training + exercise; and Group 3: aroma-massage with acupressure + cognitive training. A consort flow diagram of the above procedures is provided in Figure 1.

Ethical Considerations

This trial was not registered with the clinical trial registry because Hong Kong did not require researchers to register clinical trials at the time of the implementation of this study. However, institutional ethical approval was separately sought from the Department of Rehabilitation Sciences of the Hong Kong Polytechnic University and the organization from which the participants were recruited. Individual written consent was also obtained from the guardians or carers of the participants before data collection began. All guardians and carers of the participants were fully aware of the basic information of the study in terms of its aims, implementation details, and possible risks before they signed their consent forms.

Interventions

Each group received a three-month biweekly intervention beginning from the time of inclusion.

Aroma massage with acupressure: The protocol was developed in collaboration with a

traditional Chinese medicine (TCM) practitioner. The acu-points were selected based on the literature (Lin *et al.* 2009), TCM theory, and clinical experience. These acu-points were located in different parts of the body that were easy to reach, could be exposed for acupressure and were less sensitive to touch. For patients who were contra-indicated in any one of the chosen accu-points, other acu-points were used to serve a similar purpose. The aroma massage with the acupressure protocol together with the selected acu-points are described in detail in Table 1: the Heart Meridian, Pericardium Meridian, and Governor Vessel. First, the Heart was the leader of the other organs, which is also referred to as "mind" in TCM theory. Three acu-points, including Lingdao (HT4), Tong Li (HT5), and Shenmen (HT7), located in the forearm and hand in this meridian, had a calming effect and reduced restlessness. Second, the Neiguan acu-point (PC6) of the Pericardium Meridian was used to protect the heart and, thus, the mind. Third, Baihui (GV20), which is the conjunction of several meridians and vessels and is effective for calming, was chosen, along with the Governor Vessel. We also included Fengchi (GB20), Shenting (GV24), Taiyang (Ex-HN5) and Yintang (Ex-HN3), located at the head, which were used for improving memory, calming, and relieving headaches. Finally, Sanyinjiao (SP6), which was the conjunction of three meridians located above the ankle, was chosen to manage nervous breakdowns. Trained carers or therapists provided no more than 20 minutes of aromatherapy, combining therapeutic massage with blended 2% lavender essential oil in a sunflower-based oil. Acupressure on the selected acu-points was integrated into the massage treatment session.

Cognitive training: Trained care staff or therapists provided 20 minutes of cognitive training which aimed to improve attention, short-term memory, calculation, or orientation using work sheets and puzzles.

Exercises: In this study, exercise was considered as "activity as usual" or "passive control" because it was well recognized as part of the routine treatment for older persons in an

institutional setting. In fact, using exercise as the control group has been reported in many studies (Hsu *et al.* 2016). Trained care staff or therapists assisted the participants to perform 20 minutes of stretching exercises, as outlined by a physiotherapist.

The above interventions were introduced to the care staff and an occupational therapist in each setting during two sessions with tutorials, practices, and examinations. Adverse side effects, if any, were recorded. A quality assessment was performed by the occupational therapists for all care staff.

Concomitant drug use was allowed, and the medications prescribed remained the same throughout the intervention period.

Outcome Measures

The 29-item Chinese Version of Cohen-Mansfield Agitation Inventory (CCMAI-29 items, Choy, Lam, Chan, Li & Chiu, 2001) was adopted as the primary outcome measure to evaluate the frequency of the occurrence of BPSD. It was used by care staff to assess BPSD in the participants during the previous 2 weeks. The items assessed included 29 agitated behaviours, such as wandering, screaming, hurting self or others, etc. Each item was rated on a 7-point frequency scale from "1" meaning never to "7" meaning several times per hour. Internal consistency for the CCMAI, as shown by Cronbach's alpha, was 0.75, and inter-rater reliability was found to be excellent, with an intraclass correlation of 0.98. A high test-retest reliability was also reported ($r = 0.85$, $p < 0.001$) (Choy *et al.* 2001). In this study, domain scores were used for comparison.

The Neuropsychiatric Inventory (NPI) was used as another primary outcome measure to assess neuropsychological disturbances of the participants, including abnormalities of mood and psychotic phenomena. NPI assessed the severity and level of distress of 12 behavioural disturbances that are common in dementia, such as delusions, agitation, anxiety, and appetite

change. The severity of the disturbances was rated from "1" meaning mild (noticeable, but not a significant change) to "3" meaning severe (very marked or prominent, a dramatic change). Distress was rated from "1" meaning not distressing at all to "5" meaning extreme or very severe (extremely distressing, unable to cope with). Test-retest reliability was found to be 0.79 and 0.86 ($p < 0.01$) for frequency and sensitivity, respectively. For internal consistency, a Cronbach's alpha of 0.88 was reported for the total score and ranged from 0.87 to 0.88 for the individual subscales (Cumming *et al.* 1994). Cumming (1994) has also reported a high inter-rater reliability, however, no correlation was reported.

The 30-point questionnaire Cantonese Version of the Mini-Mental State Examination (CMMSE) was used in this study as a screening test for cognitive impairment and dementia and as the third primary outcome measure to assess the change in cognitive function. It included orientation, registration, attention, calculation, recall, language, and praxis tasks, which consisted of a total of 11 questions requiring verbal and written responses. Scores ranged from 0 to 30, with a cut-off score of 19 suggesting the need for further investigation of the possibility of dementia. Internal consistency for the CMMSE, as shown by Cronbach's alpha, was 0.86, and inter-rater reliability was found to be excellent, with an intraclass correlation of 0.99. A high test-retest reliability was observed ($r = 0.78$, $p < 0.001$) (Chiu, Lee, Chung & Kwong, 1994).

