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Research on treating neuropsychiatric symptoms of advanced dementia with non-pharmacological strategies, 1998–2008: a systematic literature review

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Abstract

Background—Advanced dementia is characterized by severe cognitive and functional impairments that lead to almost total dependency in self-care. Neuropsychiatric symptoms (NPS) are common in advanced dementia, diminishing quality of life and increasing the care burden. The challenge for health care providers is to find safe and effective treatments. Non-pharmacological interventions offer the potential for safer alternatives to pharmacotherapy, but little is known about their efficacy. This review evaluates the published literature on non-pharmacological interventions for treating NPS in advanced dementia.

Methods—A literature search was undertaken to find non-pharmacological intervention studies published between 1998 and 2008 that measured NPS outcomes in individuals diagnosed with advanced dementia. Strict inclusion criteria initially required that all study participants have severe or very severe dementia, but this range was later broadened to include moderately severe to very severe stages.

Results—Out of 215 intervention studies, 21 (9.8%) specifically focused on treatments for individuals with moderately severe to very severe dementia. The studies provide limited moderate to high quality evidence for the use of sensory-focused strategies, including aroma, preferred or live music, and multi-sensory stimulation. Emotion-oriented approaches, such as simulated presence may be more effective for individuals with preserved verbal interactive capacity.

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Dr. Kverno drafted the manuscript. Drs. Black, Nolan, and Rabins undertook critical revision of the paper.

Conclusions—Most studies of interventions for dementia-related NPS have focused on individuals with mild to moderate cognitive impairment. Individuals with severe cognitive impairment do not necessarily respond to NPS treatments in the same manner. Future studies should be specifically designed to further explore the stage-specific efficacy of non-pharmacological therapies for patients with advanced dementia. Areas of particular need for further research include movement-based therapies, hands-on (touch) therapies, and interventions that can be provided during personal care routines. Interventions appear to work best when they are tailored to balance individual arousal patterns.

Keywords

dementia; neuropsychiatric; behavioral and psychological symptoms associated with dementia (BPSD); non-pharmacological

Introduction

Individuals having cognitive impairment, ranging from severe to very severe, make up approximately 40% of the residents diagnosed with dementia in special care units and nursing homes in the U.S.A. (Gruneir *et al.*, 2007). Particularly challenging to healthcare providers and distressing to patients and their families are the neuropsychiatric symptoms (NPS) associated with dementia. NPS are common in dementia and the majority of individuals with advanced dementia have one or more, the most common of which are agitation or aggressive behavior, depression, apathy or withdrawal, psychosis, and aberrant motor behavior (Zuidema *et al.*, 2007; Kverno *et al.* 2008). In addition, individuals with advanced dementia are likely to be experiencing multiple medical comorbidities (Black *et al.*, 2006) and being prescribed multiple medications (Blass *et al.*, 2008). Of particular concern are the risks associated with antipsychotic medications that are used to treat NPS. The complex issues raised by the pharmacological therapy of NPS, and a focus on improving the quality of life of individuals with advanced dementia, has led to a renewed emphasis on non-pharmacological treatment strategies.

The most recent American Psychiatric Association practice guidelines for treating patients with dementia (Rabins *et al.*, 2007) advocate for the development of stage-specific treatment plans. Stage-specific treatment plans rely on the synthesis of current knowledge. Numerous systematic reviews of the literature have examined the treatments for NPS associated with dementia, yet to our knowledge none have examined the literature especially relevant to treating these symptoms in advanced dementia.

The purpose of this systematic review of the literature was to identify and summarize the literature of the past decade relevant to the treatment of NPS in advanced dementia. Non-pharmacological treatment strategies can be divided into four broad categories: emotion-oriented, stimulation-oriented, behavior-oriented, and cognitive-oriented (Rabins *et al.*, 2007). Due to impaired capacity for using language, we hypothesized that individuals with advanced dementia would show the greatest benefit from the less cognitively demanding types of non-pharmacological interventions. The focus of the review was not on palliative or end-of-life care, typically defined as providing comfort during the last six months of life. Rather, the focus was on identifying non-pharmacological NPS treatments for those individuals who are severely cognitively impaired, whether or not they are receiving palliative care. The goal of reducing NPS is to improve quality of life, regardless of the stage of dementia.

One decade ago, Opie *et al.* (1999) systematically reviewed the 43 studies they identified that examined the efficacy of psychosocial approaches to behavioral disorders in dementia

and recommended that future studies use more rigorous methods, enroll larger numbers of subjects, and include a wider range of settings. The review presented here sought answers to the following questions: (1) What progress has been made in the last decade in treating NPS in advanced dementia? (2) What are the critical elements for clinicians to address, given what we know now? (3) What are the critical elements for researchers to address in identifying relevant treatments for advanced dementia?

Methods

We systematically searched electronic databases for articles published from as early as 1974 through May 2008, including MEDLINE, CINAHL, Psyc-INFO, EMBASE, Dissertations International, and the Cochrane Database of Systematic Reviews. In addition, we manually searched the reference lists of systematic reviews and continued to manually search databases up through September 2008. For each database, we used master heading terms relevant to dementia and stage (advanced, severe, or late stage) and treatments (treatments, therapies, interventions, psychotherapy). We limited the searches to research, systematic reviews, meta-analyses and practice guidelines. This broad search strategy identified interventions studies related to all types of treatments (pharmacological and non-pharmacological) for NPS in dementia. We saved all identified articles to an online research management database and then excluded all studies that did not meet inclusion criteria.

Inclusion criteria

English-language intervention studies published in peer-reviewed journals were reviewed that included: (i) all participants meeting criteria for severe or very severe dementia documented by the use of a validated cognitive or functional measurement instrument, and (ii) measures of NPS as the primary outcome variable(s). As shown in Table 1, severe dementia was defined by the: (a) Mini-mental State Examination (MMSE; Folstein *et al.*, 1975) with scores ranging from 0 to 10 out of a possible 30; (b) the Clinical Dementia Rating (CDR; Hughes *et al.*, 1982) stage 3 (Perneczky *et al.*, 2006); (c) the Global Deterioration Scale (GDS; Reisberg *et al.*, 1982) stages 6 (severe) and 7 (very severe); (d) the Functional Assessment Staging (FAST; Sclan and Reisberg, 1992) stages 6 (severe) and 7 (very severe); and (e) the International Classification of Diseases (ICD-10; World Health Organization, 2007) stage severe. By definition, cognitive impairment worsens with each increasing stage of dementia. For individuals who fall below a score of 6 on the MMSE, the Severe Impairment Rating Scale (Rabins and Steele, 1996) provides a measure of preserved cognitive function for very basic tasks.

In addition, studies that stratified participant responses by severity of cognitive impairment were included when they met all other criteria. When the range of severity scores was not reported, the determination of severity for inclusion in the review was based upon the mean cognitive impairment scores plus two standard deviations from the mean falling between 0 and 10 on the MMSE or an equivalent measure. (The cognitive impairment criterion was later broadened to include 0–17 on the MMSE or the equivalent.)

Exclusion criteria

Studies were excluded that: (i) had a primarily pharmacological treatment focus, or a combined pharmacological and non-pharmacological focus, including the use of herbal or dietary treatments; (ii) examined the effects of electrical stimulation; (iii) focused on palliative or end-of-life care (unless the focus was specifically on relieving NPS); (iv) focused on sleep dysfunction or sleep architecture in dementia (unless other NPS such as agitation were also outcomes of interest); or (v) were single case reports, observational studies, or qualitative studies.

