Complementary and alternative medicine in relation to the behavioural and psychological symptoms in people with dementia: A systematic review

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PREFACE

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Stavanger, May 2017

Ting Xu

Table of Contents

PART 1: Thesis

SUMMARY

The purpose of this thesis is to assess the efficacy of Complementary and Alternative Medicine in people with dementia with behavioural and psychological symptoms. A literature search was undertaken. Three databases, Medline, EMBASE, and PsycINFO were searched. Only peer-reviewed journal articles in English published in 1990s or later with clinic trials for humans were included in the current review. Randomized clinical trials or studies with control groups employing five following complementary and alternative therapies (Acupuncture/Acupressure, Aromatherapy, Massage, BLT, and TENS) for managing BPSD in people with dementia were included in our systematic review. In the review 565 related studies were identified, where 30 RCTs or studies with control group met the inclusion criteria for this systematic review. 22 studies of which 17 were RCTs, out of the total 30 studies selected and analysed in this work have demonstrated effectiveness of CAM. In conclusion, dementia as a medical problem currently can not be cured, but the symptoms of dementia and the quality of life of patients with dementia can be improved by different therapies. Although not all studies demonstrated consist statistic significant improvement, there were obviously benefited evidences or positive trend from CAM. More research, however, is needed to provide definitive evidence about the benefits of CAM.

1.0 INTRODUCTION

There are 35 million people with dementia worldwide, and many of them reside in nursing homes (Ballard et al., 2016). In Norway, there are over 77,000 people suffering from dementia, and the number will probably double itself within 2040. It is clearly a heavy burden for those caring for relatives with dementia at home, and many informal carers are elderly and frail themselves (Department of Health, 2009). Behavioural and psychological symptoms of dementia (BPSD) affecting 90% of people with the condition at some point, in particular, agitation, aggression, psychosis and depression are the major causes of distress for patients with dementia and those caring for them, presenting a significant challenge for treatment and care (Engedal, 2008; Testad et al., 2014).

1.1 BACKGROUND

Antipsychotic drugs as conventional medicine are often used for the management of behavioural and psychological symptoms in dementia (Banerjee, 2009). Recently, antipsychotic medications in treating dementia have limited efficacy and significantly increased the risk of stroke and mortality, and have being questioned these years (Gill et al., 2007; Schneider, Dagerman, & Insel, 2006; Wang et al., 2005). Current clinical guidance recommends non-pharmacologic interventions as the first choice for people with dementia (Salzman et al., 2008; Selbæk et al., 2016; Wood-Mitchell, James, Waterworth, Swann, & Ballard, 2008).

CAM has some intersections with pharmacologic treatments and non-pharmacologic interventions. In one side, complementary therapies are often used in addition to pharmacologic treatments. Alternative therapies are used instead of pharmacologic treatments. In other side, CAM and non-pharmacological interventions have many common therapies, such as music therapies, massage and so on. Several reviews have already discussed the effectiveness of non-pharmacological interventions to for people with BPSD. Nowadays CAM as a green wave has received great interest within the field of dementia treatment. There is an urgent need to summarize available research on complementary and alternative treatments of dementia.

1.2 PREVIOUS RESEARCH

A good and meaningful life is an important goal of our society, as evidenced by Dementia Plan 2020 "The good day" (Helse- og omsorgsdepartementet, 2015). A person-centered approach in the care of people with dementia involves an individual approach that emphasizes the uniqueness of the individual throughout the course of the disease, and shall be emphasized in this field

Determining the most suitable complementary or alternative treatment for a specific case will depend on several factors, including the specific symptoms that need to be treated and the surroundings that could comfort the person with dementia. The goals of treatment range from improving memory to providing relaxation. Each person will experience the therapy differently, and some treatments are tailored to individual needs. This can lead to different experiences and different levels of effectiveness.

Behavioral and psychological symptoms of dementia (BPSD) affecting 90% of people with the condition at some point, in particular, agitation, aggression, psychosis and depression are major causes of distress for patients with dementia (Testad et al., 2014).

Today, many are interested in alternative therapies and their importance to our health, and many patients with dementia use some forms of complementary or alternative therapies (CAM). There is an urgent need to summarize available research on complementary and alternative treatments of dementia. In the current work, the aim is to find out which complementary and alternative treatments are effective for treating dementia and improve behavioral and psychological symptoms in patients with the condition.

1.3 PURPOSE OF STUDY

The purpose of this project is to seek insights into what research says about the various types of alternative methods in connection with the treatment and symptomatic relief of dementia. Based on such findings I shall come with implications for medicinal practice and further research.

1.4 THE ISSUE

An essential question has been raised about complementary and alternative treatments of dementia. It is of great interest to attain more knowledge about this.

The issue is as follows:

Does complementary and alternative treatment have effectiveness for demented patients with behavioural and psychological symptoms of dementia?

2.0 THEORETICAL FOUNDATION

2.1 DEMENTIA

Engedal (2008) defined dementia in this way:

“Dementia is a brain organic syndrome and a generic term for a number of pathological conditions characterized by acquired cognitive failure, failure of emotional control and weak functionality compared to daily life functions. The disease is characterized by impaired mental capacity and result in failure of psychological processes such as memory, attention, learning, thinking and communication. Changed behaviour is common. The condition is chronic, which cannot be cured and worsen often over time” (p.217).

There are many different forms of dementia that affect the elderly, but Alzheimer’s disease is the most common and accounts for 60 to 80 percent of all dementias. Other types of dementia include vascular-based dementias, the second most frequent type of dementia, and Lewy body dementia.

Dementia refers to changes in memory and other cognitive skills severe enough to affect a person’s ability to perform daily social and occupational activities. Dementia is usually categorized as either AD or non-Alzheimer’s dementia.

Whether in the community or institutionalized, the person with dementia is an individual with the same desires for autonomy and respect as any other person. However, because dementia typically results in dependency and disability, persons with dementia are at risk of being denied the opportunity for autonomy and respect for personhood.

2.2 BPSD

The term BPSD stands for "behavioral and psychological symptoms of dementia," and has been used to describe a group of heterogeneous symptoms that occur during dementia and are distressing and difficult to manage, for both caregivers and health professionals (Trivedi et al., 2013).

Symptoms include depression, psychosis, aggression, wandering or walking / getting lost, agitation, apathy and emotional distress. Together or separately they affect the patients' ability to maintain daily activities, and reduce the quality of life for both people with dementia and their caregivers (Finkel, 2000). The consequences of BPSD can be disturbed sleep, fatigue, increased risk of falls and injuries, inadequate nutrition (Aselage & Amella, 2010; Manthorpe & Watson, 2003) and increased stress of caregivers.

2.3 COMPLEMENTARY AND ALTERNATIVE MEDICINE

There is a trend in society, "the green wave". We are more aware and have greater interest for in the balance and diversity of nature. Complementary and alternative therapies have many benefits for the patient. They are not restrictive. The patient has more control of treatment and greater choices above their health (Fowler & Newton, 2006).

The term 'complementary and alternative medicine' refers to a wide range of treatments, which are used to treat or prevent illness and promote wellbeing. NCCAM (the National Center for Complementary and Alternative Medicine, US) defines CAM (complementary and alternative medicine) as a broad domain of healing resources that encompasses all health systems, modalities and practices, and their accompanying theories and beliefs, other than those intrinsic to the politically dominated health systems of a particular society or culture in a given historical period. CAM includes all such practices and ideas self-defined by their users as preventing or treating illness or promoting health or well-being. Boundaries between CAM and within the CAM domain and that of the dominant health care system are not always sharp or fixed" (National Institutes of Health, 2016).

Clearly the conjunction of "alternative" and "complementary" is a little confusing. In the simplest of explanations, Complementary therapies are often used in addition to conventional medicine. Alternative therapies are used instead of conventional medicine (Alzheimer's Society, 2014). A combination of conventional medicine and CAM is regarded by the NCCAM as integrated medicine (National Institutes of Health, 2016).

CAM focuses on the whole person and includes physical, emotional, mental and spiritual health. For example, CAM includes mind-body medicine (such as meditation, acupuncture and music therapy), manipulative and body-based practices (such as massage therapy and aromatherapy), and natural products (such as herbs, dietary supplements, bright light therapy).

Complementary and alternative treatment is based on the body's nutritional power which is the body's self-healing and repair capability. The aim is to strengthen the body's own ability to heal (Sosial-og helsedepartementet, 1998). Everything living is seen as pervaded by vital force. Practitioners of alternative and complementary therapies often attempt to stimulate this power or energy, which is part of the body's defence system (Norheim, 2009). The vital force seeks to keep strains that can cause disease at such an external plane as possible, but when the body is weakened / the vitality is reduced, the plagues penetrate deeper into the body's system. The focus is thus prevention for better health.

2.3.1 Holism

Holism used within CAM treatment systems considers all aspects of the patient. Within holistic treatment systems are terms ECIWO (Embryo Containing the Information of Whole Organism), holographic learn (totality is reflected in parts / single organs in person) and quantum physics (the discovery of quarks) parts of explanatory models (Norheim, 2009). Holism also means to see the body, spirit, life situations, pains, thoughts, resources and vulnerability as a whole.

When it comes to seeing things in context as an important feature in a comprehensive or holistic approach, it is all about relationships among the mental, physical, social and spiritual dimensions of the human being, and it applies to a greater extent than a mere connection between the clinician and the patient. Moreover, it also applies to relationships between the person and the environment, especially the nature. These relationships are considered to be very significant for health.

The energy concept (prana, qi, reiki, dynamis) expresses a dynamic part of CAM that is central to the body's self-healing and regenerating ability. A disturbance, degradation or

deterioration of the person's energies is, in parts of CAM, the basis for perception of illness and for design of treatment (Norheim, 2009).

3.0 METHODS

Vilhelm Aubert defines a method as a means to solve problems and come up with a new knowledge. Any means that serves this purpose belongs to be concept of methods (Dalland, 2007). The method is a tool for us to find the knowledge. The right means will lead us to find the answer we want.

I chose literature study method, where I systematically collected data on existing research and literature. The studies can be both qualitative and quantitative methods.

3.1 DATA RETRIEVAL

First, I did preliminary searches where I went wide with keywords. Depending on the combinations of keywords I started the "real information query" to the problem and research questions. I read the titles and related abstracts. I selected 10 articles that meet my criteria for inclusion.

3.2 DATABASE/ SOURCE SEARCH

The following databases were searched: Medline/Pubmed, EMBASE, PsycInfo. I chose these databases because they include all fields of health sciences, meanwhile they represent different disciplines in health sciences.