Barthel Index-20 (BI20) was used as a secondary outcome measure to assess the level of functional dependence/independence for 10 daily living activities related to the personal care and mobility of the participants. It was sensitive to either declines or improvements in functional levels. The score ranges from 0 to 20 and a higher score was associated with higher independence and a greater likelihood of being able to live at home. The reliability and validity of BI20 were rated highly as test-retest reliability was found to be 0.989, inter-rater reliability was 0.994, and the Cronbach's alpha score was 0.935 (Collin *et al.* 2009).

Data Collection

Data books containing demographic data collection forms, BI20, CMMSE, CCMAI, and NPI were completed by the case therapists, who were trained to rate BPSD. They were asked to do so in the service units that the older persons attended. Observations occurred pre- and post-intervention period, and 3 months post-intervention. Raters were only partially blinded due to the nature of the interventions. The raters were blinded to the study design but not the group allocation.

Data Analysis

SPSS version 22 was used for the data analysis. We performed one way ANOVA to detect differences in the baseline scores. BI20 scores for Group 2 and Group 3 were found to be significantly different. Descriptive statistics and Chi Squared tests were used to analyse demographic data. The "attention span" of Group 1 was found to be significantly different from the other groups. Because longer attention span contributed to better cognitive function (Sikkes *et al.* 2012) and hence fewer BPSD, the "attention span" measure was adjusted as a covariate in a later analysis.

Multiple comparison procedures by repeated measures and parametric data were conducted through repeated measures analysis of covariance (ANCOVA) with the Bonferroni correction. BI20 (pre-test) was used as a post hoc decision to detect between-group differences (groups consisted of 3 levels), within-subject differences (time consisting of three endpoints: pre-, post-, and 3-month), and the interaction effect between group and time. When a significant interaction was identified, post hoc analysis was performed to determine which time point contributed to it.

Two 3-month follow-up datasets were unable to be collected due to subjects in Group 1

dropping out of the study. A last observation carried forward (LOCF) approach was used to treat these missing data. Data from all 60 participants were analysed.

RESULTS

Demographic Data

Sixty older adults (18 males and 42 females) ranging in age from 63 to 100 years (mean = 84.02 years, *SD* = 7.62) were recruited and randomly assigned to the three groups. Table 2 summarizes the demographics of the participants. There were no significant differences in the demographic data of the three groups, except with regard to their attention span ($p = 0.04$).

Results of Outcome Measures

Table 3 shows the baseline results for the three groups, and Table 4 shows the results from the post-test and 3-month follow-up assessments for the three groups.

The CMMSE scores of the three groups at the time points pre-test, post-test, and 3-month post-test showed no significant differences. Repeated measure ANCOVA revealed no interaction between the three groups across time ($p = 0.33$, observed power = 0.36).

The mean BI20 pre-test scores for the three groups were 15.56 (*SD* = 4.76), 13.32 (*SD* = 6.51), and 10.84 (*SD* = 4.43), respectively. One way ANOVA test revealed an overall significant difference between the groups ($p = 0.03$, $df = 2$). Post hoc multiple comparison (LSD) showed a significant difference between Group 3 and Group 2 with $p = 0.03$, $f = 3.932$ as shown in Figure 2a. For the three time points, repeated measure ANCOVA revealed no interaction between the scores of the three groups across time ($p = 0.05$, $df = 2$, observed power = 0.64).

The three domain scores (“aggressive behaviour”, “physically nonaggressive behaviour”, and “verbally agitated behaviour”) of CCMAI of the three groups at three time points were

not significantly different. Moreover, repeated measure ANCOVA revealed no significant time × group effect in "aggressive behaviour" ($p = 0.06$, $f = 2.397$, $df = 2$, observed power = 0.67), "physically nonaggressive behaviour" ($p = 0.16$, $f = 1.722$, $df = 2$, observed power = 0.47), and "verbally agitated behaviour" ($p = 0.63$, $f = 0.595$, $df = 2$, observed power = 0.17).

In the comparison of the NPI sub-scores, significant time × group effects were found in the "severity score" ($p = 0.04$, $f = 2.889$, $df = 2$, observed power = 0.69), and "distress score" ($p = 0.04$, $f = 3.022$, $df = 2$, observed power = 0.68) after the effects of attention and BI20 score were controlled. To determine which time point contributed to it, a post hoc comparison was performed; the results are shown in Table 5.

The mean "severity score" dropped significantly from 3.70 ($SD = 3.30$) in the pre-test to 2.55 ($SD = 2.48$) ($p = 0.01$) and to 1.85 ($SD = 1.46$) at the 3-month post-test in Group 1 ($p = 0.01$). There was also a significant reduction of the mean score from 3.60 ($SD = 3.05$) at the pre-test to 2.35 ($SD = 2.26$) at the 3-month follow-up in Group 3 ($p = 0.01$). These two differences contributed to the overall significance ($p = 0.04$, $f = 2.889$, $df = 2$, observed power = 0.69). These results are shown in Figure 2b.

In terms of the "distress score", there was a significant reduction from 5.8 ($SD = 5.09$) in pre-test to 4.25 ($SD = 3.78$) in the post-test ($p = 0.02$), and a reduction of the mean scores from the post-test: 4.25 ($SD = 3.78$) to the 3-month post-test: 2.75 ($SD = 2.66$) in Group 1 ($p = 0.02$). When comparing the pre-test mean score 5.80 ($SD = 5.09$) with the 3-month post-test score stated above, a significant reduction was found ($p = 0.02$) in Group 1. Similar changes were found in Group 3 at the pre-test (5.40 ± 4.53) ($p = 0.01$) and 3-month follow-up (2.95 ± 3.02) ($p = 0.01$). The above differences contributed to the overall significance ($p = 0.04$, $f = 3.022$, $df = 2$, observed power = 0.68), as shown in Figure 2c.