Data synthesis

All studies meeting inclusion criteria were appraised for design strength and quality of evidence using an adapted version of the Johns Hopkins Nursing Evidence-Based Practice (JHNEBP) model (Newhouse *et al.*, 2007). The JHNEBP model includes three levels of strength referring to the rigor of the study design, and three broadly defined levels of quality that address sample size, experimental control, and the definitiveness of the conclusions. The same quality guidelines were used with the addition of a fourth component, the consistency of the direction of effects across studies, to evaluate groups of studies within intervention categories. The JHNEBP model was operationalized using criteria from the Forbes (1998) Validity Rating Tool.

Using the adapted rating tool (Table 2), the studies were first rated for strength of design. Experimental designs received a strength rating of Level I and quasi-experimental designs received a rating of Level II. Non-experimental Level III designs were not included in the review. Because of the difficulties inherent in doing clinical research with this frail population, nearing the end-of-life, we included in the Level I strength category the factorial or crossover designs in which individuals were randomly assigned to groups and participated in all conditions. Studies that lacked experimental control or the ability to randomize were included in the Level II category. The quality ratings were determined as follows: scoring proceeded top down, from high to low. For a study to have an evidence rating as high, all of the quality ratings had to be in the high category, with one exception. The only allowable diversion from the high grade for studies that qualified as high was the absence of a power analysis, as long as the criteria for sample selection were clear and the sample size was sufficiently large. Studies rated as having a moderate quality of evidence met all criteria from the moderate category or a combination of moderate and high categories. Finally, a low rating was given to studies that had any of the low quality of evidence indicators.

Results

Selection of studies

Of the 3826 manuscripts or dissertations identified by the initial search strategy, 3366 were excluded based on title and abstract. The majority were pharmacological interventions. Other initial exclusions included case studies, studies that were unrelated to dementia or neuropsychiatric symptoms, and duplicates that were not initially identified by the online research management software due to the format used in different electronic databases. The remaining 460 unique manuscripts, all related to non-pharmacological treatments in dementia, were retained and categorized in the online research management database. An additional seven systematic literature reviews and 30 manuscripts were located by manually searching online databases and references from systematic reviews. Eleven of the additional manuscripts were added after searching online databases for studies involving touch or massage therapies because the initial search did not identify them.

The next stage of the selection process involved eliminating manuscripts that were not relevant for reasons outlined in exclusion criteria (ii)–(v). In addition, we eliminated studies published prior to 1998 and systematic reviews that either did not include studies from the last ten years or that were not focused on the treatment of NPS in dementia. At this stage of the review, the 215 intervention studies were sorted into the four APA categories of non-pharmacological psychosocial treatments for dementia, identified within the most recent American Psychiatric Association (APA) practice guidelines (Rabins *et al.*, 2007). The studies were broadly categorized by the focus of the treatment, not by the actual NPS that were targeted by the treatment. For example, sensory-oriented treatments included studies

that used any treatment modality that would stimulate the senses (e.g. exercise, aromatherapy, music listening). Sensory-oriented treatments were sometimes targeting withdrawal behaviors (e.g. apathy) and other times targeting more disruptive behaviors (e.g. agitation). Emotion-oriented treatments were focused on increasing pleasure or reducing distress (e.g. validation therapy, and simulated presence). Behavior-oriented treatments considered were those that specifically focused on creating a safe and positive environment (e.g. adequate space, low noise and commotion, special care units) for individuals with advanced dementia. Although behavioral techniques including differential reinforcement and redirection would have been included in the behavior category, we did not find any studies that fit our inclusion criteria. Cognitive-oriented treatments would have included language-based treatments such as reality orientation, cognitive retraining, and skills training, but again, we found none for the treatment of NPS in advanced dementia.

The final stage of the selection process was to identify the studies that examined non-pharmacological treatments for advanced dementia. Of the 215 potentially relevant intervention studies, four studies examined interventions treating NPS in individuals with severe dementia defined by MMSE scores between 0 and 10, or the equivalent. By broadening the inclusion criteria of dementia severity to include studies using participant samples with moderately severe to severe dementia, that is, MMSE 0–17 (Tombaugh and McIntyre, 1992) or the equivalent, an additional 17 studies were identified. All of the selected studies are summarized in Table 3.

None of the systematic reviews was devoted to studies of individuals with advanced dementia. Out of the 22 relevant systematic reviews comprising 143 distinct intervention studies published between 2000 and 2008, only 11 studies (7.7%) described interventions developed specifically for individuals with advanced dementia characterized by moderately severe to very severe cognitive impairment. Complete references for the systematic reviews are presented as supplementary material (Appendix S1) in the online version of this paper available at www.journals.cambridge.org/jid_IPG.

Data synthesis

All four studies that focused on treating participants who met strict criteria for severe dementia examined the effects of non-language-based, sensory interventions on behaviors related to agitation. Three examined the effects of aromatherapy and one examined the effects of bright light therapy. After adding the additional 17 intervention studies that used patient samples meeting criteria for moderately severe to severe dementia (MMSE 0–17), the breakdown was as follows: four examined emotion-oriented approaches, three examined behavioral/environmental approaches, and 15 examined sensory-stimulation (including sensory-integration) approaches. One study (Garland *et al.*, 2007) compared the effects of an emotion-oriented (simulated presence) with a sensory-oriented (music) treatment and was therefore counted in both categories. None of the studies utilized cognitive-oriented interventions.

Emotion-oriented approaches

Four studies utilized emotion-oriented approaches to treat NPS in moderately severe to severe dementia. All used experimental Level I designs. Three were rated as providing high quality research evidence and the fourth was rated as moderate.

VERBAL AND NON-VERBAL EMOTION-FOCUSED CARE—Two multi-center randomized controlled studies examined the effects of specific emotion-oriented care on NPS in moderately severe to severe dementia. In both studies, nursing assistant caregivers in the experimental groups were trained to provide emotion-focused care, or an alternative (i.e.

usual care with equivalent attention). The emotion-focused care in the Magai *et al.* (2002) study relied on recognizing and validating non-verbal expressions of emotion. Several measurement tools were used to detect changes in NPS; however, the only significant effect was greater positive affect in the group receiving emotionally sensitive care in the six weeks following caregiver training. The integrated emotion-focused care in the Finnema *et al.* (2005) study involved training nursing assistants to integrate emotion-focused strategies (e.g. validation, reminiscence) into 24-hour care with the goal of improving emotional and social functioning. Participants with mild to moderate dementia showed an improvement in emotional adaptation following the intervention; however, there was no benefit to participants with severe dementia.

Although the findings from the two studies were inconsistent, the Magai *et al.* study specifically focused on non-verbal aspects of emotion, whereas in the Finnema *et al.* study, some of the interventions relied on preserved verbal capacity (e.g. reminiscence). Overall, the studies suggest that, for individuals with advanced dementia, sensitivity to non-verbal aspects of emotion may have some short-term positive effects on emotion, whereas strategies that depend on language capacity may not be as effective.

SIMULATED PRESENCE—Simulated presence therapy involves videotaped or audiotaped recordings of family members, including conversations, stories, or shared memories. Two studies (Camberg *et al.*, 1999; Garland *et al.*, 2007) examined the effects of simulated presence on agitated behavior in nursing home residents with moderately severe to severe dementia. Both studies required that participants have verbal interactive capacity, thus excluding individuals with the most advanced stage of dementia. Both compared a simulated presence audio recording to a neutral recording (news, gardening) and to usual care (no recording). In neither study were the interventions given during times of personal care.