Medline	Medline is considered as a **main** source for biomedical research. References and abstracts to journal articles in medicine, preclinical sciences and other related areas. Here registered articles from nearly **5,700 international journals.**	Access PubMed: freely available on the Internet.
EMBASE	European oriented database with references to journal articles in biomedicine and pharmacology. Covering a variety of topics: drug discovery, pharmaceuticals, toxicology, odontology, psychology and **alternative medicine**. In relation to Medline: several European magazines and especially good coverage within pharmacological topics.	Access Ovid: subscription via UiS network and through the Health Library

PsycINFO	Covering **psychological** literature in education, research and practice of about 45 countries and over 30 languages. PsycINFO includes relevant material from related disciplines such as medicine, **psychiatry**, education, social work, law, criminology, social and organizational behavior.	Access Ovid: subscription via UiS network and through the Health Library

3.3 SEARCH TERMS

Search terms encompassing complementary and alternative therapies, dementia , Alzheimer disease, behavioural symptoms, psychological symptoms. In all key words all subthemes were included.

There are very many different types of methods and measures that fall under the term alternative treatment. Alzheimer's Society (the leading support and research charity for people with dementia, their families and carers) has recommended some complementary and alternative therapies for people with dementia. I have chosen these therapies, as well as some of the clinic widely used alternative treatments for literature: ***Acupuncture, Aromatherapy, Massage, BLT, TENS.***

3.4 EXCLUSION CRITERIA FOR ARTICLES

Studies associated with herbal remedies/vitamin supplements, diet, exercise, spiritual therapy, psychotherapy, cognitive therapy, or prevention of dementia was excluded.

3.5 INCLUSION CRITERIA FOR ARTICLES

Only peer-reviewed journal articles in English published in 1990s or later with clinic trials for humans were included in the current review. Randomized clinical trials or studies with control groups employing five following complementary and alternative therapies: Acupuncture/Acupressure, Aromatherapy, Massage, BLT, and TENS (Table 1) for managing BPSD in people with dementia were included in our systematic review.

Table 1. Descriptions of different therapies

Complementary and Alternative Medicine	**Descriptions**
General	**Complementary and Alternative Medicine (CAM)** was defined as "diagnosis, treatment and/or prevention which complements mainstream medicine by contributing to a common whole, satisfying a demand not met by orthodoxy, or diversifying the conceptual framework of medicine" (Ernst, Pittler, & Wider, 2001).
Acupuncture/Acupressure	**Acupuncture** is one of the foremost forms of treatment in Chinese medicine. It involves the use of sharp, thin needles that are inserted into the body at very specific points. This process is believed to adjust and alter the body's energy flow into healthier patterns, and is used to treat a wide variety of illnesses and health conditions (Zhao et al., 2009).**Acupressure** is a non-invasive variation of acupuncture involving constant pressure to stimulate meridians or acupoints of the human body to balance energy, thus promoting individual well-being (Lin et al., 2009)
Aromatherapy	**Aromatherapy** is the use of pure essential oils from fragrant plants to help relieve health problems and improve the quality of life in general (Forrester et al., 2014).
Massage	**Massage therapy**, defined as manipulation of soft tissue areas of the body, is offered in clinical settings to assist relaxation, facilitate sleep, and relieve muscular aches and pains (Vickers & Zollman, 1999).
Bright Light Therapy (BLT)	**BLT** is a method of maintaining or restoring the natural circadian rhythm by assisting daytime awakening using bright lights (Taguchi, Yano, & Kido, 2007).
Transcutaneous Electrical Nerve Stimulation (TENS)	**TENS**, a type of peripheral nerve stimulation, is the application of an electrical current through electrodes attached to the skin. The most common clinical application of TENS is for pain management. TENS is also used occasionally for the treatment of a range of neurological and psychiatric (Cameron, Lonergan, & Lee, 2003).

3.6 TYPES OF OUTCOME MEASURES

The search included studies that measured changes on specific variables. The primary outcomes are key BPSD defined as depression, agitation and anxiety, in addition to impact on antipsychotic medication prescribing.

3.7 SEARCH STRATEGIES

The following databases were explored: Medline through Pubmed; and OVID for EMBASE and PsycInfo. There are many different types of methods and measures that fall under the term ”Alternative Treatment”. The search strategy was conducted with the help of the librarian from Stavanger University with professional guidance provided by colleagues in scientific environment at SESAM.

To conduct a search:

- Choose PubMed or Ovid EMBASE, PsycINFO (Advanced Search)
- For complementary and alternative therapies:

1.Enter terms best describing the inventions

2.Possible subheadings (f.eks: acup*[tiab] for acupuncture, acupressure, acupoint …for broadest coverage or most frequently used)

- For dementia or BPSD:

1. Enter terms best describing the outcome.
2. Possible subheadings (f.eks: dement*[tiab] or Alzheimer*[tiab] for dementia for broadest coverage or most frequently used)

- Combine the first two search statements, using the Boolean operator "AND""OR" and combine the final subject statement with the quick filter (hedge) below.

Pubmed:

Pubmed	Acup*	Massage*	Aroma*	BLT	TENS
2.Dementia	acup*[tiab] and dement*[tiab]	massage[tiab] and dement*[tiab]	aroma*[tiab] and dement*[tiab]	Light therap*[tiab] and dement*[tiab]	transcutaneous electrical nerve stimulation*[tiab] and

					dement*[tiab]
Results	115	56	91	84	6
3.Alzheimer*	acup*[tiab] and Alzheimer*[tiab]	massage*[tiab] and Alzheimer*[tiab]	aroma*[tiab] and Alzheimer*[tiab]	Light therap*[tiab] and Alzheimer*[tiab]	transcutaneous electrical nerve stimulation*[tiab] and Alzheimer*[tiab]
Results	70	16	352	50	17
2 OR 3	175	67	410	100	19
4.BPSD	(("behavioral symptoms") OR "psychological symptoms") OR "agitation") OR "depression") OR "anxiety"))				
4 AND (2 OR 3)	27	37	60	48	3

EMBASE

EMBASE	Acup	Massage	Aroma	BLT	TENS
Index terms	Acupuncture.sh OR acupuncture.ti OR acup$.tw	massage.sh OR massage.ti	aromatherapy.sh OR aroma$.ti	light therapy.sh OR light therapy.ti	transcutaneous electrical nerve stimulation.sh. or transcutaneous electrical nerve stimulation$.ti.
Dementia	Dementia.sh OR dementia.ti OR Alzheimer disease.sh OR Alzheimer$.ti				
BPSD	Behavioral symptoms.sh OR behav$.ti OR psychological stress.sh OR mental stress.sh OR psyc$.ti OR mental$.ti OR depression.sh OR depression.tw OR agitation.sh OR agitation.tw OR anxiety.sh OR anxiety.tw				
Results	96	91	110	32	8

PsycINFO

PsycINFO	Acup	Massage	Aroma	BLT	TENS
Index terms	Acupuncture.sh OR acupuncture.ti OR acup$.tw	massage.sh OR massage.ti	aromatherapy.sh OR aroma$.ti	light therapy.sh OR light therapy.ti	transcutaneous electrical nerve stimulation.sh. or transcutaneous electrical nerve stimulation$.ti.
Dementia	Dementia.sh OR dementia.ti OR Alzheimer disease.sh OR Alzheimer$.ti				
BPSD	Behavioral symptoms.sh OR behav$.ti OR psychological stress.sh OR mental stress.sh OR psyc$.ti OR mental$.ti OR depression.sh OR depression.tw OR agitation.sh OR agitation.tw OR anxiety.sh OR anxiety.tw				
Results	27	37	60	48	5

(**$:** To allow for different endings or spellings in these keywords i have truncated words and tested each phrase by doing a title search for each one before added them to my logic grid.

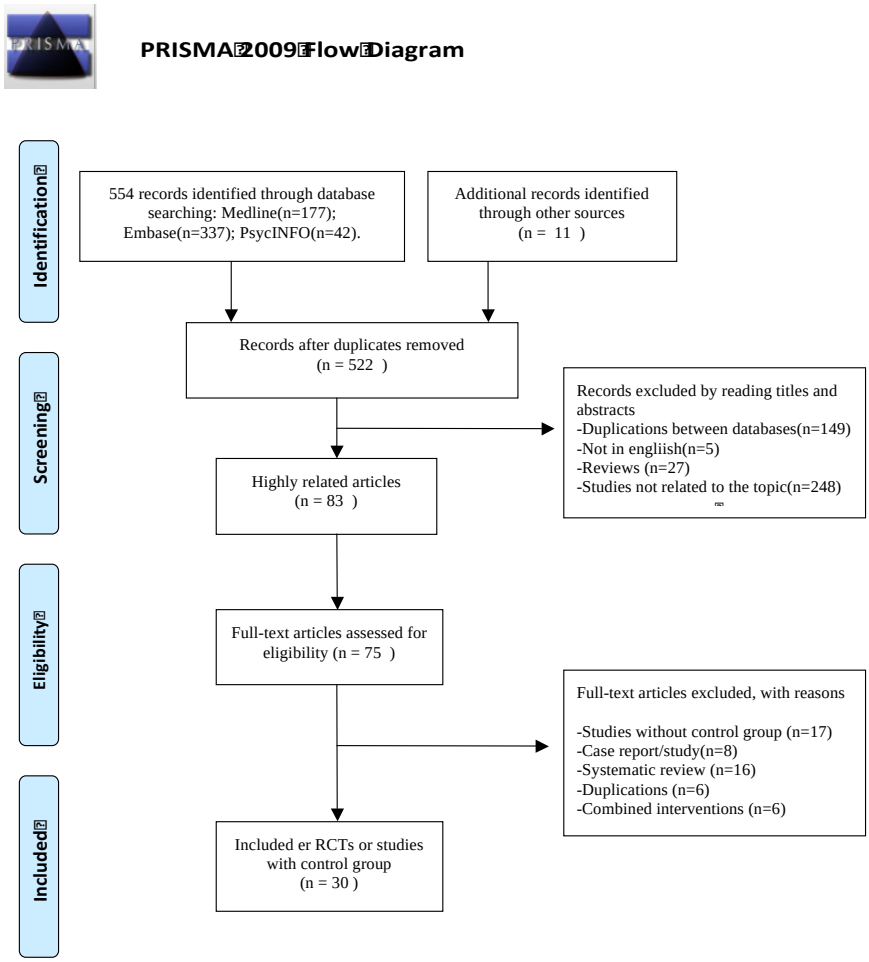
.tw: I have used .tw instead of .ti OR .ab

.tw searches not just titles and abstracts, but also key concepts which are terms the indexers use to supplement Thesaurus terms. Key concepts aren´t standardized like the thesaurus language but contain a variety of words and phrases from ordinary language.)

3.8 SELECTION OF ARTICLES

The selected articles will illuminate and answer my research questions. I chose articles that provide the basis for the analysis on the basis of their content. The selected articles should illuminate and answer my research questions. On the basis of this I chose out articles that high related on these therapies, which I have chosen for this study. 565 studies were identified in the initial search, of which 535 were excluded. 30 studies were included.

Figure 1. Flow chart of trial selection process for this review



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit www.prisma-statement.org.

First of all, I used the search strategy in these databases to find out articles on relevant therapies and dementia/AD. I read the titles and abstracts to select the most relevant articles that are related to my topic. I also used textbooks from previous subjects to investigate whether these referred to the relevant articles I could use in my essay. I also searched through the references of these articles I chose, to look for other articles that could be relevant.