In comparing the "severity score" and "distress score" among the three groups at the three time points, the statistical analysis did not show any significant differences. The effects

of the covariates (attention and BI20 pre-test score) were controlled for in the above analysis.

No adverse side effects were observed in the participants during the entire research period.

DISCUSSION

Overall, there was no significant finding when comparing the three groups through ANCOVA and after adjusting for attention and BI pre-test. However, when compared within each group at three different time-points, the participants in Groups 1 and 3 showed significant reductions in the severity and distress caused by BPSD from the pre-test to the post-test and to the 3-month post-test, whereas group 2 did not demonstrate similar effects. Aroma massage with acupressure used either with cognitive training or exercise (activity as usual) significantly reduced the severity and distress caused by BPSD. With this result, the first hypothesis was supported. In other words, the newly developed protocol combining aroma-massage with acupressure was as effective as cognitive training in reducing BPSD. However, it could not be implied that this effect was better than that for those who received only conventional interventions, such as cognitive training and exercise.

Other interesting observations were made based on this clinical trial. First, some of the significant results were not obtained at the post-test but during the follow-up period, meaning that positive outcomes only appeared after at least three months. Second, we noticed that the protocol was implemented by carers during the follow-up period, as they learned through observing the care staff during the treatment period, which indicates that the aroma massage with acupressure treatment protocol is easy to learn and can be implemented by non-professionals. The willingness of carers to learn has additional value, as this process may have improved the relationship between them and the older adults, as observed by the researchers. Third, significant effects were not reported in the cognitive training + exercise group,

implying that the aroma massage with acupressure protocol is more effective when combined with either cognitive training or exercise. When the participants received aroma massage with acupressure, they were relaxed and calm. In contrast, cognitive training may irritate them and was not effective in helping to improve their cognitive function or behaviour.

Finally, the CMMSE scores in the aroma massage with acupressure + cognitive training group had an upward trend, which was not observed in the other groups. Although this change was not significant, it raises the question of whether aroma massage with acupressure protocol may have enhanced the effect of cognitive training in this group. There were no significant differences in the secondary outcome measures. The significant improvement in the severity and distress of BPSD measured by NPI in Group 1 and Group 3 took three months to appear. The aroma massage with acupressure treatment protocol, as found in other studies, is likely to produce a positive effect on relationships, engagement, and BPSD, but not on function (Ballard *et al.* 2002, Burns *et al.* 2011) or cognition (Lin *et al.* 2007, Snow *et al.* 2004). The pleasant experience of aroma massage with acupressure protocol calmed the participants from their agitated state during cognitive training and enabled them to function better when performing table tasks for 20 minutes. Thus, the second hypothesis is also supported by this finding. In short, aroma massage with acupressure was found to further enhance the effect of cognitive training, and future study should be performed to verify this finding.

Aromatherapy, therapeutic massage, and acupressure are independently found to be effective in reducing BPSD. For aromatherapy alone, some studies have reported positive results (Lin *et al.* 2007, Jimbo *et al.* 2009, Ballard & Howard 2006), while others have not reported positive findings (Burns *et al.* 2011, O'Connor *et al.* 2013). The combined effects of these three treatments, however, have not been clearly documented, despite the fact that clinical experience shows that, when used together with acupressure, client satisfaction levels are higher (Yang *et al.* 2015), which suggests that this combination of therapies can be

effective in managing dementia-associated agitation. Thus, the innovative aspect of this study is that we combined the three interventions using the aroma massage with acupressure protocol and reported its positive clinical outcomes in treating BPSD which adds to our knowledge in this aspect.

Despite some positive findings and contribution resulting from this study, there are limitations that should be noted. The first limitation is related to the small sample size. Second, there are no outcome measures regarding desirable behaviours, such as increase in social engagement and interaction with others. Third, the raters were only blinded to the design of the study but not to the group allocations, which may lead to subjective judgement regarding the effects of treatments. Finally, the anti-psychotics and concomitant drugs consumed by the participants during the study were not controlled.

RELEVANCE TO CLINICAL PRACTICE

Aromatherapy and therapeutic massage are found to be effective in improving sleep, alleviating anxiety and depression, and reducing the occurrence of BPSD. It is well documented that these two interventions, when used together, reduce the occurrence of BPSD. In addition, acupressure is separately found to be effective in the reduction of BPSD. When it is combined with aromatherapy, more positive outcomes have been reported than when using aromatherapy alone. Although the above three interventions have been found to be effective independently, their combined effects have not been clearly documented. Clinical experiences suggest that, when used together, client satisfaction is higher.

This study adds to the existing literature by providing evidence on the effectiveness of the combination of the three interventions in the management of BPSD. The findings of this RCT indicate that aroma massage with acupressure protocol is safe, well-tolerated and easy to administer by non-professional staff, with a minimal level of training required for professional

staff, such as occupational therapists. Further large-scale studies are required to investigate the mechanisms and differential effects in comparison with the three intervention elements used alone. With more supporting evidence, this protocol could be recommended as a complementary therapy to mainstream interventions, such as antipsychotic medication, cognitive training and exercise, to enhance outcomes in the treatment of BPSD in people with late-stage dementia.