The studies were consistent in showing that agitated behaviors decreased to a significantly greater extent during the simulated presence of a family member compared to a placebo recording and usual care. Camberg *et al.* reported reductions in agitation 67% of the time during simulated presence compared to reductions 46% of the time for placebo and 59% of the time for usual care. Garland *et al.* reported that 43% of the residents experienced a reduction of 50% or more in physical and/or verbal agitation while the simulated presence tapes were played. (However, Garland *et al.* also note that the placebo narration by a non-family member was just as effective as simulated presence in reducing verbal agitation.) Simulated presence was effective in reducing withdrawn behaviors 69% of the time compared to reductions of 55% with usual care and 34% with placebo (Camberg *et al.*, 1999).

The simulated presence recordings were simple to administer and were well received by most participants. Camberg *et al.* reported greater frequencies of happy expressions with simulated presence compared to the placebo and reported a low (9%) refusal rate. There do not appear to be lasting benefits. Although Garland *et al.* report that the reductions in physical and verbal agitation following simulated presence were still evident 15 minutes following treatment, Camberg *et al.* reported no significant difference in the reduction of agitation measured between simulated care phases and usual care phases as measured by a weekly short CMAI agitation inventory. Taken together, the two studies provide limited high quality evidence that simulated presence can be effective in reducing agitation and withdrawn behavior during (and shortly after) the time that it is provided.

Behavior or environment-oriented approaches

Three studies examined the effects of special care units on NPS in advanced dementia. The studies used quasi-experimental Level II designs with non-equivalent, naturally formed groups, and the interventions focused on the reduction of NPS.

SPECIAL CARE UNITS (SCUS)—Two multisite studies conducted in the Lombardy region of Italy report on the effectiveness of long-term special care units. Both presumably relied on the superior training of staff in treating NPS associated with moderately severe and severe dementia. Bellelli *et al.* (1998) describe the training of staff in SCUs to recognize behavioral problems, look for potential causes, and adapt medical procedures. Nurses were taught how to reduce high auditory and visual stimuli, with emphasis on gentle care and non-pharmacological therapies. They were also taught to promote and maintain functional performances through amusing activities, maintain nutritional intake, prevent falls, and reduce the unnecessary use of physical and pharmacological restraints. Frisoni *et al.* (1998) compared behavioral disturbances of residents from traditional nursing homes and SCUs at admission and at three months. They did not report specific intervention methods. Both studies reported reductions in NPS between admission and follow-up, although in the Frisoni *et al.* study, these were not significantly greater than the reductions of NPS in residents receiving traditional nursing home care. Because the interventions in the studies by Bellelli *et al.* and Frisoni *et al.* are not clearly specified or controlled, the studies were given a low quality rating and the findings cannot be generalized.

ENVIRONMENTAL MODIFICATIONS—Morgan and Stewart (1998) examined the behavioral effects of care environments that provide greater social and physical space for residents. Behaviors of residents with moderately severe to severe dementia were compared as one cohort of two was moved from existing high density SCUs to new low density SCUs. The lower density SCUs were created with more space (409 square feet per resident compared to 212 square feet), including private rooms. Over the 12-month follow-up period, disruptive behaviors decreased to a significantly greater extent in the low density as compared to the high density units. Because other uncontrolled factors such as the staff response to the new, modernized environment may have had some unspecified effect, the results of this study can only provide modest evidence that reducing social crowding may improve NPS in advanced dementia.

Sensory stimulation-oriented approaches

The majority (71%) of the intervention studies examining non-pharmacological treatments for NPS in advanced dementia involved sensory stimulation. Sensory-oriented approaches for advanced dementia included aroma, bright light, movement, multi-sensory, music and touch therapies.

AROMATHERAPY—Three of the four studies that specifically examined non-pharmacological treatments for NPS in severe dementia, used aromas. Aromatherapy involves the diffusion of an aromatic oil into the environment. Two oils that have been used to treat agitation are lavender and Melissa oil (lemon balm). In the four studies examining the effects of aromatic oils in patients with moderately severe to severe dementia, oils were delivered via a communal area diffuser (Holmes *et al.*, 2002), individual bedside diffusers (Lin *et al.*, 2007), sachets (Snow *et al.*, 2004), and skin cream (Ballard *et al.*, 2002). Dosage and exposure times varied greatly.

Holmes *et al.* (2002) reported that 60% of participants with behavioral problems showed a reduction in agitation with lavender compared with water steam. Lin *et al.* (2007) reported significant reductions in agitation, irritability, aberrant motor behaviors and dysphoria with

lavender therapy compared to placebo. The quality of evidence for these studies was moderate. Snow *et al.* (2004) reported no effect; however, the quality of evidence was low due to the use of a small (*n*=7) convenience sample.

Only one Level I high quality study, by Ballard *et al.* (2002), examined the effects of lemon balm on agitation in individuals with severe dementia. Agitation was significantly reduced by 35% with a lemon balm skin lotion compared to a placebo reduction of 11%. In addition to agitation, Ballard *et al.* reported a significant reduction in the percentage of time spent socially withdrawn and an increase in the percentage of time engaged in constructive activities among people receiving the lemon balm treatments.

With few exceptions, aromatherapy was well accepted and easy to administer. None of the studies carried out any long-term follow-up so it is unclear whether there are any persisting benefits of aromatherapy. Overall, the limited moderate to high quality evidence suggests that lavender- and lemon balm-based aromatherapies may be effective in reducing agitation and apathy during the time that they are administered.

BRIGHT LIGHT THERAPY—Fragmented sleep-wake cycles in dementia can be associated with aberrant behaviors (wandering, yelling, delirious episodes). Two studies examined the effects of bright light treatment on sleep-rest cycle and aberrant behaviors of dementia. Skjerve *et al.* (2004) exposed 10 participants with severe dementia to morning bright lights for 45 minutes each morning for four weeks. Mishima *et al.* (1998) used a randomized crossover design to expose 22 participants with moderate to severe dementia to two light dosages: bright light and dim light. Lights were presented for two hours per day for two weeks with a 4-week interval between sessions. Activity was monitored continuously with wrist actigraphs. Both studies reported a significant reduction in aberrant behavior with bright light treatment; however, the overall quality of the evidence is low. Skjerve *et al.* (2004) had a small sample and did not include data from one participant who had increased agitation and confusion during the second week and was dropped from the study. Mishima *et al.* (1998) monitored physical activity but used no other agitation or NPS measures.

MOVEMENT THERAPY—Although many individuals with advanced dementia are frail, many are motivated to move, and display wandering behaviors or agitated physical behaviors. Two studies have examined the effects of structured movement therapies on NPS in moderately severe dementia. Both combined movement with interactive activities such as balloon volleyball, clapping hands, passing a ball (Holliman *et al.*, 2001) and imagined bread baking, swimming, and flying with birds (Heyn *et al.*, 2003). Heyn *et al.* incorporated exercise into a multi-sensory activity that also included music and storytelling in their intervention. Holliman *et al.* found no differences between the experimental and control groups, but reported good participation in the interactive activities with an increase in positive participation (81.6%) relative to other behaviors (18.4%). Heyn *et al.* reported that 61.5% of the participants looked happier, calmer, or friendlier after participating in the exercise. Although there is consistency between the findings of the two studies in terms of participation and engagement, the sample sizes were small and the study by Holliman *et al.* did not describe the activities or size of the control group. Overall, the two studies have major flaws that limit the interpretation of evidence for the possible benefits of movement therapies on NPS in advanced dementia.