As results showing in the Figure 1, we can see that some of the articles are totally irrelevant to my topics; some of them address only therapies or dementia/AD or symptoms of dementia; some of them are systematic reviews. I filed the related articles and imported them to Endnote. Using Endnote has helped me to find duplications, analyse articles and organize articles into different groups.

Then I used different databases and searched tools to get access to the full text of these articles. Full texts were not available for a few of these articles.

4.0 ANALYSIS

Braun and Clarke (2006) defined thematic analysis as: ”A method for identifying, analysing and reporting patterns within data”. Thematic analysis has been chosen to provide a critical summary of all my selected papers. Table 2 is an overview of these 30 articles. It gives a summary of the information I have collected.

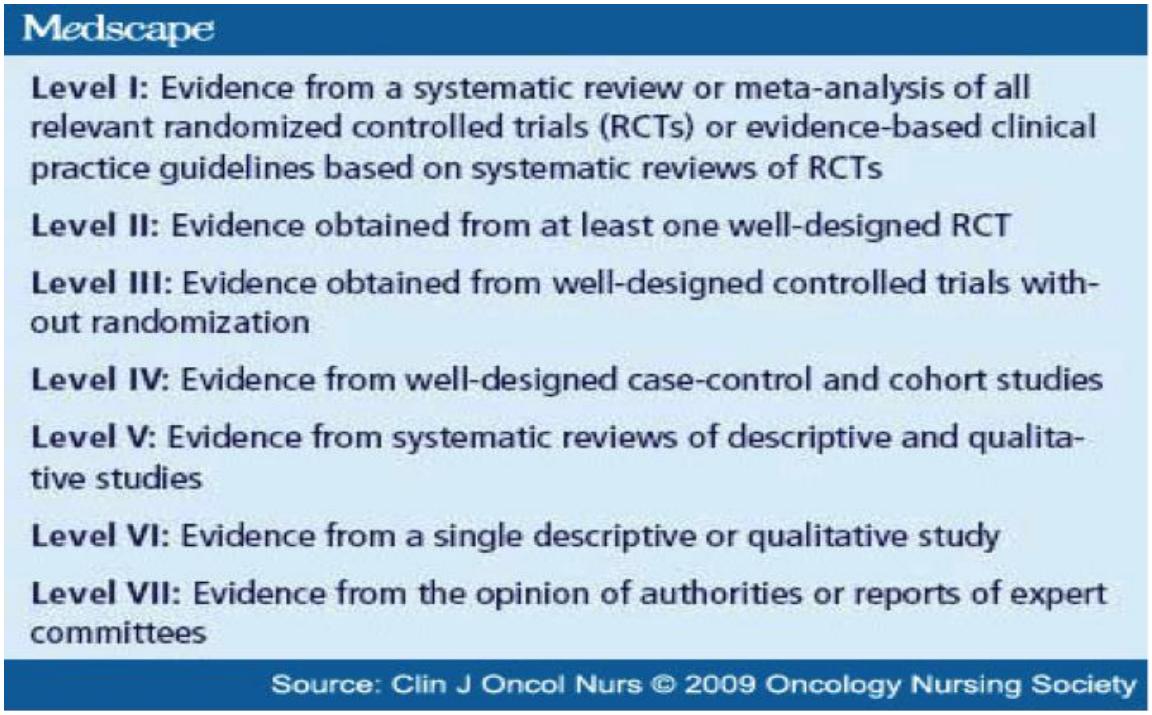
4.1 ANALYSIS PROCESS

I read each study many times to immerse myself in these articles I have carefully chosen and become familiar with them. Through analysis process, I tried to notate the details of each of my selected articles, including the strengths and limitations of each. It is very useful to compile a table to assist me in this process. It gave me an overview of all the studies I have looked into, and the different approaches used in each one. The article was assigned to five different directories according to the different interventions. This method helped me to understand these papers and see how they are related to each other. The different articles that eventually totalled my findings were then placed under the five research fields, which are acupuncture/acupressure, aromatherapy, massage, BLT and TENS.

4.2 QUALITY ASSESSMENT

The methodological quality assessment was measured by the Melynk`s level of evidence (Melnyk & Fineout-Overholt, 2011) (Figure 2). Two reviewers have assessed these studies independently. If there was disagreement, the third reviewer was consulted. All the three reviewers discussed and made consensus.

Figure 2. The Melynk`s level of evidence



4.3 VALIDITY AND RELIABILITY

The validity, also called relevance, applies to both the search of the literature and using people as a source of information (Dalland, 2007, p.95). The literature study in this thesis applies the search and discovery of literature. Keywords and short titles have been used frequently during the searching and selection process of scientific articles. Being critical in the selection of articles, and sometimes critical assessment of several analogous articles, is to determine whether they cover the issue of the project and if they provide authoritative information, has also increased the validity.

Reliability is all about collecting data reliably. For this requirement to be fulfilled, all steps in the process should be free of inaccuracies (Dalland, 2007, p.96). Regarding reliability, it may be challenging with qualitative study and related interviews, as not all questions have to be answered in a reliable manner. From this, one could imagine that a literature study can provide increased reliability, although one must be aware of the qualitative approach that is present in the searching process.

Reliability refers to the degree of measurement precision or measurement errors (Befring, 2007) . Since I have used literature study, this is not relevant to me since I

have not used surveys or interviews. In the other hand, I questioned the material's accuracy; not all I have found are relevant to the issue/project. It's about what data were used, how they were collected and how they were processed. One way to try out the data's reliability is that others were doing the same type of survey. High reliability could be suggested with similar results from these parallel surveys. Therefore, it is important to explain the process from data collection, presentation to discussion of findings. By detailing the entire research process transparency could be achieved (Johannessen & Tufte, 2002). Another way to make reliable findings is by assuring that the articles were peer reviewed and published in well-recognized journals.

4.4 DATA SYNTHESIS

Data from the selected 30 studies were synthesized according to the following characteristics: author and year (setting), intervention type, attention control, study design, length, number of times, length of each session, sample population, outcome focus, outcome measures, impact and Level of evidence (Table 2). A narrative synthesis approach was performed to examine the results. These studies were conducted in the following settings: Taiwan (n = 3), China (n = 1), Spain (n=1), UK (n=5), Australia (n=4), Japan (n = 3), USA (n=7), Hong Kong (n = 1), Canada (n=1), and the Netherlands (n = 4).

4.5 OUTCOME FOCUS AND BPSD MEASURES

Specific norms and scales for measuring agitation include the Cohen-Mansfield Agitation Inventory (CMAI) (Cohen-Mansfield, Marx, & Rosenthal, 1989) and the Pittsburgh Agitation Scale (PAS) (Rosen et al., 1995). Additionally, norms for some general behavioral symptoms such as The Neuropsychiatric Inventory (NPI) (Cummings et al., 1994), the Behavioral Pathology in Alzheimer’s disease rating scale (BEHAVE-AD) (Reisberg, Borenstein, Salob, & Ferris, 1987) and the Agitated Behavior Rating Scale (ABRS) (Bliwise & Lee, 1992) include subscales that specifically apply to agitation. A higher score obtained from these scales indicates a higher level of agitation with increased severity.

The Cornell Scale for Depression in Dementia (CSDD) (Alexopoulos, Abrams, Young, & Shamoian, 1988) for depression symptoms is a reliable and valid instrument. The

Neuropsychiatric Inventory-Nursing Home (NPI-NH) (Cummings et al., 1994) assesses either 10 or 12 behavioral disturbances commonly found in dementia, where a higher score indicates greater severity. Cognitive status was mostly measured by administering the Mini–Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975).

Actigraphy has been shown to correlate well with electroencephalogram recording and direct observation (Ancoli-Israel, Clopton, Klauber, Fell, & Mason, 1997). Wrist actigraphy allows continuous measurement of movement for consecutive days or weeks and provides a feasible technique for studying the rest-activity rhythm in persons with dementia. It is also an appropriate means for assessing treatment effects (Ancoli-Israel et al., 2003).

5.0 RESULTS

The routine for conducting the reviewing process was presented (Figure 1). 565 related studies were identified via automatic search in different databases as well as manual search from the reference lists of selected articles. With duplicates removed, the remained 522 records were screened by their titles and abstracts. Among them, 83 studies were considered highly relevant and 75 of these available were assessed for eligibility based on their full-texts. 30 studies that met the inclusion criteria for this systematic review were eventually selected and read through by two reviewers independently. The characteristics of these included studies are summarized in Table 2.

5.1 ACUPUNCTURE/ACUPRESSURE

Four studies evaluated acupuncture and acupressure therapies in treating people with BPSD. Two were double-blinded RCT (Lin et al., 2009; Rodriguez-Mansilla et al., 2013), one single-blinded RCT (Shi et al., 2015) and one quasi-experimental study (Yang, Wu, Lin, & Lin, 2007). The studies had from 31 and 133 participants with duration of 4 to 12 weeks, the frequency of acupuncture or acupressure intervention varied from every 15 days to twice a day, and the length of each session varied from 15 to 30 minutes. Two RCTs (Rodriguez-Mansilla et al., 2013; Shi et al., 2015) evaluated acupuncture therapy by qualified acupuncturists using a specific protocol with body acupuncture or ear acupuncture. Both outcomes of these studies were measured by MMSE and ADL. The first was double-blinded RCT study (Rodriguez-Mansilla et al., 2013) indicated significant benefit compared to the comparison group. In contrast, the results of a single-blinded RCT (Shi et al., 2015) reported no significant difference among groups was observed. This trial has two parts: Randomized acupuncture group (R-acupuncture); Nonrandomized acupuncture group (NR-acupuncture), or control group. No significant differences of MMSE scores among the three groups but MMSE ($p=0.014$), ADL ($p=0.003$) scores of pooled-acupuncture group were significant higher than control group.

Other outcome, such as the Ease-of-care, was consistently evaluated across studies. The other two studies (Lin et al., 2009; Yang et al., 2007) measured agitation med CMAI as a specific outcome. The results indicated significant improvement with acupressure therapy intervention when compared to the control group.

5.2 AROMATHERAPY

Nine studies were included (Ballard, O'Brien, Reichelt, & Perry, 2002; Burns et al., 2011; Moyle, & Cooke, 2013; Gray & Clair, 2002; Holmes et al., 2002; Lin, Chan, Ng, & Lam, 2007; O'Connor, Eppingstall, Taffe, & van der Ploeg, 2013; Smallwood, Brown, Coutler, Irvine, & Copland, 2001; Yang et al., 2015), of which two were double-blinded RCTs, four single-blinded RCTs, one RCT with cross-over design and two quasi-experimental studies. The studies included between 13 and 186 participants with duration of 2 to 12 weeks. The frequency of aromatherapy intervention varied from once per day to three times per day, and the length of each session varied from 2 minutes to 4 hours. Inhalation or topical applications to the skin with scented essential oil from plants, such as Lavender and Melissa, was used as aromatherapy intervention for the treatment of physical and psychological health. In our included aromatherapy studies, two RCTs used Melissa oil and the other seven RCTs or quasi-experimental studies used Lavender oil. Aromatherapy was delivered via drops on clothing, cotton-ball, diffused in the air, sprayed onto chest, or applied as lotion directly on skin. Agitation was the main outcome focus among these seven included studies (Ballard et al., 2002; Burns, Allen, Tomenson, Duignan, & Byrne, 2009; Fu et al., 2013; Holmes et al., 2002; Lin et al., 2007; O'Connor et al., 2013; Yang et al., 2015). The observed effectiveness of these included studies in treating dementia patients had shown mixed results.