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TABLE AND FIGURE LEGENDS

Table 1. Aroma massage with acupressure protocol

Table 2. Demographic data of the subjects in the three groups

Table 3. Comparison of the various outcome measures at the baseline assessments among the three groups

Table 4. Comparison of the various outcome measures at the post-test and 3-month follow-up assessments among the three groups

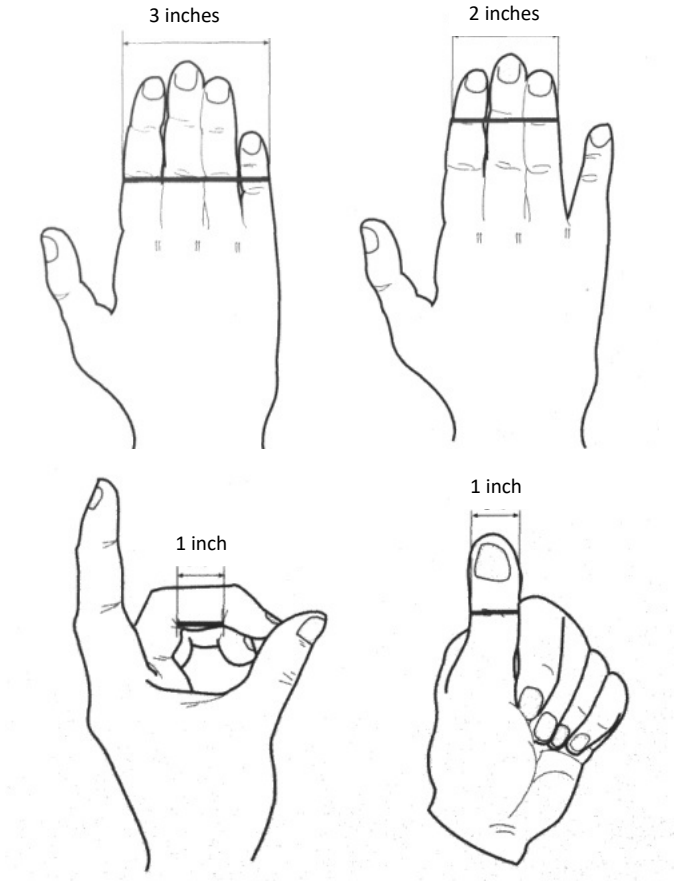
Table 5. Significant differences found in the NPI sub-scores at the post-test and 3-month follow-ups for Group 1 and Group 3

Figure 1. Consort flow diagram

Figure 2(a) to (c). Diagrams showing the mean scores of the measured outcomes, with significant results.

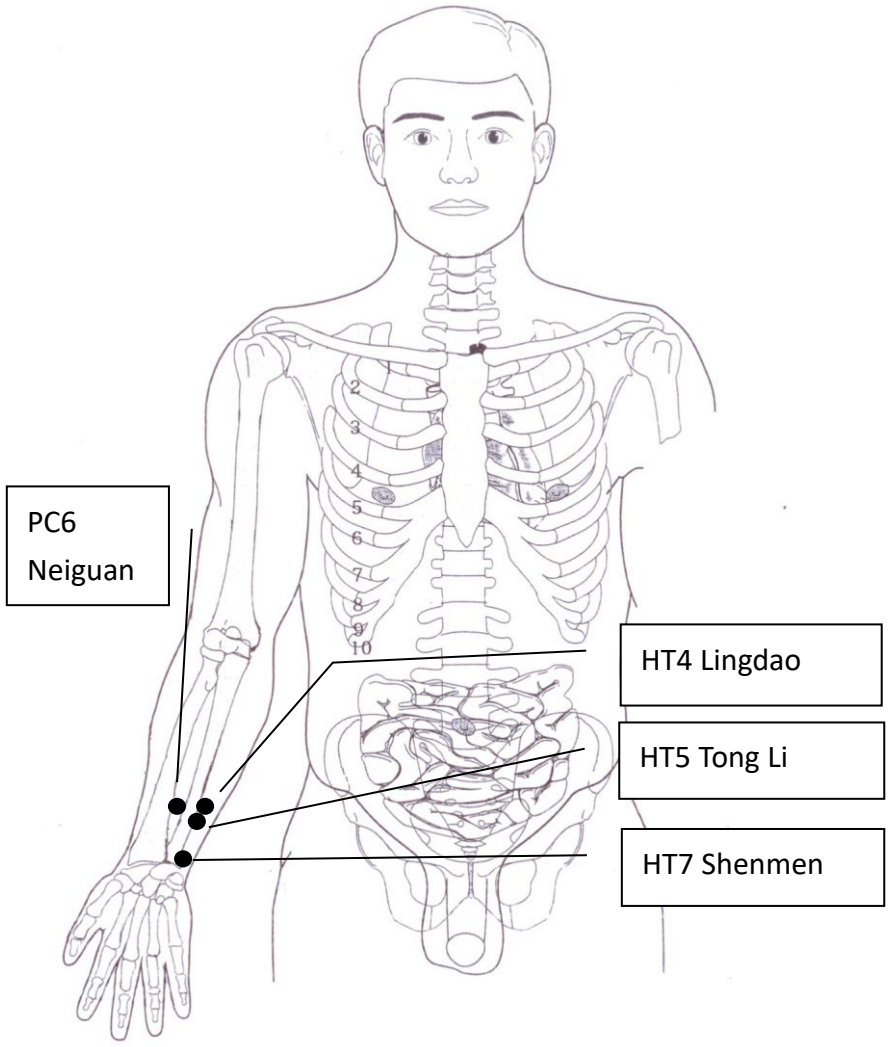
Table 1 Aroma-massage with Acupressure Protocol

Important notes	
Duration	Not more than 20 minutes
Positioning and environment	Prepare the participant in a comfortable chair/wheelchair. Worker sits face to face to the elderly person. Room temperature should be warm with a range of 23 to 26 degree. Environmental distraction, such as noises of a radio, should be kept to minimal.
Procedures and sequencing	3 parts: forearm, head, and lower leg. With the sequence: forearm→head→lower leg. Areas not massaged and the underlying reasons should be clearly recorded, e.g., hypersensitivity and aggressiveness.
Acupressure techniques used	Use pressing and kneading techniques with the thumb. Press downward vertically with the tip of the thumb, knead with clockwise direction for 20 strokes, and then 20 strokes in anti-clockwise direction. Note: the finger nails should be kept short.