MUSIC—Three studies examined the effects of music on NPS in moderately severe to severe dementia (MMSE 0–17; GDS 5–7). Garland *et al.* (2007) compared responses of participants selected for behavioral disturbances across randomly ordered presentations of pre-recorded preferred music, simulated presence (recorded conversations by family members), a placebo recorded narration from a gardening book, and usual care. The 15-

minute audiotaped recordings were each presented three times per week interspersed by a washout period. Svansdottir and Snaedal (2006) compared behavioral responses to interactive live familiar music with usual care. Residents in the lively music group listened to familiar songs and joined in as desired. The groups lasted 30 minutes each and were presented three times a week over a six-week period. Holmes *et al.* (2002) compared responses of participants selected for apathy across three 30-minute back-to-back randomly ordered music sessions that included live, pre-recorded music that was the same popular music as in the live session, and silence.

All three studies reported significant reductions in NPS during music therapy. Agitated behaviors were reduced to a greater extent with live (Svansdottir and Snaedal, 2006) or pre-recorded preferred music (Garland *et al.*, 2007) than usual care. In the Garland *et al.* study, 50% of the participants demonstrated a reduction in agitated behaviors of 50% or more during preferred music. In the Holmes *et al.* (2006) study, apathy was reduced to a greater extent with live music (69% of participants showed positive engagement) than prerecorded music (25% engaged) or silence (12.5% engaged). Lasting benefits of music therapy were found to be present at 15 minutes (Garland *et al.*), but not at four weeks (Svansdottir and Snaedal) post-treatment. Overall there is limited but good quality evidence supporting the use of music therapy for the short-term reduction of agitation and apathy. Interactive live music and preferred music appear to be more beneficial than pre-recorded music for individuals with advanced dementia.

MULTI-SENSORY STIMULATION (MSS)—Multi-sensory stimulation, otherwise known as Snoezelen therapy, stimulates the senses through the provision of unpatterned visual, auditory, olfactory, and tactile stimuli. Individuals are given the opportunity to explore a variety of stimuli in a specially prepared room. The purported goal is to create a pleasant non-verbal experience for individuals with severe dementia, and it is generally considered to be an emotion-oriented approach. It is included in the stimulation-oriented approaches here because of the overlap with other sensory stimulation approaches. Two studies by Baker *et al.* (2001; 2003) examined the effects of MSS on samples of participants with moderately severe to severe dementia. Both were randomized controlled trials comparing four weeks of MSS to a control activity requiring intellectual or physical skills (playing cards, doing quizzes, and looking at photographs).

Using a sample of participants from a day hospital, Baker *et al.* (2001) found significant reductions in dysphoric mood and behavior following MSS (later in the day after participants returned to their residences) compared to activity therapy. In a replication of the study with a larger sample of participants from three different countries, Baker *et al.* (2003) found no differences in NPS between the MSS and activity conditions. Only when they compared individuals with severe dementia (MMSE 0–9) to individuals with moderately severe dementia (MMSE 10–17) did they see a difference between conditions. Participants with severe dementia showed a reduction in apathy following MSS and an increase in apathy following the activity group. In contrast, individuals with moderately severe dementia showed the opposite pattern with an increase in apathy following the MSS intervention and a decrease in apathy following the activity intervention. Although interesting, Baker *et al.* (2003) do not report the number of participants in the severe and moderately severe stratified subgroups and apparently performed these analyses *post hoc*, so the interpretation of these results is limited. Overall, there is high quality, but very limited, evidence suggesting that non-verbal MSS is more effective than intellectual interventions for reducing apathy in individuals with severe dementia.

TOUCH—Touch therapies can include massage, hand massage, therapeutic touch, and craniosacral therapies. Craniosacral still point technique is thought to induce relaxation and

increase symmetry and amplitude of the craniosacral rhythm (Gerdner *et al.*, 2008). Gerdner *et al.* are the only researchers to publish findings related to the treatment of agitation in moderately severe dementia (GDS 5–7) using this technique. They report a significant reduction in physical and verbal agitation from pretreatment to post-treatment following six weeks of daily craniosacral therapy. The sample size was very small, and required the use of certified craniosacral therapists. No other touch therapy studies met criteria for the review. Overall there is insufficient evidence to support the use of touch therapies to treat NPS in advanced dementia.

BALANCING AROUSAL CONTROLS EXCESSES (BACE)—Kovach *et al.* (2004) developed the BACE intervention based upon Kovach's Model of Imbalance of Sensoristasis (MIS). The model posits that agitated behaviors in advanced dementia may be initiated or exacerbated when there is an imbalance between sensory-stimulating and sensory-calming activity. In a randomized controlled trial, Kovach *et al.* determined whether arousal imbalances (defined as sustained arousal states lasting 1.5 hours or longer) existed in the experimental group, and then implemented individualized activity schedules for those who had imbalanced arousal states (defined as 2.5 or more hours of imbalance over a 12-hour observation period) that balanced the arousal states throughout the day. Compared with the treatment-as-usual group, the mean agitation level decreased significantly in the experimental group following the intervention. Although the experimental intervention was only conducted over a 12-hour period, the study provides moderate quality evidence supporting interventions that balance arousal states for the treatment of agitation in advanced dementia.

Discussion

This systematic review examined published studies of non-pharmacological interventions aimed at reducing NPS in advanced dementia. All of the identified studies took place in day hospitals or residential care facilities. Eleven countries were represented. The number of studies examined was limited by the use of only those studies published in the English language and by limiting the review to the decade spanning from 1998 to 2008. One challenge the review faced was that many studies report mean and standard deviations for MMSE scores but not the range of scores. Because these measures of central tendency are affected by sample size, it was not always clear whether all participants fell within the range of moderately severe to very severe dementia. Only studies reporting that all participants met the dementia severity criteria were included in this review. This decision rule resulted in the exclusion of some important studies that reported mean cognitive impairment scores within the range of severe impairment. A review of a sample of these studies indicated that their findings were consistent with the conclusions of this review (e.g. Gerdner, 2000; Lawton *et al.*, 1998).

What progress has been made in the last decade in treating NPS in severe dementia?

Ten years ago, Opie *et al.* (1999) reviewed the progress of the previous ten years of research on psychosocial interventions for treating behavioral disorders of dementia. Without examining interventions by cognitive severity level, they found only one study of the 43 reviewed that had strong validity. They recommended that future studies be conducted in more than one facility, include greater numbers of participants, and use multivariate analyses or multiple outcome measures. They recommended that staff receive adequate training and that the final report provide sufficient details to permit replication. This review demonstrates that some progress has been made in reaching these goals. Of the 21 identified intervention studies from 11 different countries that focused specifically on individuals with moderately severe to very severe dementia, 12 used randomized controlled trial designs, 15

collected data from multiple facilities allowing access to larger sample sizes, and 20 used valid and reliable NPS outcome measurement tools.