Two studies used Melissa oil to treat agitation in people with dementia. Both studies were double-blinded RCTs, but they have conflicting results. The Melissa oil was integrated into a body cream and the cream was gently applied to the skin on patients` hands and faces (Ballard et al., 2002), or hands and arms (Burns et al., 2011). In the study by Ballard et al, the total CMAI scores were significantly reduced in people with severe dementia compared to placebo treatment ($p<0.00001$) and quality of life indices were significantly improved ($p=0.005$). In contrast, the other study by Burns et al. with patients who had probable or possible AD showed that there was no significant difference among groups at week 4 and week 12. Nevertheless, there were substantial improvements in all three participant groups in the PAS and NPI over 12 weeks.

The next seven RCTs with single-blinded/crossover design or quasi-experimental studies used varied percentages of Lavender oil to manage BPSD in people with dementia. Four of the seven studies (Holmes et al., 2002; Lin et al., 2007; Smallwood et al., 2001; Yang et al., 2015) demonstrated significant improvement after aromatherapy interventions and the other three studies (Fu et al., 2013; Gray & Clair, 2002; O'Connor et al., 2013) showed positive but not significant effects when compared with control group. In these studies, one of the largest single-blinded RCT studies randomized 186 participants with dementia to aroma-acupressure, aromatherapy or usual care (Yang et al., 2015); A study by Lin et al. included 70 residents with dementia and they were allocated randomly into two groups, aromatherapy by inhalation of lavender oil or placebo therapy with sunflower oil. This RCT study had a crossover design. Both of the two studies demonstrated that aromatherapy had significant effect in agitation for people with dementia. A single-blinded RCT study by Fu et al. had three groups: aromatherapy (spray lavender oil to the chest), aromatherapy and hand massage, and a control group with water sprayed onto the chest; In O´Conner et al. study, 64 patients were included. The study had a single-blinded and crossover design. It included two types of treatment: aromatherapy and inactive control oil (jojoba oil) administered. Even through they do not find the significant effects in their results, the intervention groups showed positive effects. The other three RCT or quasi-experimental studies (Gray & Clair, 2002; Holmes et al., 2002; Smallwood et al., 2001) with small samples as evidence showed the effect of aromatherapy.

5.3 MASSAGE

Four studies, of which three RCTs and one quasi-experimental study (Hicks-Moore & Robinson, 2008; Moyle et al., 2014; Remington, 2002; Suzuki et al., 2010) were identified. Three of them tested the efficacy of massage on agitation and for BPSD in general. The studies included between 40 and 68 participants, with durations ranged from 2 to 6 weeks. The frequency of each intervention not available in each study, two studies given massage therapy once a day, every weekday. The length of each session varied from 10 minutes to 20 minutes. All these studies demonstrated positive effects of massage therapy on reducing a range of conditions of BPSD, especially agitation, in people with dementia. Three studies (Hicks-Moore & Robinson, 2008; Moyle et al., 2014; Remington, 2002) focused on agitation as an outcome, which indicated that

massage therapy conferred significant advantage in negative affect. One RCT by Hicks-Moore et al. reported randomizing 41 residents with mild to moderate dementia to hand massage, music, combined, or control; A double-blinded, cross-over RCT conducted by Moyle and colleagues compared foot massage with attention control; A quasi-experiment study by Suzuki et al. made a comparison between tactile massage group and control group; and a study employed single-blinded RCT by Remington compared hand massage with no treatment. In addition, there were two RCTs characterized under acupressure and aromatherapy categories on the efficacy of massage for behaviour disorders in people with dementia (Rodriguez-Mansilla et al., 2013; Smallwood et al., 2001). Massage intervention group in these two RCTs reported positive results in dementia patients. These two studies were of a sufficient methodological rigour to count as evidence to answer the question of effect.

5.4 BRIGHT LIGHT THERAPY

Eight RCTs or quasi-experimental studies assessed the efficacy of BLT to manage BPSD among dementia residents in nursing homes and assisted living facilities. Three RCT studies measured agitation (Ancoli-Israel et al., 2003; Burns et al., 2009; Lyketsos, Veiel, Baker, & Steele, 1999); two RCT studies measured activity rhythms (Ancoli-Israel et al., 2003; Dowling et al., 2008), one quasi-experimental study measured sleep disorder (Mishima et al., 1994); and the other two RCTs measured cognitive functions, especially depression (Dowling, Graf, Hubbard, & Luxenberg, 2007; Graf et al., 2001). Comparison groups received exposure to standard light, dimmed red light, or no treatment. The studies had between 14 and 92 participants and duration of 10 days to 10 weeks. Patients were exposed to bright light variably as 2500 lux to 10,000 lux. The frequency of bright light therapy interventions varied from every other day to every day, and the length of each session varied from 1 hour to 2 hours per day at varying times of day. All these included studies showed positive results such as improved night sleep, reduction in agitation, and improvement in cognitive performance. Nevertheless, only a few studies have demonstrated bright light intervention with clinically significant effect. Significant advantage compared to comparison group was identified in four of the eight studies examining BPSD (Dowling et al., 2007; Graf et al., 2001; Lyketsos et al., 1999; Mishima et al., 1994), including three of the four RCTs examining this outcome. However, three studies with significant improvement had small size sample of 14 to 23

patients. Only one study employed a RCT design by Dowling et al. included 70 residents who were diagnosed with AD. Bright light was administered for one hour daily for 10 weeks. They tested the effects of morning or afternoon bright light exposure compared with usual indoor light for neuropsychiatric behaviours in patients. The results of this study revealed statistically significant differences between groups on agitation, depression and other varied neuropsychiatric behaviours.

5.5 TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION

Five RCTs evaluated the benefit of TENS therapy, of which four of the five RCTs were authored by Scherder and colleagues, one double-blinded RCT were conducted by Hozumi et al. Three RCTs focused on memory or affective behaviour (Scherder, Bouma, & Steen, 1995; Scherder & Bouma, 1999; Scherder, Bouma, & Steen, 1998; Van Someren, Scherder, & Swaab, 1998), one on sleep-wake and behaviour disorder (Hozumi et al, 1996) and the last on rest-activity rhythm (Scherder et al, 1999). Scherder and his colleagues used a similar intervention protocol for these five RCTs. The studies had between 14 and 18 participants and duration was 6 weeks, the frequency of TENS intervention was 5 days a week, and the length of each session was 30 minutes. In all cases, the control intervention was sham TENS. The main difference among the studies existed in the different type of TENS: short-term, isolated, or burst TENS. According two studies conducted by Scherder et al., they proved that 160 Hz/ 100μs, 30 minutes every weekday for 6 weeks would be a effective set of stimulation parameters for nonverbal or verbal memory, and short-term and long-term visual memory. Results from all these included studies were very consistent. The results demonstrated that TENS had great clinically significant effects in people with dementia. Two of these six RCTs employed double-blinded design (Hozumi et al., 1996; Scherder et al., 1998). Hozumi et al. included 27 participants with multi-infarct dementia and were selected on the basis of irregular sleep-wake patterns in conjunction with nocturnal behaviour disorders. The frequency of their TENS intervention was 6-80 Hz. Treatment duration was 20 minutes daily for 2 weeks. Significant improvements were found in motivation behaviour disorder, sleep disorder and subjective complaints. Scherder et al. tested the effect of ”isolated” TENS, single-blinded design, for memory and affective behaviour in people with AD during the treatment. The frequency of TENS was 160 Hz and duration was 30 minutes every weekday for 6 weeks. The results of the study

showed that isolated TENS had significant treatment effects on patients` cognitive and independent function, whereas patients` affective behaviour did not improve.

6.0 DISCUSSION

This systematic review examined 30 published studies of complementary and alternative medicine aimed at managing BPSD in people with dementia. Of these 30 studies, there were four on acupuncture and acupressure, nine on aromatherapy, four on massage, eight on BLT, and five on TENS. 25 studies employed an RCT design in our included studies, although others used studies with control conditions can be worked as good evidence to show the great diversity in these interventions.

In the initial searching process, it was hard to find clinical trials on acupuncture intervention in related to dementia but many studies with animal model were founded. In previous reviews, few high-quality RCTs published in international journals on acupuncture therapy reported that this intervention had effectiveness to dementia. Therefore, more well design clinical trials were needed to demonstrate that acupuncture has great efficacy to BPSD in people with dementia. Acupressure as a simple and non-intrusive therapy has been increasingly studied. Acupressure treatment conforms to the same principles as acupuncture involving constant pressure to stimulate meridians or acupoints of the human body to balance energy (Zhao et al., 2009). Acupressure is not only to relax the human body, but also stimulate the channels governing the flow of energy to promote health and offer comfort (Chen, Lin, Wu, & Lin, 1999; Weaver, 1985).

In this systematic review, acupuncture and acupressure each intervention only has two studies found to be of sufficient methodological quality to produce reliable evidence regarding effectiveness. The limited amount of reliable evidence available is impossible in scope to allow for general conclusions. Overall, the limited moderate to high quality evidence suggests that acupuncture and acupressure therapies may be effective in managing BPSD.

There are two ways for essential oil to be applied externally, by which they may reach the bloodstream: absorption by olfactory system or skin absorption (Gould, 2003). Essential oil molecules can enter through the nose, and can also pass through the epidermal barrier and enter the bloodstream without causing injury or triggering inflammation or water loss. Our bodies can become sedated, stimulated or relaxed by the action of certain oils.

Comparing with these positive and negative studies in aromatherapy, we might find that the method of administration of the treatment was different. In the negative studies (Burns et al., 2011; Fu et al., 2013; Gray & Clair, 2002; O'Connor et al., 2013), the site of administration of the essential oil was relatively far from the olfactory system. The perceived quality of the essential oil odor was the most relevant factor for determining how an individual would respond to it both emotionally and physiologically (Herz, 2009). Snow and colleagues did not find that the use of a purely olfactory form of aromatherapy can decrease agitation in impaired olfactory sense participants with severe dementia (Snow, Hovanec, & Brandt, 2004).

Meanwhile, based on the comparison of these included studies, it is hard to determine whether Melissa and Lavender oil was associated with effectiveness of aromatherapy. Differences in essential oil formulation, delivery methods, participant numbers, length of each session, selection criteria, outcome measures and time frames make it almost impossible to compare studies (Holt et al., 2003).

Massage as an alternative therapy has been used in dementia care with the aim of managing related psychological and behavioral manifestations and improving quality of life in people with dementia (Cohen-Mansfield, 2001). The small amount of evidence currently available is in favor of massage intervention; more research is needed to provide definitive evidence about the benefits of massage intervention.