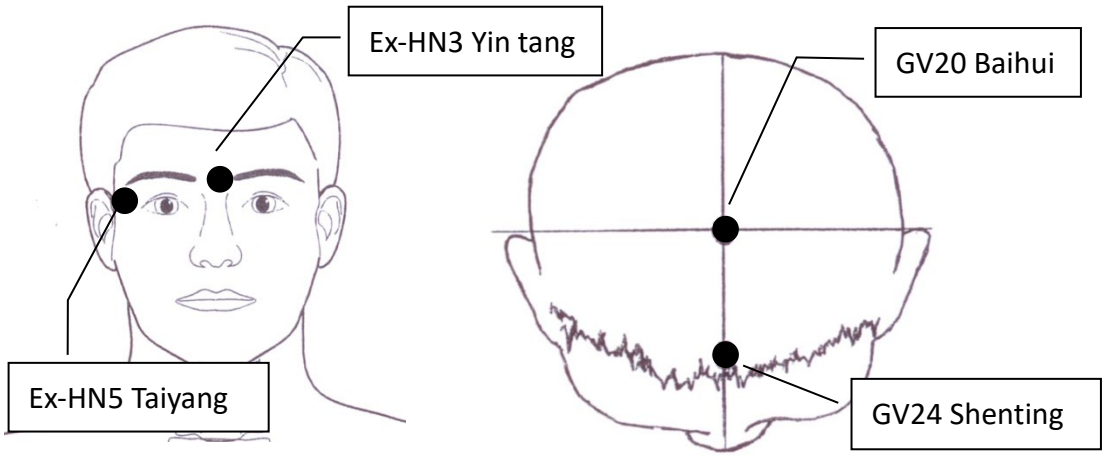
Measurement of "Chinese inch": (mentioned as "inch" in this table)	
Getting started	
Material and equipment	Massage oil (blended lavender essential oil in sunflower base oil with concentration of 2%) in glass container; Alcohol wrap tissue × 5 packs; and tissue paper × 1 box.
Explain treatment procedures	"Today, I will perform 20 minutes of aroma-massage with acupressure on your forearm, head, and leg. The purpose is to help you relax and have a peaceful mind. You may feel tenderness or numbness during acupressure. Please let me know if you are feeling uncomfortable or want me to press with more or less strength. Let's get started." We must explain the procedures to every elderly person even they may not

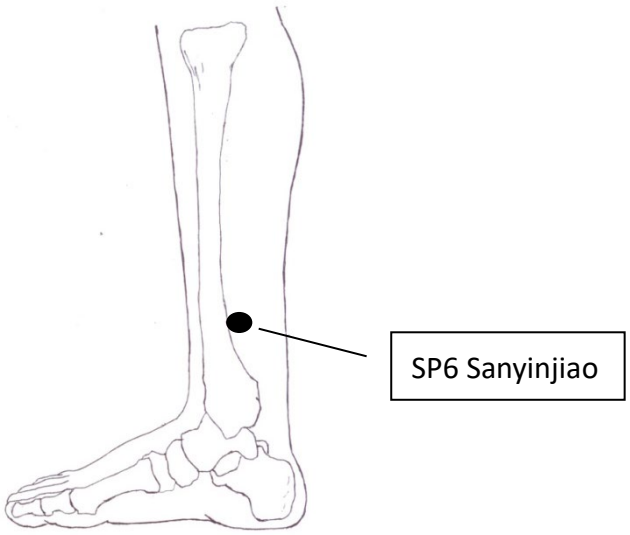
	understand or have no response.
Sterilization	Use a large alcohol wrapping tissue to clean you own hands. Then, use another one for cleaning each forearm and another one for each leg of the elderly person.
Prepare your hands	Use some massage oil to rub and warm your hands before you start to perform the procedures on the elderly person.

Forearm



Warm up	Use some oil on the elderly person's hand and forearm with palm facing upward. Hold his/her hand with your hands. Use your two thumbs to massage the palm from the middle of the palm to both sides 5 times. Massage the forearm with the same technique until the forearm is covered with massage oil. Check for the elderly person's facial expression and their responses. If the elderly person seems not warmed up yet, extend the period up to not more than 2 minutes. Use your non-dominant hand to hold the forearm and then use your dominant hand to perform acupressure. You can start with less force and ask how they feel for every acu-points. If the elderly person suffers from dysphasia, observe for any adverse facial expression or reaction.
HT7 Shenmen	At the wrist cease of the palmer side of the wrist, proximal to the carpal bone, next to the tendon above the head of ulnar bone (lateral side).
HT5 Tong Li	One inch above the above acu-point.
HT4 Lingdao	Half inch above the above acu-point.
Heart meridian	Extend your thumb, friction along the meridian with hard surface of the distal joint for 10 times.
PC6 Neiguan	Ask the elderly person to make a fist, two tendons will be slightly protruded and the acu-point is located between the two tendons at the point 2 inches

	proximal to the wrist cease.
Having finished the acu-points of the left side, repeat the above procedures on the right side.	
Head  	
Ex-HN5 Taiyang	1 inch behind the conjunction of the end of the eye blow and edge of the eye, there is a concave area. Another side of the head should be supported during acupressure. Perform acupressure on the right side after the left side is done.
Ex-HN3 Yintang	Stand behind the elderly person, help to extend his/her neck to 40 degrees. The acu-point is located at the midpoint of the two eye blows. Then, friction along the midline towards the hair line and to the next acu-points. The back of the head should be well supported during this step.
GV24 Shenting	Upward along the vertical midline of the face and 0.5 inch behind the hair line. Back of the head should be well supported during this step.
GV20 Baihui	Neck in neutral position, this acu-point is located at the conjunction of a line collecting tips of two ears and the midline of the head. When acupressure is

	applied on this point, the head should be supported by holding the chin.
GB20 Fengchi	At the end of the curve at the back of the skull, there are two major muscles at both sides of the mid line. Across the muscle to the lateral side, there is a depression point at the conjunction of the muscle and the curve of the head. Chin should be supported during acupressure at this acu-point. Perform the right side after the left side is completed.
Leg	
Warm up	Elderly person in supine position or sitting with lower leg resting on a stool or a chair.
	Use some massage oil to massage the lower leg.
SP6 Sanyinjiao	3 inches above the medial malleolus and along the edge of the tibia.
Spleen meridian	Extend your thumb, friction along the meridian with hard surface of the distal joint for 10 times.