Despite the progress that has been made in understanding and treating NPS in advanced dementia, questions remain. Only 21 out of the 215 (9.8%) studies identified from this systematic review of the literature sought to identify non-pharmacological treatments specific to individuals with moderately severe to very severe dementia, and only four (1.9%) examined treatments specific to severe or very severe dementia. Given that approximately 40% of nursing home residents with dementia have severe to very severe cognitive impairment (Gruneir *et al.*, 2007) and that the great majority of those residents suffer from NPS (Zuidema *et al.*, 2007; Kverno *et al.*, 2008), there remains much to be learned. In advanced dementia, as the ability to understand language decreases, the prevalence of resistiveness to care, often labeled as aggressiveness, increases up to eightfold (Volicer *et al.*, 2007). This highlights the importance of identifying efficacious non-pharmacological strategies to reduce distress during personal care.

What are the critical elements for clinicians to address, given what we know now?

It is now clear that NPS do not “burn out” or become less problematic as dementia progresses. Individuals with advanced dementia are likely to be suffering from distressing symptoms that can have multiple etiologies. For example, NPS can represent discomfort, unmet physical care needs, person-environment conflicts (arousal imbalances), and stress responses. The approach taken to address these symptoms will depend, at least in part, upon the identified etiology and the assessed meaning of the symptom. Nonetheless, given that the overarching goal of identifying and treating NPS is to improve comfort and enhance quality of life, we found moderate to high quality, albeit limited, evidence of efficacy for the following interventions:

- physical environments that minimize social and spatial crowding (Morgan and Stewart, 1998);
- staff that are trained to be sensitive to and validate the non-verbal expression of emotion (Magai *et al.*, 2002);
- individualized schedules that utilize a variety of activities or interventions to correct identified arousal imbalances (Kovach *et al.*, 2004);
    - Interventions for reducing underarousal states (apathy) or increasing engagement include:
        - simulated presence (Camberg *et al.*, 1999)
        - aromatherapy with lemon balm (Ballard *et al.*, 2002)
        - multi-sensory stimulation (Baker *et al.*, 2001; 2003) especially for individuals with severe cognitive impairment
        - listening to live music (Holmes *et al.*, 2006).
    - Interventions for reducing overarousal states such as agitation, aberrant motor behavior, and irritability include:
        - simulated presence or recorded conversation (Camberg *et al.*, 1999; Garland *et al.*, 2007)
        - aromatherapy with lavender (Holmes *et al.*, 2002; Lin *et al.*, 2007) or lemon balm (Ballard *et al.*, 2002)

- listening to preferred, or live interactive music (Garland *et al.*, 2007; Svansdottir and Snaedal, 2006).

It is important to note that the studies using simulated presence required participants to have verbal interactive capacity, so the findings may not apply to individuals with severe cognitive impairment. For these individuals, non-demanding, non-verbal, sensory-based treatments for NPS (music, aromatherapy, and multisensory stimulation) appear the most efficacious. Other potentially promising non-verbally based interventions involving hands-on (touch) therapies, movement therapies, and personal care approaches need to be further explored.

What are the critical elements for researchers to address in identifying relevant treatments for advanced dementia?

Many published intervention studies did not meet criteria for inclusion in this review because they included individuals with a broad range of severity levels without stratifying or using a standardized measure of severity. We believe that the data are convincing that interventions aimed at reducing NPS must examine disease severity as a moderating feature and that assuming that interventions will be equally efficacious across severity levels is a mistake. This is particularly true since many interventions appear to rely on relative preservation of language and cognitive skills (e.g. reminiscence) or on preserved psychomotor functioning (e.g. movement therapies). For example, three studies in this review showed that individuals with advanced dementia respond differently than individuals with mild-moderate dementia to non-pharmacological interventions. Individuals with advanced levels of dementia did not benefit as much as individuals with mild to moderate severity from integrated emotion-oriented care (Finnema *et al.*, 2005), language based activities such as card games (Baker *et al.*, 2003), and pre-recorded music (Holmes *et al.*, 2006). In contrast, they benefited to a greater extent from non-verbal patterned multisensory stimulation (Baker *et al.*, 2003). At a minimum, researchers should either stratify participant samples by severity or limit inclusion to individuals with advanced disease.

Issues of treatment fidelity are important when evaluating the effectiveness of research interventions. For example, Kovach *et al.* (2006) deconstructed the negative findings of a randomized controlled multi-site intervention study using a combined pharmacological and non-pharmacological serial treatment intervention (STI) to address NPS and discomfort in advanced dementia and noted that the consecutive steps of the protocol were not followed for nearly half of the participant residents, despite the seven hours of classroom protocol instruction, site visits, and compliance checks given to the 22 experienced nurses across 14 different nursing care centers. Given the range of potential barriers to fidelity (e.g. staffing, workload, perceptions of relevance), researchers must attend to this issue for studies to guide future care.

The key effective elements of many interventions are often not clear. For example, in the study by Garland *et al.* (2007), individuals with advanced dementia (MMSE 0–12) showed similar decreases in verbal agitation in response to recorded voices whether or not they were familiar (simulated presence) or relevant (gardening narration). In the study by Camberg *et al.* (1999), weekly staff surveys suggested that usual care and simulated presence were equally effective in increasing positive affect compared with placebo. These findings bring up questions regarding whether observed benefits of non-pharmacological treatments result from the specific types of treatments or perhaps some other unidentified effects such as novelty, or the non-demanding calm presence of a caregiver or human voice. Finally, when measuring behavior change, the importance is to identify clinically meaningful changes that reduce distress and improve quality of life. Despite the apparent lack of long-term consequences of the identified sensory-oriented non-pharmacological interventions, the

short-term benefits of decreased agitation or increased engagement would appear to be clinically meaningful.

Recommendations for the next decade of research on treating NPS in advanced dementia include those mentioned by Opie *et al.* (1999) a decade ago: use of rigorous methods, larger numbers of subjects, a wider range of settings, and multiple methods and measures. Terms such as agitation and aggression are often non-specific and must be operationalized by both clearly describing the behaviors and by specifying the context (e.g. combativeness during personal caregiving activities). Promising non-pharmacological, intellectually non-demanding interventions for NPS that have been examined in individuals with mild to moderate dementia should be tested for efficacy in advanced dementia. A variety of existing models for behavioral care (e.g., Finnema *et al.*, 2000; Volicer and Hurley, 2003) provide excellent frameworks for future research.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Staging of advanced dementia

SCALE	SEVERITY LEVEL	CHARACTERISTICS
Clinical Dementia Rating (CDR; Hughes *et al.*, 1982)	CDR 3: Severe	Severe memory loss; only fragments remain. Orientation to person only. Unable to make judgments or solve problems. No significant function in home outside of own room. Requires much help with personal care; often incontinent.
Functional Assessment of Alzheimer Disease (FAST; Sclan and Reisberg, 1992)	Stage 6: Moderately Severe	Requires physical assistance in putting on clothes properly. Requires assistance in bathing properly. Requires assistance with mechanics of toileting. Urinary incontinence. Fecal incontinence.
	Stage 7: Severe	Speech limited to about six words in the course of an average day. Intelligible vocabulary generally limited to a single word in the course of an average day. Ambulatory ability lost. Ability to sit up lost. Ability to smile lost. Ability to hold head up lost.
Global Deterioration Scale (GDS; Reisberg *et al.*, 1982)	Stage 5: Moderately Severe	Patients can no longer survive without assistance. They cannot recall major relevant aspects of current lives. May be disoriented to time or place. They require no assistance with toileting or eating but may require help choosing proper clothing and dressing.
	Stage 6: Severe	Largely unaware of all recent events and experiences. Retain some knowledge of past lives. Unaware of surroundings. Require substantial assistance with ADLs. May be incontinent. Frequently exhibit neuropsychiatric symptoms.
	Stage 7: Very Severe	All verbal abilities are lost. Incontinent of urine. Requires assistance in toileting and in eating. Loss of psychomotor skills. Generalized cortical and focal neurologic signs and symptoms are frequently present.
International Classification of Diseases (ICD-10; World Health Organization, 2007)	Severe	The degree of memory loss is characterized by the complete inability to retain new information. Only fragments of previously learned information remain. The individual fails to recognize even close relatives. The decline in other cognitive abilities is characterized by an absence, or virtual absence, of intelligible ideation.
Mini-mental State Examination (MMSE)	Moderately severe*	Score range is 11–17 *Tombaugh and McIntyre (1992)
Folstein *et al.* (1975)	Severe	Score range is 0–10
Severe Impairment Rating Scale (SIRS) Rabins and Steele (1996)	Very Severe	Determines severity level for individuals who score less than 6 on the MMSE.