The BLT studies included in this review revealed positive effects of this intervention in BPSD, especially in agitated, sleep disturbance and circadian activity rhythms. However, little evidence with small amount sample studies demonstrated that this intervention has significant effects. In contrast, there was a large, pre-and post-test design RCT (Ancoli-Israel et al., 2003) reported that bright light had no significant effects on the observational ratings of agitation in any of the light-treatment groups, importantly, they also observed a worsening of verbal agitation in the evening bright light group. In future study, the safety of complementary and alternative intervention should be assessed in the design of the experiment.

The included studies in TENS therapy readily fall into the Dutch studies and the Japanese study. Five of the six RCTs were authored by Scherder and his colleagues, of which one RCT focus on rest-activity and others on memory and affective behaviour

used similar experimental design, subjects, interventions and outcome measures. In contrast, the study from Japan conducted by Hozumi et al. focused on irregular sleep-wake patterns and nocturnal behaviour disorders and/or delirium in people with multi-infarct dementia. The results employing TENS intervention had significant effects, however, all these studies were conducted before 2000 and the numbers of subjects in each study was small. No more studies on TENS in related to BPSD in people with dementia were published in recent years.

Complementary and alternative therapies, due to their different experimental designs, have many inconsistent results. This requires a very critical evaluation of the design of each research experiment in order to achieve a consistent conclusion. Even if it is a well-designed RCT, there may still be conflicting results. It may because of the different types of patients or the different measurements of the indicators. Different experimental design may cause different results. These led to a lack of comparability among experiments. Consequently, the significance of these clinical experiments could not be easily stated in a reliable, statistical manner.

In one hand, an effective, repeatable and safety therapy protocol is urgent and it is also an important way to improve BPSD condition and quality of life of people with dementia. Further research is required to identify very effective and practical protocol for each complementary and alternative medicine and guide their clinic practice. In the other hand, it is good to try to combine these two or three effective complementary and alternative therapies together and the results might be enhanced. It would be great potential value to people with dementia. Among the various complementary therapies, acupressure, massage and aromatherapy are commonly used and seen as relatively non-invasive procedures for managing a variety of symptoms, especially agitation/aggression. The combination of aromatherapy and massage or acupressure (Fujii et al., 2008; Smallwood et al., 2001; Turten Kaymaz & Ozdemir, 2016; Yang et al., 2015; Yang, Lee, Chao, Hsu, & Wang, 2016) showed the greatest improvement in agitation and other behaviour disorders of BPSD compared with aromatherapy or massage or acupressure treatment only.

6.1 LIMITATIONS

Several limitations are acknowledged in this study. Due to time limitation, this systematic review did not include all the categories of complementary and alternative therapies. Only five interventions (Acupuncture/Acupressure, Aromatherapy, Massage, BLT, and TENS) were assessed whether they had efficacy in reducing behaviour and psychological symptoms in patients with dementia. More complementary and alternative therapies should be assessed in future research on their effectiveness and safety in related to improve BPSD in people with dementia. Furthermore, we choose only three databases, which probably include most relevant articles. However, manual search from the reference lists of selected articles is a very effective method to find other highly related studies. An additional limitation is that we did not discuss the safety of complementary and alternative medicine. Although there was few studies reported that some of CAM has side effects in persons with dementia, it is also important to reduce or avoid any possible risks.

7.0 CONCLUSION

Dementia as a medical problem currently can not be cured, but the symptoms of dementia and the quality of life of patients with dementia can be improved by different therapies. Although not all studies demonstrated consist statistic significant improvement, there were obviously benefited evidences or positive trend from CAM. More research, however, is needed to provide definitive evidence about the benefits of CAM.

REFERENCES

Alexopoulos, G. S., Abrams, R. C., Young, R. C., & Shamoian, C. A. (1988). Cornell scale for depression in dementia. *Biological psychiatry, 23*(3), 271-284.

Alzheimer's Society. (2014). Complementary and alternative medicine and dementia. Retrieved from http://lx.iriss.org.uk/sites/default/files/resources/Complementary_and_alternative_medicine_and_dementia.pdf

Ancoli-Israel, S., Clopton, P., Klauber, M. R., Fell, R., & Mason, W. (1997). Use of wrist activity for monitoring sleep/wake in demented nursing-home patients. *Sleep, 20*(1), 24.

Ancoli-Israel, S., Cole, R., Alessi, C., Chambers, M., Moorcroft, W., & Pollak, C. (2003). The role of actigraphy in the study of sleep and circadian rhythms. American Academy of Sleep Medicine Review Paper. *Sleep*, *26*(3), 342-392.

Ancoli-Israel, S., Gehrman, P., Martin, J. L., Shochat, T., Marler, M., Corey-Bloom, J., & Levi, L. (2003). Increased light exposure consolidates sleep and strengthens circadian rhythms in severe Alzheimer's disease patients. *Behavioral Sleep Medicine, 1*(1), 22-36.

Ancoli-Israel, S., Martin, J. L., Gehrman, P., Shochat, T., Corey-Bloom, J., Marler, M., . . . Levi, L. (2003). Effect of light on agitation in institutionalized patients with severe Alzheimer disease. *The American journal of geriatric psychiatry, 11*(2), 194-203.

Aselage, M., & Amella, E. (2010). An evolutionary analysis of mealtime difficulties in older adults with dementia. *Journal of Clinical Nursing, 19*. doi: 10.1111/j.1365-2702.2009.02969.x

Ballard, C., Orrell, M., YongZhong, S., Moniz-Cook, E., Stafford, J., Whittaker, R., . . . Fossey, J. (2016). Impact of Antipsychotic Review and Nonpharmacological Intervention on Antipsychotic Use, Neuropsychiatric Symptoms, and Mortality in People With Dementia Living in Nursing Homes: A Factorial Cluster-Randomized Controlled Trial by the Well-Being and Health for People With Dementia (WHELD) Program. *The American Journal of Psychiatry, 173*(3), 252-262. doi: 10.1176/appi.ajp.2015.15010130

Banerjee, S. (2009). *The use of antipsychotic medication for people with dementia: Time for action*. London: Department of Health.

Befring, E. (2007). *Forskningsmetode med etikk og statistikk.* Oslo: Det norske samlaget.

Bliwise, D. L., & Lee, K. A. (1992). Development of an Agitated Behavior Rating Scale for discrete temporal observations. *Journal of Nursing Measurement, 1*(2), 115-124.

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative research in psychology, 3*(2), 77-101.

Burns, A., Allen, H., Tomenson, B., Duignan, D., & Byrne, J. (2009). Bright light therapy for agitation in dementia: a randomized controlled trial. *International Psychogeriatrics, 21*(4), 711-721. doi: 10.1017/s1041610209008886

Burns, A., Perry, E., Holmes, C., Francis, P., Morris, J., Howes, M.-J., & Ballard, C. (2011). A double-blind placebo-controlled randomized trial of Melissa officinalis oil and donepezil for the treatment of agitation in Alzheimer's disease. *Dementia and Geriatric Cognitive Disorders, 31*(2), 158-164.

Cameron, M., Lonergan, E., & Lee, H. (2003). Transcutaneous electrical nerve stimulation (TENS) for dementia. *Cochrane Database of Systematic Reviews* (3), Cd004032. doi: 10.1002/14651858.cd004032

Chen, M.-L., Lin, L.-C., Wu, S.-C., & Lin, J.-G. (1999). The effectiveness of acupressure in improving the quality of sleep of institutionalized residents. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 54*(8), M389-M394.

Cohen-Mansfield, J. (2001). Nonpharmacologic interventions for inappropriate behaviors in dementia: a review, summary, and critique. *The American journal of geriatric psychiatry, 9*(4), 361-381.

Cohen-Mansfield, J., Marx, M. S., & Rosenthal, A. S. (1989). A description of agitation in a nursing home. *Journal of Gerontology, 44*(3), M77-M84.

Cummings, J. L., Mega, M., Gray, K., Rosenberg-Thompson, S., Carusi, D. A., & Gornbein, J. (1994). The Neuropsychiatric Inventory comprehensive assessment of psychopathology in dementia. *Neurology, 44*(12), 2308-2308.

Dalland, O. (2007). *Metode og oppgaveskriving for studenter*. Oslo: Gyldendal akademisk.

Department of Health. (2009). Living well with dementia: A national dementia strategy. Retrieved from https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/168220/dh_094051.pdf.

Dowling, G. A., Burr, R. L., Van Someren, E. J., Hubbard, E. M., Luxenberg, J. S., Mastick, J., & Cooper, B. A. (2008). Melatonin and Bright-Light Treatment for Rest–Activity Disruption in Institutionalized Patients with Alzheimer's Disease. *Journal of the American Geriatrics Society, 56*(2), 239-246.

Dowling, G. A., Graf, C. L., Hubbard, E. M., & Luxenberg, J. S. (2007). Light treatment for neuropsychiatric behaviors in Alzheimer's disease. *Western Journal of Nursing Research, 29*(8), 961-975. doi: 10.1177/0193945907303083

Engedal, K. (2008). *Alderspsykiatri i praksis : Lærebok* (2. utg. ed.). Tønsberg: Nasjonalt kompetansesenter for aldring og helse.

Ernst, E., Pittler, M. H., & Wider, B. (2001). *The desktop guide to complementary and alternative medicine: an evidence-based approach*: Mosby Hartcourt.

Finkel, S. (2000). Introduction to behavioural and psychological symptoms of dementia (BPSD). *International Journal of Geriatric Psychiatry, 15*, S2-S4.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*(3), 189-198.

Forrester, L. T., Maayan, N., Orrell, M., Spector, A. E., Buchan, L. D., & Soares-Weiser, K. (2014). Aromatherapy for dementia. *The Cochrane Library*.

Fowler, S., & Newton, L. (2006). Complementary and alternative therapies: the nurse's role. *Journal of Neuroscience Nursing*, *38*(4), 261-268.

Fu, C. Y., Moyle, W., & Cooke, M. (2013). A randomised controlled trial of the use of aromatherapy and hand massage to reduce disruptive behaviour in people with dementia. *BMC Complementary and Alternative Medicine, 13*, 165. doi: 10.1186/1472-6882-13-165

Fujii, M., Hatakeyama, R., Fukuoka, Y., Yamamoto, T., Sasaki, R., Moriya, M., . . . Sasaki, H. (2008). Lavender aroma therapy for behavioral and psychological symptoms in dementia patients. *Geriatrics & Gerontology International, 8*(2), 136-138. doi: 10.1111/j.1447-0594.2008.00461.x

Gill, S. S., Bronskill, S. E., Normand, S.-L. T., Anderson, G. M., Sykora, K., Lam, K., . . . Herrmann, N. (2007). Antipsychotic drug use and mortality in older adults with dementia. *Annals of internal medicine, 146*(11), 775-786.

Gould, F. (2003). *Aromatherapy for holistic therapists*: Nelson Thornes.