When the acu-points of the left side are completed, repeat the above procedures on the right side.

Table 2 Demographic data of subjects in the three groups

	Group 1: aroma-massage with acupressure + exercise (*n* = 20)	Group 2: cognitive training + exercise (*n* = 20)	Group 3: aroma-massage with acupressure + cognitive training (*n* = 20)	*P*-value
Gender				0.50†
Male	4(20%)	7(35%)	7(35%)	
Female	16(80%)	13(65%)	13(65%)	
Age (range, mean ± SD)	66-92 (82.13 ± 7.69)	78-100 (84.33 ± 7.85)	65-97 (mean = 84.11 ± 7.33)	0.33φ
Marital Status				0.22†
Single	7(35%)	1(5%)	0(%)	
Married	13(65%)	9(45%)	5(25%)	
Widowed	0	10(50%)	15(75%)	
Diagnosis				
Dementia	13(65%)	15(75%)	12(60%)	0.60†
Hypertension	14(70%)	12 (60%)	14(70%)	0.75†
Parkinsonism	3(15%)	2(10%)	1(5%)	0.58†
Diabetes Mellitus	8(40%)	4(20%)	5(25%)	0.35†
Bilateral cataract	7(35%)	11(55%)	6(30%)	0.24†
Cerebral vascular accident	5(25%)	7(35%)	7(35%)	0.74†
Skeletal disorder	2(10%)	3(15%)	5(25%)	0.43†
Others	9(45%)	4(20%)	9(45%)	0.52†
Activity Level				
Bed-chair bound	1(5%)	3(15%)	4(20%)	0.10†
Homebound	11(55%)	12(60%)	15(75%)	
Outdoor	7(35%)	5(25%)	1(5%)	

Education Level				
Illiterate	11(55%)	10(50%)	11(55%)	0.97†
1-2 years	2(10%)	3(15%)	2(10%)	
>2 years	7(35%)	7(35%)	7(35%)	
Alertness				
Alert	19(95%)	19(95%)	19(95%)	1.00†
Sleepy	0	0	1(5%)	
Drowsy	1(5%)	1(5%)	0	
Communication				
Follow verbal command	20(100%)	18(90%)	18(90%)	0.35†
Gesture	0	2(10%)	2(10%)	
Attention Level				
> 5 mins	15(75%)	8(40%)	8 (40%)	*0.04*†
2-5 mins	4(20%)	9(45%)	8(40%)	
< 2 mins	1(5%)	3(15%)	4(20%)	

Values are number of subjects and percentage (except age). †Chi's Square test was performed between groups for count data, and ᵠOne-way ANOVA test for continuous data.

Table 3 Comparison of various outcome measures at baseline assessments among the three groups

	Group 1: aroma-massage with acupressure + exercise (n = 20) Mean (SD)	Group 2: cognitive training + exercise (n = 20) Mean (SD)	Group 3: aroma-massage with acupressure + cognitive training (n = 20) Mean (SD)	One Way ANOVA		LSD
				p-value	*f-value*	*p-value*
CCMAI Domain Score:						
Aggressive behaviour	14.60 (1.90)	15.35 (4.36)	13.85 (1.93)	0.29	1.283	
Physically nonaggressive behaviour	12.75 (5.74)	13.00 (5.53)	13.90 (6.88)	0.82	0.198	
Verbally agitated behaviour	12.40 (4.80)	12.75 (7.07)	13.30 (6.78)	0.90	0.103	
NPI Sub-scores:						
Severity score	3.70 (3.30)	2.65 (2.98)	3.60 (3.05)	0.50	0.694	
Distress score	5.80 (5.09)	3.70 (4.57)	5.40 (4.53)	0.34	1.111	
BI20	15.56 (4.76)	13.32 (6.51)	10.84 (4.34)	*0.03*	3.932	*0.01* §
CMMSE	10.30 (6.64)	9.30 (6.53)	6.48 (0.41)	0.41	0.904	

Post hoc test was performed when significant between groups difference was found: §LSD (group 2 vs group 3)

Table 4 Comparison of various outcome measures of post-test and 3-month follow-up assessments among the three groups

		Group 1: aroma-massage with acupressure + exercise (n = 20) Mean (SD)	Group 2: cognitive training + exercise (n = 20) Mean (SD)	Group 3: aroma-massage with acupressure + cognitive training (n = 20) Mean (SD)	3 Time-point x 3 groups Interaction measured by repeated measure ANCOVA p-value	*f*-value	Observed Power (Post hoc power)
CMMSE	Post-	10.00 (6.67)	8.55 (6.55)	10.80 (6.74)	0.33	1.172	0.36
	3M FU	10.25 (6.60)	8.95 (6.50)	11.25 (7.13)			
CCMAI Domain Score:							
Aggressive behaviour	Post-	13.35 (0.93)	14.95 (3.52)	14.95 (3.56)	0.06	2.397	0.67
	3M FU	13.50 (1.00)	13.80 (1.99)	14.10 (2.77)			
Physically nonaggressive	Post-	12.80 (7.18)	13.65 (5.84)	13.15 (6.71)	0.16	1.722	0.47
behaviour	3M FU	13.30 (7.75)	13.75 (6.04	12.90 (7.77			
Verbally agitated behaviour	Post-	11.20 (4.56)	12.70 (7.41)	12.60 (5.93)	0.63	0.595	0.17
	3M FU	11.80 (4.79)	12.85 (7.01)	12.80 (6.00)			
NPI Sub-scores:							
Severity score	Post-	2.55 (2.48)	2.00 (2.70)	2.75 (2.17)	*0.04*	2.889	0.69
	3M FU	1.85 (1.46)	2.35 (2.64)	2.35 (2.26)			
Distress score	Post-	4.25 (3.78)	3.00 (3.33)	4.50 (3.50)	*0.04*	3.022	0.68
	3M FU	2.75 (2.66)	3.05 (2.80)	2.95 (3.02)			