Table 2

Strength and quality of research evidence rating scheme for individual studies

LEVEL	STRENGTH OF EVIDENCE/DESIGN	YES	OR NO
I	Evidence obtained from an experimental study/randomized controlled trial. Includes factorial or crossover designs where individuals were randomly assigned to groups that each had a different order of treatment.	—	—
II	Evidence obtained from a pre-experimental or quasi-experimental study that lacked either randomization or control.	—	—
III	Evidence obtained from a non-experimental study, qualitative study, or meta-synthesis.	—	—
GRADE	QUALITY OF RESEARCH EVIDENCE		
High	• Sample: power analysis reported	—	—
	• Control: confounders controlled, equivalent groups, equivalent attention and diversion in treatment and control conditions	—	—
	• Methods: description permits replication	—	—
	• Conclusion validity:		
	• Attrition: ≤10% or use of intent-to-treat or other appropriate methods for analyzing missing data	—	—
	• Use of at least one validated and reliable outcome measurement tool	—	—
	• Investigators blinded to participant group allocation	—	—
Moderate	• Sample: clear criteria for how sample was selected	—	—
	• Control: non-equivalent groups or unequal attention and diversion in comparison condition(s)	—	—
	• Methods: major details are described	—	—
	• Conclusion validity:		
	• Attrition: 11–20% or analysis of attrition rates and group equivalency	—	—
	• Use of at least one validated and reliable outcome measurement tool	—	—
	• Some attempt to limit potential investigator/rater bias	—	—
Low/major flaw(s)	• Sample size: no explanation, small convenience sample (n ≤ 10)	—	—
	• Control: no attempt made to control relevant confounders	—	—
	• Methods: inadequate description	—	—
	• Conclusion validity:		
	• Attrition >20%, not analyzed, or not reported	—	—
	• Data collection did not use validated measures (of NPS)	—	—
	• Potential investigator/rater bias	—	—

Note: Adapted from *Johns Hopkins Nursing Evidence Based Practice* (JHNEBP: Newhouse *et al.*, 2007) and the Validity Rating Tool (Forbes, 1998). A criterion of consistency of findings was also included when evaluating intervention evidence across related studies.

Table 3

Summary of studies examining non-pharmacological treatments for NPS in moderately severe to severe dementia (MMSE 0–17; Tombaugh and McIntyre, 1992)

AUTHORS AND LOCATION	SEVERITY OF COGNITIVE IMPAIRMENT	TREATMENT AND COMPARISON GROUPS	NPS SYMPTOMS AND OUTCOME MEASURES	TIMING OF DATA COLLECTION PERIODS AND FOLLOW-UP	RESEARCH DESIGN	RESULTS	STRENGTH / QUALITY
EMOTION-ORIENTED TREATMENTS							
Finnema *et al.* (2005) Netherlands: 16 psychogeriatric wards in 14 nursing homes	Stratified by severity: Severe (GDS 5–6): n = 70 Moderate (GDS 3–4): n = 69 Mild (GDS 1–2): n = 7	Integrated emotion-oriented care: n = 67 Usual care: n = 79 146/194 completed: 25% attrition	Behavioral and mood disturbances Measures: CSDD CMAI	Baseline, 3, and 7 months.	Pretest-posttest, cluster (by ward), RCT. Matched nursing assistants, blinded to which residents were participating, were trained to administer either protocol and integrate it into 24 hr care. (High attrition, mostly due to death, was equally distributed.)	No benefit over usual care for participants with severe dementia. Participants with mild and moderate severity of dementia benefited from emotion-focused care, showing greater emotional adaptation than those in usual care.	Level I / Moderate
Magai *et al.* (2002) U.S.A.: 3 nursing homes	MMSE 3.4 ± 5.0	1. Non-verbal sensitivity: n = 41 2. Behavioral placebo: n = 23 3. Control (waitlist): n = 27 8% attrition.	Affect & Behavior Measures: BEHAVE-AD CMAI CSDD Facial expression	Baseline and every three weeks until 12 wk post-training (of caregivers)	Double-blind, cluster (by nursing home) RCT with repeated measures. Manualized caregiver training administered over 2 weeks by a psychologist who was blind to condition and hypotheses. Blinded research assistants completed all ratings.	No differences in behaviors between groups. Positive affect increased sharply during the first 6 wk following non-verbal sensitivity training*, but no differences between groups remained by 12 wks.	Level I / High
• **Simulated Presence (SP)**							
Camberg *et al.* (1999) U.S.A.: 9 nursing homes	MMSE 5.1 ± 4.4 Excluded residents who did not have verbal interactive capacity.	1. SP 2. Placebo 3. Usual care N = 54. Partial attrition (n = 5) did not affect analyses.	Agitation, withdrawal Measures: Direct observation Weekly staff survey included: Short CMAI MOSES	Direct observation on pre-determined schedule for 3 hr, 20min/wk. Staff documented responses to treatments. Weekly staff surveys.	Double-blind, Latin-square, 3-factor with restrictive randomization of treatments. Treatments: were each continued for 17 days over a 4-wk period with a 10-day washout. Nursing staff observers were blinded to the interventions.	Staff observations: SP was better in reducing agitation and withdrawal than usual care*** or placebo***. Weekly staff surveys on CMAI and MOSES did not show any benefit from SP over usual care and both resulted in more positive affect than placebo***.	Level I / High