Graf, A., Wallner, C., Schubert, V., Willeit, M., Wlk, W., Fischer, P., . . . Neumeister, A. (2001). The effects of light therapy on mini-mental state examination scores in demented patients. *Biological psychiatry, 50*(9), 725-727.

Gray, S. G., & Clair, A. A. (2002). Influence of aromatherapy on medication administration to residential-care residents with dementia and behavioral challenges. *American Journal of Alzheimer's Disease and Other Dementias, 17*(3), 169-174.

Helse- og omsorgsdepartementet. (2015). *Demensplan 2020: Et mer demensvennlig samfunn*. Oslo: Helse- og omsorgsdepartementet.

Herz, R. S. (2009). Aromatherapy facts and fictions: a scientific analysis of olfactory effects on mood, physiology and behavior. *International Journal of Neuroscience, 119*(2), 263-290.

Hickman, S. E., Barrick, A. L., Williams, C. S., Zimmerman, S., Connell, B. R., Preisser, J. S., . . . Sloane, P. D. (2007). The effect of ambient bright light therapy on depressive symptoms in persons with dementia. *Journal of the American Geriatrics Society, 55*(11), 1817-1824.

Hicks-Moore, S. L., & Robinson, B. A. (2008). Favorite music and hand massage: Two interventions to decrease agitation in residents with dementia. *Dementia: The International Journal of Social Research and Practice, 7*(1), 95-108.

Holmes, C., Hopkins, V., Hensford, C., MacLaughlin, V., Wilkinson, D., & Rosenvinge, H. (2002). Lavender oil as a treatment for agitated behaviour in severe dementia: a placebo controlled study. *International Journal of Geriatric Psychiatry, 17*(4), 305-308.

Holt, F. E., Birks, T. P., Thorgrimsen, L. M., Spector, A. E., Wiles, A., & Orrell, M. (2003). Aroma therapy for dementia. *Cochrane Database of Systematic Reviews, 3*.

Hozumi, S., Hori, H., Okawa, M., Hishikawa, Y., & Sato, K. (1996). Favorable effect of transcranial electrostimulation on behavior disorders in elderly patients with dementia: a double-blind study. *International Journal of Neuroscience, 88*(1-2), 1-10.

Johannessen, A., & Tufte, P. A. (2002). *Introduksjon til samfunnsvitenskapelig metode.* . Oslo: Abstrakt.

Lin, L. C., Yang, M. H., Kao, C. C., Wu, S. C., Tang, S. H., & Lin, J. G. (2009). Using Acupressure and Montessori-Based Activities to Decrease Agitation for Residents with Dementia: A Cross-Over Trial. *Journal of the American Geriatrics Society, 57*(6), 1022-1029. doi: 10.1111/j.1532-5415.2009.02271.x

Lin, P. W., Chan, W. C., Ng, B. F., & Lam, L. C. (2007). Efficacy of aromatherapy (Lavandula angustifolia) as an intervention for agitated behaviours in Chinese older persons with dementia: a cross-over randomized trial. *International Journal of Geriatric Psychiatry, 22*(5), 405-410. doi: 10.1002/gps.1688

Lyketsos, C. G., Veiel, L. L., Baker, A., & Steele, C. (1999). A randomized, controlled trial of bright light therapy for agitated behaviors in dementia patients residing in long-term care. *International Journal of Geriatric Psychiatry, 14*(7), 520-525.

Manthorpe, J., & Watson, R. (2003). Poorly served? Eating and dementia. *Journal of Advanced Nursing, 41*. doi: 10.1046/j.1365-2648.2003.02520.x

Melnyk, B. M., & Fineout-Overholt, E. (2011). *Evidence-based practice in nursing & healthcare: A guide to best practice*: Lippincott Williams & Wilkins.

Mishima, K., Okawa, M., Hishikawa, Y., Hozumi, S., Hori, H., & Takahashi, K. (1994). Morning bright light therapy for sleep and behavior disorders in elderly patients with dementia. *Acta Psychiatrica Scandinavica, 89*(1), 1-7.

Moyle, W., Cooke, M. L., Beattie, E., Shum, D. H., O'Dwyer, S. T., & Barrett, S. (2014). Foot massage versus quiet presence on agitation and mood in people with dementia: a randomised controlled trial. *International Journal of Nursing Studies, 51*(6), 856-864. doi: 10.1016/j.ijnurstu.2013.10.019

National Institutes of Health. (2016). National Center for Complementary and Alternative Medicine. Retrieved from http://nccam.nih.gov.

Norheim, A. J. (2009). *Komplementær og alternativ medisin: en innføring for helsepersonell*. Kristiansand: : Høyskoleforlaget.

O'Connor, D. W., Eppingstall, B., Taffe, J., & van der Ploeg, E. S. (2013). A randomized, controlled cross-over trial of dermally-applied lavender (Lavandula angustifolia) oil as a treatment of agitated behaviour in dementia. *BMC Complementary and Alternative Medicine, 13*(1), 315.

Reisberg, B., Borenstein, J., Salob, S. P., & Ferris, S. H. (1987). Behavioral symptoms in Alzheimer's disease: phenomenology and treatment. *Journal of Clinical Psychiatry*.

Remington, R. (2002). Calming music and hand massage with agitated elderly. *Nursing research, 51*(5), 317-323.

Rodriguez-Mansilla, J., Gonzalez-Lopez-Arza, M. V., Varela-Donoso, E., Montanero-Fernandez, J., Jimenez-Palomares, M., & Garrido-Ardila, E. M. (2013). Ear therapy and massage therapy in the elderly with dementia: a pilot study. *Journal of Traditional Chinese Medicine, 33*(4), 461-467.

Rosen, J., Burgio, L., Kollar, M., Cain, M., Allison, M., Fogleman, M., . . . Zubenko, G. S. (1995). The Pittsburgh Agitation Scale: a user-friendly instrument for rating agitation in dementia patients. *The American journal of geriatric psychiatry, 2*(1), 52-59.

Salzman, C., Jeste, D., Meyer, R. E., Cohen-Mansfield, J., Cummings, J., Grossberg, G., . . . Maslow, K. (2008). Elderly patients with dementia-related symptoms of severe agitation and aggression: consensus statement on treatment options, clinical trials methodology, and policy. *Journal of Clinical Psychiatry, 69*(6), 889.

Scherder, E., Bouma, A., & Steen, L. (1995). Effects of simultaneously applied short-term transcutaneous electrical nerve stimulation and tactile stimulation on memory and affective behaviour of patients with probable Alzheimer's disease. *Behavioural Neurology, 8*(1), 3-13.

Scherder, E. J. A., & Bouma, A. (1999). Effects of transcutaneous electrical nerve stimulation on memory and behavior in Alzheimer's disease may be stage-dependent. *Biological psychiatry, 45*(6), 743-749.

Scherder, E. J. A., Bouma, A., & Steen, L. M. (1998). Effects of 'isolated' transcutaneous electrical nerve stimulation on memory and affective behavior in patients with probable Alzheimer's disease. *Biological psychiatry, 43*(6), 417-424.

Scherder, E. J. A., Van Someren, E. J. W., & Swaab, D. F. (1999). Transcutaneous electrical nerve stimulation (TENS) improves the rest–activity rhythm in midstage Alzheimer's disease. *Behavioural Brain Research, 101*(1), 105-107. doi: http://dx.doi.org/10.1016/S0166-4328(98)00150-8

Schneider, L. S., Dagerman, K., & Insel, P. S. (2006). Efficacy and adverse effects of atypical antipsychotics for dementia: meta-analysis of randomized, placebo-controlled trials. *The American journal of geriatric psychiatry, 14*(3), 191-210.

Selbæk, G., Aarsland, D., Ballard, C., Engedal, K., Langballe, E. M., Benth, J. Š., & Bergh, S. (2016). Antipsychotic Drug Use Is Not Associated With Long-Term Mortality Risk in Norwegian Nursing Home Patients. *Journal of the American Medical Directors Association, 17*(5), 464. e461-464. e467.

Smallwood, J., Brown, R., Coutler, F., Irvine, E., & Copland, C. (2001). Aromatherapy and behaviour disturbances in dementia: A randomized controlled trial. *International Journal of Geriatric Psychiatry, 16*(10), 1010-1013.

Snow, L. A., Hovanec, L., & Brandt, J. (2004). A controlled trial of aromatherapy for agitation in nursing home patients with dementia. *Journal of Alternative and Complementary Medicine, 10*(3), 431-437. doi: 10.1089/1075553041323696

Sosial- og helsedepartementet. *Alternativ Medisin* NOU 1998-21.

Suzuki, M., Tatsumi, A., Otsuka, T., Kikuchi, K., Mizuta, A., Makino, K., . . . Saruhara, T. (2010). Physical and psychological effects of 6-week tactile massage on elderly patients with severe dementia. *American Journal of Alzheimer's Disease & Other Dementias, 25*(8), 680-686. doi: 10.1177/1533317510386215

Taguchi, T., Yano, M., & Kido, Y. (2007). Influence of bright light therapy on postoperative patients: a pilot study. *Intensive and Critical Care Nursing, 23*(5), 289-297.

Tataryn, D. J. (2002). Paradigms of health and disease: a framework for classifying and understanding complementary and alternative medicine. *Journal of Alternative and Complementary Medicine, 8*(6), 877–892.

Testad, I., Corbett, A., Aarsland, D., Lexow, K. O., Fossey, J., Woods, B., & Ballard, C. (2014). The value of personalized psychosocial interventions to address behavioral and psychological symptoms in people with dementia living in care home settings: a systematic review. *International Psychogeriatrics, 26*(7), 1083-1098. doi: 10.1017/S1041610214000131

Trivedi, D., Goodman, C., Dickinson, A., Gage, H., McLaughlin, J., Manthorpe, J., . . . Iliffe, S. (2013). A protocol for a systematic review of research on managing behavioural and psychological symptoms in dementia for community-dwelling older people: evidence mapping and syntheses. *Systematic Reviews, 2*(1), 70. doi: 10.1186/2046-4053-2-70

Turten Kaymaz, T., & Ozdemir, L. (2016). Effects of aromatherapy on agitation and related caregiver burden in patients with moderate to severe dementia: A pilot study. *Geriatric Nursing*. doi: 10.1016/j.gerinurse.2016.11.001

Van Someren, E. J., Scherder, E. J., & Swaab, D. F. (1998). Transcutaneous electrical nerve stimulation (TENS) improves circadian rhythm disturbances in Alzheimer disease. *Alzheimer Disease & Associated Disorders, 12*(2), 114-118.

Vickers, A., & Zollman, C. (1999). ABC of complementary medicine: Massage therapies. *British Medical Journal, 319*(7219), 1254.

Wang, P. S., Schneeweiss, S., Avorn, J., Fischer, M. A., Mogun, H., Solomon, D. H., & Brookhart, M. A. (2005). Risk of death in elderly users of conventional vs. atypical antipsychotic medications. *New England Journal of Medicine, 353*(22), 2335-2341.

Weaver, M. T. (1985). Acupressure: an overview of theory and application. *The Nurse Practitioner, 10*(8), 38-42.