Repeated measures ANCOVA adjusted for attention and BI pre-test.
3M FU, 3-month follow-up; CMMSE, Cantonese Version of Mini-mental Status Examination; BI, Barthel Index; CCMAI, Chinese Cohen-Mansfield Agitation Inventory; NPI, Neuropsychiatric Inventory.

Table 5 Significant differences found in NPI sub-scores at post-test and 3-month follow-up in Group 1 and Group 3

	aroma-massage with acupressure + exercise						
Group 1	NPI sub-scores:	Pre-test	Post-test	3M FU			
(*n* = 20)		Mean (SD)	Mean (SD)	Mean (SD)	*t*	*p*-value	95% CI
	Severity score	3.70 (3.30)	2.55 (2.48)		2.93	*0.01*	[.33, .197]
		3.70 (3.30)		1.85 (1.46)	3.00	*0.01*	[.56, 3.14]
	Distress score	5.80 (5.09)	4.25 (3.78)		2.58	*0.02*	[.29, 2.81]
		5.80 (5.09)		2.75 (2.66)	3.27	*0.00*	[1.10, 5.00]
			4.25 (3.78)	2.75 (2.66)	2.64	*0.02*	[.31, 2.69]
Group 3	Severity score	3.60 (3.05)		2.35 (2.26)	2.80	*0.01*	[.32, 2.18]
(*n* = 20)	Distress score	5.40 (4.53)		2.95 (3.02)	2.92	*0.01*	[.70, 1.91]
			4.50 (3.50)	2.95 (3.02)	2.68	*0.02*	[.34, 2.76]