AUTHORS AND LOCATION	SEVERITY OF COGNITIVE IMPAIRMENT	TREATMENT AND COMPARISON GROUPS	NPS SYMPTOMS AND OUTCOME MEASURES	TIMING OF DATA COLLECTION PERIODS AND FOLLOW-UP	RESEARCH DESIGN	RESULTS	STRENGTH / QUALITY
Garland *et al.*, 2007 Australia: 9 nursing homes	MMSE 2.5, range 0–12 Excluded residents who did not have verbal interactive capacity.	1. SP 2. Preferred music 3. Placebo 4. Usual care N = 30. No attrition.	Agitation Measures: CMAI	Direct observation before during and after exposure to 15 minute tapes.	Repeated measures with randomized crossover. Random assignment to groups that received treatments in different orders. Conditions delivered by 15 min. audiotape 3days/wk for each condition. Researchers were blinded to tape content.	Decreased physical agitation during treatment with SP compared to placebo** and usual care**. Decreased verbal agitation during treatment with SP compared to usual care*. No difference between SP and music.	Level I/High
BEHAVIORAL AND ENVIRONMENTAL TREATMENTS							
Bellelli *et al.* (1998) Italy: 8 SCUs	MMSE 6.1 ± 5.0, range 0–14	Consecutive patients: N = 55 Attrition not reported.	Behavioral and mood disturbances Measures: NPI	Measurements at baseline, 3 months, and 6 months after admission.	Single-group pretest-posttest. Special training of nursing staff provide gentle care while reducing high auditory stimuli and fast movements.	Decreases in agitation*, apathy**, and aberrant motor*** at 3 mos. Decreases in agitation***, apathy*, and aberrant motor*** at 6 mos.	Level II / Low
Frisoni *et al.* (1998) Italy: 43 nursing homes, 25 with SCUs	MMSE range 0–16	SCU: n = 31 NH usual care: n = 35 Attrition not reported.	Behavioral disturbances Measures: NPI, CMAI, CSDD.	Baseline and 3 months after admission	Non-equivalent groups, pretest-posttest. Treatment not described.	Reduction in NPI motor subscale** and CSDD* in both groups after 3 mos., although the patterns of specific NPS reductions differed.	Level II / Low
Morgan and Stewart (1998) Canada: 2 long-term care facilities	GDS 5–6 Excluded GDS 7 (due to immobility)	Low density SCU n = 39 Traditional SCU n = 11 53/59 completed: 10% attrition.	Disruptive and non-disruptive behavior Measures: EBIC	Baseline, 6 months and 12 months following re-location.	Non-equivalent groups, 2×3 factorial. Convenience sample of nursing home residents moving from their SCU to other SCUs with lower social and spatial densities. Comparison group sample remained in the traditional SCU.	Greater decrease over time in disruptive behaviors in the experimental (low-density) group than in the comparison (constant high density) group**.	Level II / Moderate
SENSORY-ORIENTED TREATMENTS							
• **Aromatherapy**							

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AUTHORS AND LOCATION	SEVERITY OF COGNITIVE IMPAIRMENT	TREATMENT AND COMPARISON GROUPS	NPS SYMPTOMS AND OUTCOME MEASURES	TIMING OF DATA COLLECTION PERIODS AND FOLLOW-UP	RESEARCH DESIGN	RESULTS	STRENGTH / QUALITY
Ballard *et al.* (2002) U.K.: 8 nursing homes	CDR3	Melissa oil: n = 36 (35 completed) Sunflower oil: n = 36 71/72 completed: 3% attrition	Agitation Measures: CMAI NPI (Aberrant motor subscale)	Baseline, and weekly for 4 wk.	Double-blinded cluster (by facility) RCT. Eight facilities, randomly assigned to treatment or placebo. The oils were applied within a skin cream to face and arms twice per day over a 4 wk period.	Reductions in agitation** in both groups. Irritability and aberrant motor improved to a greater extent with aromatherapy compared to placebo***. Greater reduction in social withdrawal and increase in time spent in constructive activities with aromatherapy compared to placebo**.	Level I / High
Holmes *et al.* (2002) U.K.: Long-term stay unit for patients with behavioral problems.	ICD-10 severe dementia	1. Lavender oil 2. Water N = 15	Agitation Measures: PAS	During treatment only. No baseline or follow-up.	Single-group repeated measures, with alternating daily aroma treatments 2 hr/day for 10 days. Aroma-streams were administered in a communal area. Raters were blinded (nose calipers) to treatment.	The median PAS score was lower (reduced agitation) during aromatherapy compared with placebo*.	Level II / Moderate
Lin *et al.* (2007) Hong Kong: Care and attention homes	CMMSE 7.8 ± 3.4, range 0–14	1. Lavender aroma 2. Sunflower aroma N = 70 No attrition.	Agitation Measures: Chinese versions of CMAI and NPI	Before and after each treatment period.	Repeated measures with randomized crossover. Aromas were delivered by diffuser at night for at least one hour for 3 wk, with 2 wk washout between conditions.	Decrease in agitation with lavender treatment with reduced scores on both C-CMAI and C-NPI***. No change following sunflower treatment.	Level I / Moderate
Snow *et al.* (2004) U.S.A.: Nursing home	SIRS 13.2 ± 5.25, range 8–18	3 Oils: A. Lavender B. Thyme C. Grapeseed (unscented) N = 7. No attrition.	Agitation Measure: CMAI	Every other day during the 4 wk baseline, 10 wk intervention and 2 wk post-treatment.	Single-group repeated measures (ABCBA). Oils were worn for 3 hr on a sachet near the collarbone on treatment days. Following 4 wk baseline, each treatment was given for 2 wks in the same order.	Total absence of treatment effect.	Level II / Low
• Bright Light Therapy							
Mishima *et al.* (1998) Japan: 1 long-term care facility	MMSE range 3–17	Light 1. Bright 2. Dim	Symptom: Rest-activity rhythm Measure: Actigraph	Baseline, wk 1, wk 2, and post-treatment. Continuous 1 min	Repeated measures with randomized crossover. Compared therapeutic effect of morning bright light and	Reduction in nighttime activity and percentage of nighttime activity to	Level I / Low

AUTHORS AND LOCATION	SEVERITY OF COGNITIVE IMPAIRMENT	TREATMENT AND COMPARISON GROUPS	NPS SYMPTOMS AND OUTCOME MEASURES	TIMING OF DATA COLLECTION PERIODS AND FOLLOW-UP	RESEARCH DESIGN	RESULTS	STRENGTH / QUALITY
		N = 22 with sleep and behavioral disturbances No attrition.		rest-activity monitoring.	dim light, each presented for 2 wk period, with 4 wk washout. No NPS measures.	total activity with bright light for Ss with vascular dementia** but not for those with Alzheimer's dementia.	
Skjerve *et al.* (2004) Norway: 2 psychogeriatric institutions	MMSE range 0–11 CDR 3	Bright Light Therapy N = 11 10 completed: 9% attrition	Agitation and behavioral symptoms Measures: CMAI BEHAVE-AD, and Actigraph	2 wk baseline, during, and 2 wk after treatment.	Single-group repeated measures. Bright light for 45 min each morning for 4 wk. Continuous activity monitoring for 6 wk (one week of baseline and post-treatment.	Decrease in agitation and behavioral symptoms from pre to post-treatment**. No improvement in sleep-wake measures (actigraph). (One participant was dropped due to increased agitation.)	Level I / Low
• **Movement Therapy**							
Heyn (2003) U.S.A.: Nursing home	MMSE 7.25 ± 3.4, range 1–12	Multi-sensory exercise program: N = 13 No attrition.	Engagement and mood Measures: MPES CMR	Direct assessment of engagement and mood during exercise program.	Single-group pretest-posttest. All participants received the MSS exercise program 3 times per wk for 8 wk. Duration of exercise increased over time from 15 min. to 70 min.	69% of the participants engaged in more than half of the activity (MPES). 61.5% of the participants showed improvement ratings of facial expression/ mood (CMR).	Level II / Low
Holliman *et al.* (2001) U.S.A.: Geriatric psychiatry facility	MMSE 4.6 ± 4.9, range 0–13	Interactive physical activity (E) Unspecified control N = 12. 12/14 completed: 14% attrition	Behavioral disturbances Measures: PGDRS (behavior subscale) PBRS (E group only)	Baseline, twice during intervention sessions, and once at post-test (total = 4 times) for each session.	Pretest–post-test with random assignment to either the interactive physical activity (E) or control group. E group met for 30 min. 3/ wk for 2 wk. Socialization with snack followed activity. Repeated measures on PBRS for E group only. Control group was not described.	E group participants had less disruptive behavior and more positive behavior during group sessions than before (PBRS). No lasting benefits: E group had more disruptive behavior than control group (PGDRS) following sessions*.	Level II / Low
• **Music Therapy**							
Garland *et al.* (2007) See emotion-oriented treatments for full summary.						Decreased physical agitation during preferred music compared to usual care (no treatment)*.	Level I / High