Wood-Mitchell, A., James, I. A., Waterworth, A., Swann, A., & Ballard, C. (2008). Factors influencing the prescribing of medications by old age psychiatrists for behavioural and psychological symptoms of dementia: a qualitative study. *Age and Ageing, 37*(5), 547-552.

Yang, M. H., Lin, L. C., Wu, S. C., Chiu, J. H., Wang, P. N., & Lin, J. G. (2015). Comparison of the efficacy of aroma-acupressure and aromatherapy for the treatment of dementia-associated agitation. *BMC Complementary and Alternative Medicine, 15 (1)*.

Yang, Y. P., Lee, F. P., Chao, H. C., Hsu, F. Y., & Wang, J. J. (2016). Comparing the Effects of Cognitive Stimulation, Reminiscence, and Aroma-Massage on Agitation and Depressive Mood in People With Dementia. *Journal of the American Medical Directors Association, 17*(8), 719-724. doi: 10.1016/j.jamda.2016.03.021

Zhao, M., Haley, D. R., Nolin, J. M., Dunning, K., Wang, J., & Sun, Q. (2009). Utilization, cost, payment, and patient satisfaction of rehabilitative services in Shandong, China. *Health Policy, 93*(1), 21-26.

PART 2: Article

Complementary and Alternative Medicine in relation to the Behavioural and Psychological Symptoms in people with Dementia: A systematic review

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Abstract

Objective: To assess the efficacy of Complementary and Alternative Medicine in people with dementia with behavioural and psychological symptoms.

Methods: A literature search was undertaken. Three databases, Medline, EMBASE, and PsycINFO were searched. Only peer-reviewed journal articles in English published in 1990s or later with clinic trials for humans were included in the current review. Randomized clinical trials or studies with control groups employing five following complementary and alternative therapies (Acupuncture/Acupressure, Aromatherapy, Massage, BLT, and TENS) for managing BPSD in people with dementia were included in our systematic review.

Results: 565 related studies were identified, where 30 RCTs or studies with control group met the inclusion criteria for this systematic review. 22 studies of which 17 were RCTs, out of the total 30 studies selected and analysed in this work have demonstrated effectiveness of CAM.

Conclusion: Dementia as a medical problem currently can not be cured, but the symptoms of dementia and the quality of life of patients with dementia can be improved by different therapies. Although not all studies demonstrated consist statistic significant improvement, there were obviously benefited evidences or positive trend from CAM. More research, however, is needed to provide definitive evidence about the benefits of CAM.

Keywords: dementia; Alzheimer`s Disease; Behavioural and Psychological Symptoms in Dementia; Complementary and Alternative Medicine

Introduction

There are 35 million people with dementia worldwide, and many of them reside in nursing homes (Ballard *et al.*, 2009b). In Norway, there are over 77,000 people suffering from dementia, and the number will probably double itself within 2040. It is clearly a heavy burden for those caring for relatives with dementia at home, and many informal carers are elderly and frail themselves (Department of Health, 2009). Dementia refers to changes in memory and other cognitive skills severe enough to affect a person's ability to perform daily social and occupational activities. There are many different forms of dementia that affect the elderly, but Alzheimer's disease (AD) is the most common and accounts for 60 to 80 percent of all dementias. Other types of dementia include vascular-based dementias (VsD), the second most frequent type of dementia, and Lewy body dementia.

Behavioural and Psychological Symptoms of Dementia (BPSD) affects more than 90% of people with dementia at some point, and in particular, agitation, aggression, psychosis and depression are major causes of distress for patients with dementia (Testad *et al.*, 2014). BPSD affects the patients' ability to maintain daily activities, and reduce the quality of life for both people with dementia and their caregivers (Finkel, 2000). The consequences of BPSD can be disturbed sleep, fatigue, increased risk of falls and injuries, inadequate nutrition (Aselage and Amella, 2010; Manthorpe and Watson, 2003) and increased stress of caregivers.

Antipsychotic drugs as conventional medicine are often used for the management of behavioural and psychological symptoms in dementia (Banerjee, 2009). Antipsychotic medications in treating dementia have limited effect and significantly increased the risk of stroke and mortality (Ballard *et al.*, 2009a; Gill *et al.*, 2007; Schneider *et al.*, 2006; Wang *et al.*, 2005). Current clinical guidance recommends non-

pharmacologic interventions as the first choice for people with dementia (Salzman *et al.*, 2008; Selbæk *et al.*, 2016; Wood-Mitchell *et al.*, 2008 Swann, & Ballard, 2008). In addition to pharmacological and non-pharmacological intervention, complimentary and alternative medicine (CAM) is starting to show some interesting results as well in the treatment of BPSD and dementia (Posadzki *et al.*, 2012; Sierpina *et al.*, 2005). Complementary therapies are often used in addition to conventional medicine. Alternative therapies are used instead of conventional medicine (National Institutes of Health, 2016). That is to say, complementary interventions are used together with conventional treatments, whereas alternative interventions are used instead of conventional medicine.

Meanwhile, CAM has some intersections with pharmacologic treatments and non-pharmacologic interventions. In one side, complementary therapies are often used in addition to pharmacologic treatments. Alternative therapies are used instead of pharmacologic treatments. On the other side, CAM and nonpharmacological interventions have many common therapies, such as music therapies and massage. Several reviews have already discussed the effectiveness of nonpharmacological interventions to for people with BPSD (Chen *et al.*, 2014; Cohen-Mansfield, 2013; Oliveira *et al.*, 2015). Nowadays CAM as a green wave has received great interest within the field of dementia treatment. There is an urgent need to summarize available research on complementary and alternative treatments of dementia.

The aim of this review is to assess the efficacy of Complementary and Alternative Medicine in people with dementia with behavioural and psychological symptoms.

Methods

SEARCH STRATEGY

The following databases were explored: Medline through Pubmed; and OVID for EMBASE and PsycInfo. There are many different types of methods and measures that fall under the term ”Alternative Treatment”. The search strategy was conducted with the help of the librarian from Stavanger University with professional guidance provided by colleagues in scientific environment at SESAM.

SEARCH TERMS

Complementary and Alternative Therapies terms were chosen from Alzheimer` Society in UK for this systematic review: *Acupuncture/Acupressure, Aromatherapy, Massage, Bright Light Therapy (BLT), and Transcutaneous Electrical Nerve Stimulation (TENS)* and the following key words and subthemes were adopted as search terms: (1) “Dementia” OR “Alzheimer`s Disease”; (2) “Behavioural symptoms” OR “Psychological disorder” OR “agitation” OR “depression” OR “anxiety”; (3) “Acupuncture” OR “acup*”; “Massage”; “Aromatherapy”; ”Bright Light Therapy”; “Transcutaneous electrical nerve stimulation”. Searches are primarily conducted in English.

EXCLUSION CRITERIA

Studies associated with herbal remedies/vitamin supplements, diet, exercise, spiritual therapy, psychotherapy, cognitive therapy, or prevention of dementia was excluded.

INCLUSION CRITERIA

Only peer-reviewed journal articles in English published in 1990s or later with clinic trials for humans were included in the current review. Randomized clinical trials or studies with control groups employing five following complementary and alternative therapies: Acupuncture/Acupressure, Aromatherapy, Massage, BLT, and TENS (Table 1) for managing BPSD in people with dementia were included in our systematic review.

QUALITY ASSESSMENT

The methodological quality rating was assessed by the Melynk`s level of evidence (Melnyk and Fineout-Overholt, 2011) (Figure 2). Two reviewers have assessed these studies independently. If there was disagreement, the third reviewer was consulted. All the three reviewers discussed and made consensus.

Results

The routine for conducting the reviewing process is presented as the flow chart (Figure 1). 565 related studies were identified via automatic search in different databases as well as manual search from the reference lists of selected articles. With duplicates removed, the remaining 520 records were screened by their titles and abstracts. Among them, 83 studies were considered highly relevant and 75 of these were assessed for eligibility based on their full-texts available for viewing. 30 studies that met the inclusion criteria for this systematic review were finally selected and read through by two reviewers independently. The characteristic of these included studies is summarized in Table 2.

DESCRIPTION OF STUDIES

Data from the selected 30 studies were synthesized according to the following characteristics: author and year (setting), intervention type, attention control, study

design, length, number of times, length of each session, sample population, outcome focus, outcome measures, impact and Level of evidence (Table 2). A narrative synthesis approach was performed to examine the results. These studies were conducted in the following settings: Taiwan (n = 3), China (n = 1), Spain (n=1), UK (n=5), Australia (n=4), Japan (n = 3), USA (n=7), Hong Kong (n = 1), Canada (n=1), and the Netherlands (n = 4).

Acupuncture/Acupressure

Four studies evaluated acupuncture and acupressure therapies in treating people with BPSD. Two were double-blinded RCT (Lin *et al.*, 2009; Rodriguez-Mansilla *et al.*, 2013), one single-blinded RCT (Shi *et al.*, 2015) and one quasi-experimental study (Yang *et al.*, 2007). The studies had from 31 and 133 participants with duration of 4 to 12 weeks, the frequency of acupuncture or acupressure intervention varied from every 15 days to twice a day, and the length of each session varied from 15 to 30 minutes. Two RCTs (Rodriguez-Mansilla *et al.*, 2013; Shi *et al.*, 2015) evaluated acupuncture therapy by qualified acupuncturists using a specific protocol with body acupuncture or ear acupuncture. Both outcomes of these studies were measured by MMSE and ADL. The first was double-blinded RCT study (Rodriguez-Mansilla *et al.*, 2013) indicated significant benefit compared to the comparison group. In contrast, the results of a single-blinded RCT (Shi *et al.*, 2015) reported no significant difference among groups was observed, but MMSE and ADL scores of pooled-acupuncture group were significantly higher than the control group. Other outcome, such as the Ease-of-care, was consistently evaluated across studies. The other two studies (Lin *et al.*, 2009; Yang *et al.*, 2007) measured agitation med CMAI as a specific outcome. The results indicated significant improvement with acupressure therapy intervention when compared to the control group.

Aromatherapy

Nine studies were included (Ballard *et al.*, 2002a; Burns *et al.*, 2011; Fu *et al.*, 2013; Gray and Clair, 2002; Holmes *et al.*, 2002; Lin *et al.*, 2007; O'Connor *et al.*, 2013; Smallwood *et al.*, 2001; Yang *et al.*, 2015), of which two were double-blinded RCTs, four single-blinded RCTs, one RCT with cross-over design and two quasi-experimental studies. The studies included between 13 and 186 participants with duration of 2 to 12 weeks. The frequency of aromatherapy intervention varied from once per day to three times per day, and the length of each session varied from 2 minutes to 4 hours. Inhalation or topical applications to the skin with scented essential oil from plants, such as Lavender and Melissa, was used as aromatherapy intervention for the treatment of physical and psychological health. In our included aromatherapy studies, two RCTs used Melissa oil and the other seven RCTs or quasi-experimental studies used Lavender oil. Aromatherapy was delivered via drops on clothing, cotton-ball, diffused in the air, sprayed onto chest, or applied as lotion directly on skin. Agitation was the main outcome focus among these seven included studies (Ballard *et al.*, 2002b; Burns *et al.*, 2009; Fu *et al.*, 2013; Holmes *et al.*, 2002; Lin *et al.*, 2007; O'Connor *et al.*, 2013; Yang *et al.*, 2015). The observed effectiveness of these included studies in treating dementia patients had shown mixed results.