Figure 1. CONSORT flow diagram

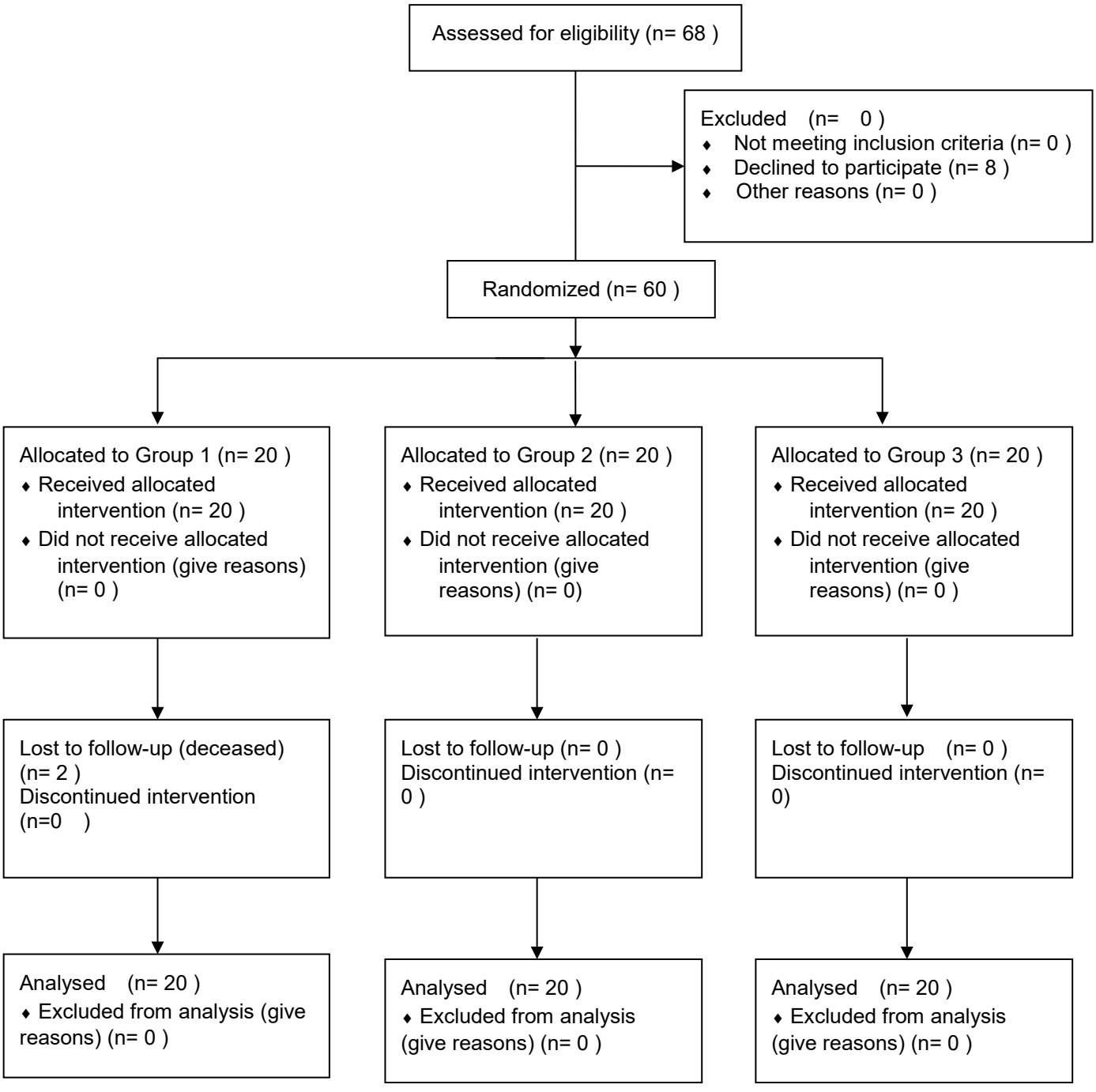
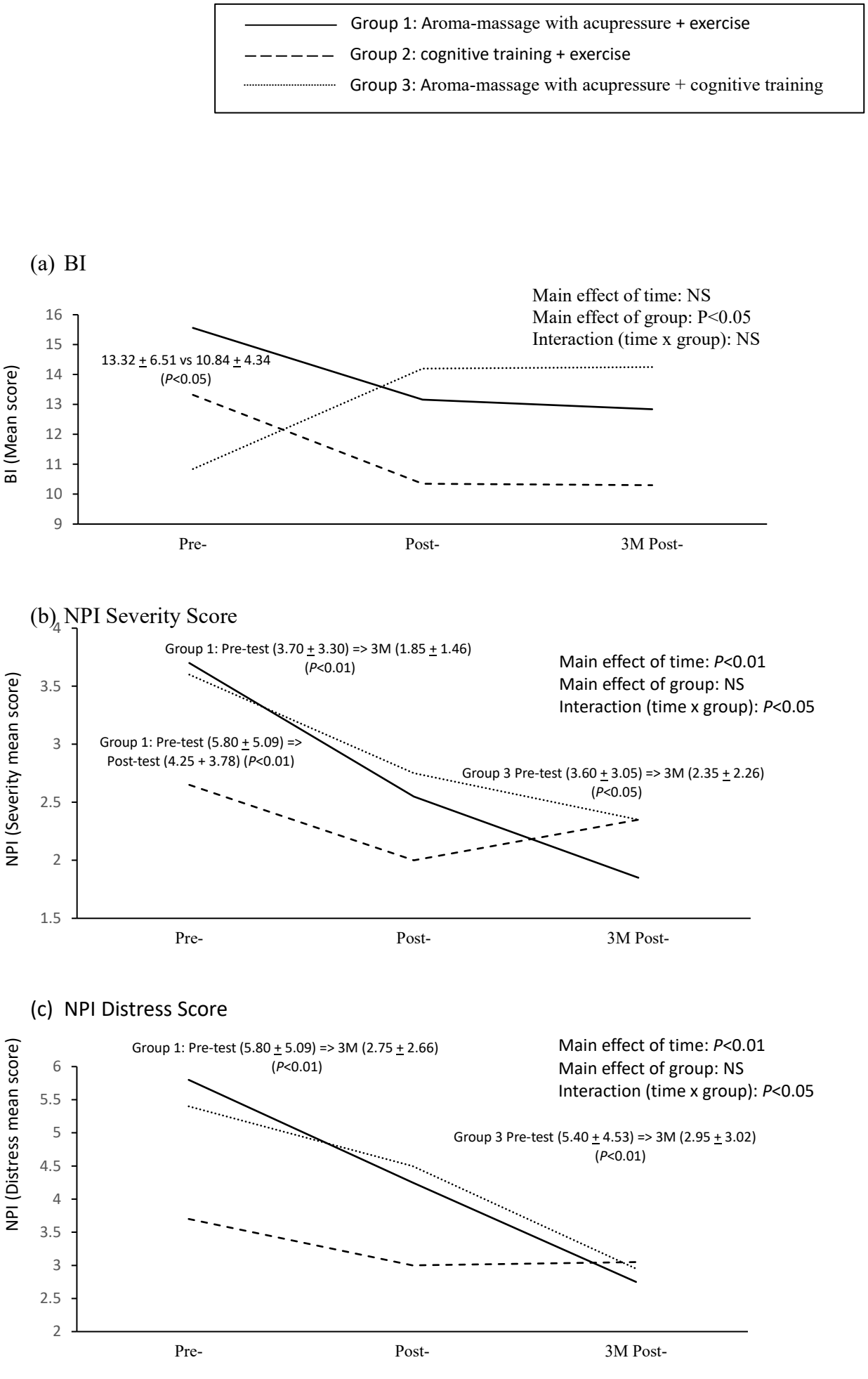


Figure 2(a) to (c). Diagrams showing mean scores of measure outcomes with significant results



CONSORT 2010 checklist of information to include when reporting a randomized trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomized trial in the title	Title page
	1b	Structured summary of trial design, methods, the results, and conclusions (for specific guidance see CONSORT for abstracts)	1-2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3-5
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	6
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	NA
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6-8
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	9-10
	6b	Any changes to trial outcomes after the trial commenced, with reasons	NA
Sample size	7a	How sample size was determined	6
	7b	When applicable, explanation of any interim analyses and stopping guidelines	NA
Randomization:			
Sequence generation	8a	Method used to generate the random allocation sequence	6
	8b	Type of randomization; details of any restriction (such as blocking and block size)	6
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	6
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned	6

		participants to interventions	
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	6
	11b	If relevant, description of the similarity of interventions	6-7
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	11
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	11
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment and were analysed for the primary outcome	12
	13b	For each group, losses and exclusions after randomization, together with reasons	11
Recruitment	14a	Dates defining the periods of recruitment and follow-up	6
	14b	Why the trial ended or was stopped	NA
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 2
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	12, Table 2
Outcomes and estimation	17a	For each primary and secondary outcome, the results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	12-13, Table 3
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	NA
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	12-13, Table 4
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	13
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	14-16
Generalizability	21	Generalizability (external validity, applicability) of the trial findings	16
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	16-17
Other information			
Registration	23	Registration number and name of trial registry	7
Protocol	24	Where the full trial protocol can be accessed, if available	NA
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	NA

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomized trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.