AUTHORS AND LOCATION	SEVERITY OF COGNITIVE IMPAIRMENT	TREATMENT AND COMPARISON GROUPS	NPS SYMPTOMS AND OUTCOME MEASURES	TIMING OF DATA COLLECTION PERIODS AND FOLLOW-UP	RESEARCH DESIGN	RESULTS	STRENGTH / QUALITY
						Decreased verbal agitation after preferred music compared to placebo**.	
Holmes *et al*. (2006) U.K.: 4 residential and nursing homes	Stratified by severity ICD-10: moderate (n = 14), and severe (n = 18) dementia	Music: 1. Live 2. Pre-recorded 3. Silence N = 32 No attrition	Apathy Measures: Participant videos were rated for engagement (category E) on the DCM	DCM category E scores were obtained 10 times during each condition for each participant.	Repeated measures with randomized crossover. Each of the three musical conditions was presented in one session lasting 1 1/2 hr (30 min per condition). Attempt to blind observer raters was ineffective.	Greater positive engagement during live music than silence**. Greater engagement during live music than pre-recorded music**. Engagement during pre-recorded music was not significantly different than silence.	Level I / Moderate
Svansdottir *et al.* (2006) Iceland: 2 nursing homes and 2 psychogeriatric wards	GDS 5–7	Music therapy: n = 23 (20 completed) Usual care: n = 23 (18 completed) 17% attrition.	Behavioral disturbances Measures: BEHAVE-AD	Baseline, 6 wk and 4 wk post-treatment	Pretest-posttest with random assignment to group. Interactive music group received 18 sessions (singing familiar music with guitar), 30 min each, 3 times/wk × 6 wk. Usual care not described. Raters blinded to condition.	Reduction in combined symptom scores for activity disturbance, aggressiveness, and anxiety**. No change in control group. Benefits of music therapy disappeared by 4 wk follow-up.	Level I / Moderate
• **Multi-sensory Stimulation (MSS)**							
Baker *et al.* (2001) U.K.: Day hospital	MSS group: MMSE 10.96 ± 6.5 Activity group: MMSE 6.08±5.07 MMSE range 0–17	MSS: n = 25 (23 completed) Activity: n = 25 48/50 completed: 4% attrition	Behavior and mood Measures: INTERACT REHAB BMD BRS	Baseline, mid-trial and post-trial. Before, during, and after sessions. Follow-up at 1 month post-treatment.	RCT with repeated measures. Two 30 min sessions / wk. over 4 wk period (8 total). Both treatments were individualized according to preferences and functional abilities.	Improved mood and interest after both treatments**. Greater increase in attentiveness to environment after MSS than activity sessions*. Greater improvement in mood and behavior at home compared to the activity group whose behavior deteriorated*. Benefits disappeared by 1 month follow-up.	Level I / High

AUTHORS AND LOCATION	SEVERITY OF COGNITIVE IMPAIRMENT	TREATMENT AND COMPARISON GROUPS	NPS SYMPTOMS AND OUTCOME MEASURES	TIMING OF DATA COLLECTION PERIODS AND FOLLOW-UP	RESEARCH DESIGN	RESULTS	STRENGTH / QUALITY
Baker *et al.* (2003) U.K.: Day hospital. Netherlands and Sweden: psychogeriatric wards.	MMSE 0–17 with post-hoc stratification by severity level.	MSS: n = 65 (62 completed) Activity: n = 71 (65 completed) 127/136 completed: 7% attrition	Behavior and mood Measures: INTERACT REHAB BMD BRS	Baseline, mid-trial and post-trial. Before, during, and after each session. Follow-up at 1 month post-treatment.	RCT with repeated measures. Two 30 min sessions / wk. over 4 wk period (8 total). All but 20 participants were randomized to treatment groups. MSS treatments were non-directive and sensory focused. Activities were focused on tasks that demanded intellectual or physical involvement.	Apathy decreased in both groups***. Severity by time interaction**. MMSE 0–9 were less apathetic at post-trial following MSS and more apathetic following activity group. MMSE 10–17 had the opposite pattern. Benefits disappeared by 1 month follow-up.	Level I / High
• Touch Therapy							
Gerdner *et al.* (2008) U.S.A.: 2 nursing homes	GDS 6.25, range 5–7	Craniosacral still point technique N = 11 9/11 completed: 18% attrition	Agitation Measures: Modified CMAI	Weekly assessments during 3 wk baseline, 6 wk of treatment, and 3 wk of post-treatment.	Single-group repeated measures. Mean treatment length was 5 minutes delivered by a certified craniosacral therapist in conjunction with Progressively Lower Stress Threshold (PLST) model of care. The M-CMAI was administered by CNAs.	Reduction in mean M-CMAI total*** and subscale scores (physically aggressive**, non-aggressive***, and verbal agitation***) at post-test. Reduction continued through post-treatment period for physically non-aggressive agitation*** and verbal agitation**.	Level II / Low
• Balancing Arousal							
Kovach *et al.* (2004) U.S.A.: 13 long-term care facilities	MMSE 0–15 FAST 6–7	BACE: n = 36 Usual care: n = 42 78/102 completed: 24% attrition	Agitation Measures: ASD Visual analog of the CMAI	Direct observation in Phases 1 and 3 of baseline, treatment and post-treatment for 3 min every 15 min from 8 am–8 pm.	Double-blind, pretest-posttest, with random assignment. BACE individualizes activity schedule to balance high-arousal and low-arousal states. Phase 1: 12hr observation, Phase 2: individualization of activity schedule, Phase 3: 12 hr. of observation.	BACE resulted in reduced agitation between pretest and posttest***, with no change in the control group. Effects mostly gone by 10 wk.	Level I / Moderate

BACE = Balancing Arousal Controls Excesses; CNA = certified nursing assistant; MSS = multi-sensory stimulation; RCT = randomized controlled trial; SCU = Special Care Unit.

Outcome measures ASD= Arousal States in Dementia Scale; BEHAVE-AD = Behavior Pathology in Alzheimer's Disease Rating Scale; BRS = Behaviour Rating Scale; BMD = Behaviour and Mood Disturbance Scale; CMR = Caregiver Mood Report; CMAI = Cohen-Mansfield Agitation Inventory; CMMSE = Chinese Mini-mental State Examination; CNPI = Chinese Neuropsychiatric Inventory; CSDD = Cornell Scale for Depression in Dementia; DCM = Dementia Care Mapping; DS-DAT = Discomfort-Dementia of the Alzheimer's Type; EBIC = Environment-Behavior Interaction Code; FAST = Functional Assessment of Alzheimer Disease; MPES = Menorah Park Engagement Scale; MMSE = Mini-mental State Examination; MOSES = Multi-dimensional Observation Scale for Elderly Subjects; NPI = Neuropsychiatric Inventory; PBRS = Patient Behavior Rating Scale; PAS = Pittsburg Agitation Scale; PARS = Philadelphia Geriatric Center Affect Rating Scale; PGDRS = Psychogeriatric Dependency Rating Scale; REHAB = Rehabilitation Evaluation.

* $p < 0.05$,

** $p < 0.01$,

*** $p < .001$.