Two studies (Ballard *et al.*, 2002a; Burns *et al.*, 2011) employing double-blinded RCTs used Melissa oil to treat agitation in people with dementia. However, the results were conflicting. In the study by Ballard et al, the total CMAI scores were significantly reduced in people with severe dementia compared to placebo treatment ($p<0.00001$) and quality of life indices were significantly improved ($p=0.005$). In contrast, the other study by Burns et al. showed that there was no significant difference among groups. The

next seven RCTs with single-blinded/crossover design or quasi-experimental studies used varied percentages of Lavender oil to manage BPSD in people with dementia. Four of the seven studies (Holmes *et al.*, 2002; Lin *et al.*, 2007; Smallwood *et al.*, 2001; Yang *et al.*, 2015) demonstrated significant improvement after aromatherapy interventions and the other three studies (Fu *et al.*, 2013; Gray and Clair, 2002; O'Connor *et al.*, 2013) showed positive but no significant effects when compared with control group.

Massage

Four studies, of which three RCTs and one quasi-experimental study (Hicks-Moore and Robinson, 2008; Moyle *et al.*, 2014; Remington, 2002; Suzuki *et al.*, 2010) were identified. Three of them tested the efficacy of massage on agitation and for BPSD in general. The studies included between 40 and 68 participants, with durations ranged from 2 to 6 weeks. The frequency of each intervention was not available in each study (Hicks-Moore and Robinson, 2008; Remington, 2002), two studies given massage therapy once a day, every weekday (Moyle *et al.*, 2014; Suzuki *et al.*, 2010). The length of each session varied from 10 minutes to 20 minutes. All these studies demonstrated positive effects of massage therapy on reducing a range of conditions of BPSD, especially agitation, in people with dementia. Three studies (Hicks-Moore and Robinson, 2008; Moyle *et al.*, 2014; Remington, 2002) focusing on agitation as an outcome which indicated that massage therapy conferred significant advantage in negative affect. In addition, there were two RCTs characterized under acupressure and aromatherapy categories on the efficacy of massage for behaviour disorders in people with dementia (Rodriguez-Mansilla et al., 2013; Smallwood et al., 2001). Massage intervention group in these two RCTs reported positive results in dementia patients.

These two studies were of a sufficient methodological rigour to count as evidence to answer the question of effect.

Bright Light therapy (BLT)

Eight RCTs or quasi-experimental studies assessed the efficacy of BLT to manage BPSD among dementia residents in nursing homes and assisted living facilities. Three RCT studies measured agitation (Ancoli-Israel et al., 2003b; Burns et al., 2009; Lyketsos et al., 1999); two RCT studies measured activity rhythms (Ancoli-Israel et al., 2003a; Dowling et al., 2008), one quasi-experimental study measured sleep disorder (Mishima et al., 1994); and the other two RCTs measured cognitive functions, especially depression (Dowling et al., 2007; Graf et al., 2001; Hickman et al., 2007). Comparison groups received exposure to standard light, dimmed red light, or no treatment. The studies had between 14 and 92 participants and duration of 10 days to 10 weeks. Patients were exposed to bright light variably as 2500 lux to 10,000 lux. The frequency of bright light therapy interventions varied from every other day to every day, and the length of each session varied from 1 hour to 2 hours per day at varying times of day. All these included studies showed positive results such as improved night sleep, reduction in agitation, and improvement in cognitive performance. Nevertheless, only a few studies have demonstrated bright light intervention with clinically significant effect. Significant advantage compared to comparison group was identified in four of the eight studies examining BPSD (Dowling *et al.*, 2007; Graf *et al.*, 2001; Lyketsos *et al.*, 1999; Mishima *et al.*, 1994), including three of the four RCTs examining this outcome. However, three studies with significant improvement had small size sample of 14 to 23 patients. Only one study employed a RCT design by Dowling et al. included 70 residents who were diagnosed with AD. The results of this study revealed statistically

significant differences between groups on agitation, depression and other varied neuropsychiatric behaviours.

Transcutaneous Electrical Nerve Stimulation (TENS)

Five RCTs evaluated the benefit of TENS therapy, of which four of the five RCTs were authored by Scherder and colleagues, one double-blinded RCT were conducted by Hozumi et al. Three RCTs focused on memory or affective behaviour (Scherder *et al.*, 1995; Scherder and Bouma, 1999; Scherder *et al.*, 1998; Van Someren *et al.*, 1998), one on sleep-wake and behaviour disorder (Hozumi *et al.*, 1996) and the last on rest-activity rhythm (Scherder *et al.*, 1999). Scherder and his colleagues used a similar intervention protocol for these five RCTs. The studies had between 14 and 18 participants and duration was 6 weeks, the frequency of TENS intervention was 5 days a week, and the length of each session was 30 minutes. In all cases, the control intervention was sham TENS. The main difference among the studies existed in the different type of TENS: short-term, isolated, or burst TENS. According two studies conducted by Scherder et al., they proved that 160 Hz/ 100μs, 30 minutes every weekday for 6 weeks would be a effective set of stimulation parameters for nonverbal or verbal memory, and short-term and long-term visual memory. Results from all these included studies were very consistent. The results demonstrated that TENS had great clinically significant effects in people with dementia. Two of these six RCTs employed double-blinded design (Hozumi *et al.*, 1996; Scherder *et al.*, 1998). Hozumi et al. included 27 participants with multi-infarct dementia and were selected on the basis of irregular sleep-wake patterns in conjunction with nocturnal behaviour disorders. Significant improvements were found in motivation behaviour disorder, sleep disorder and subjective complaints. Scherder et al. tested the effect of ”isolated” TENS, single-blinded design, for memory and affective

behaviour in people with AD during the treatment. The results of the study showed that isolated TENS had significant treatment effects on patients` cognitive and independent function, whereas patients` affective behaviour did not improve.

Discussion

This systematic review examined 30 published studies of complementary and alternative medicine aimed at managing BPSD in people with dementia. Of these 30 studies, there were four on acupuncture and acupressure, nine on aromatherapy, four on massage, eight on BLT, and five on TENS. 25 studies employed an RCT design in our included studies. Other studies with control conditions worked out with good evidence to show the great diversity in these interventions.

In the initial searching process, despite the fact that studies with animal model were found abundant, it was hard to find clinical trials of acupuncture intervention related to dementia,. In previous reviews, few high-quality RCTs published in international journals on acupuncture therapy reported that this intervention had effectiveness to dementia. Therefore, more well design clinical trials were needed to demonstrate that acupuncture has great efficacy to BPSD in people with dementia. Acupressure as a simple and non-intrusive therapy has been increasingly studied. Acupressure treatment conforms to the same principles as acupuncture involving constant pressure to stimulate meridians or acupoints of the human body to balance energy (Zhao *et al.*, 2009). Acupressure serves not only to relax the human body, but also stimulate the channels governing the flow of energy to promote health and offer comfort (Chen *et al.*, 1999; Weaver 1985).

In this systematic review, acupuncture and acupressure interventions have two studies found for each with sufficient methodological quality to produce reliable

evidence regarding effectiveness. The limited amount of reliable evidence available makes it difficult in scope to allow for general conclusions. Overall, the limited moderate to high quality evidence suggests that acupuncture and acupressure therapies may be effective in managing BPSD.

There are two ways for essential oil to be applied externally, by which they may reach the bloodstream: absorption by olfactory system or skin absorption (Gould, 2003). Essential oil molecules can enter through the nose, pass through the epidermal barrier and enter the bloodstream without causing injury or triggering inflammation or water loss. Our bodies can become sedated, stimulated or relaxed by the action of certain oils. Comparing these positive and negative studies in aromatherapy, we found that the method for administration of the treatments was different. In the negative studies (Burns *et al.*, 2011; Fu *et al.*, 2013; Gray and Clair, 2002; O'Connor *et al.*, 2013), the site of administration of the essential oil was relatively far from the olfactory system. The perceived quality of the essential oil odor was the most relevant factor for determining how an individual would respond to it both emotionally and physiologically (Herz, 2009). By using a purely olfactory form of aromatherapy, Snow and colleagues (Snow *et al.*, 2004) did not observe a decrease of agitation in participants with severe dementia and impaired olfactory sense.

Meanwhile, based on the given information of these included studies, it is hard to determine whether and how Melissa and Lavender oil was associated with effectiveness of aromatherapy. Differences in essential oil formulation, delivery methods, participant numbers, length of each session, selection criteria, outcome measures and time frames make it almost impossible to perform unbiased comparison (Holt *et al.*, 2003).

Massage as an alternative therapy has been used in dementia care with the aim of managing related psychological and behavioral manifestations and improving quality of

life in people with dementia (Cohen-Mansfield, 2001). The limited evidence currently available is in favor of massage intervention. More research is needed to provide definitive evidence on the benefits of massage intervention.

The BLT studies included in this review revealed positive effects of this intervention in BPSD, especially in agitated, sleep disturbance and circadian activity rhythms. However, little evidence with small amount sample studies demonstrated that this intervention has significant effects. In contrast a large, pre-and post-test design RCT (Ancoli-Israel *et al.*, 2003b) reported that bright light had no significant effects on the observational ratings of agitation in any of the light-treatment groups. Importantly, they also observed a worsening of verbal agitation in the evening bright light group. In future study, the safety of complementary and alternative intervention should be assessed in the design of the experiment.

The studies of TENS therapy included in our systematic review readily fall into the Dutch studies and the Japanese study. They used similar experimental design, subjects, interventions and outcome measures. In contrast, the study from Japan conducted by Hozumi et al. focused on irregular sleep-wake patterns and nocturnal behaviour disorders and/or delirium in people with multi-infarct dementia. The results employing TENS intervention had significant effects. However, all these studies were conducted before 2000 with confined subjects studied in each work. A consistent weakness of all the studies is a small sample size, which reduces the likelihood of detecting an effect of TENS. Furthermore, few studies on TENS related to BPSD in people with dementia were published in recent years.

Complementary and alternative therapies with different experimental designs may lead to inconsistent results. This requires a very critical evaluation of the design of each research experiment in order to achieve a consistent conclusion. Even with well-

designed RCT studies, there may still be conflicting results due to different types of patients or different measurements of the indicators. These led to a lack of comparability among experiments. Consequently, it is difficult to quantitatively describe the significance of these clinical experiments in a reliable, statistical manner.

On one hand, an effective, repeatable and safe therapy protocol is urgent as an important way to improve BPSD condition and quality of life for people with dementia. Further research is required to identify more effective and practical protocol for each complementary and alternative medicine and guide their clinic practice. On the other hand, it is plausible to try combinations of two or three effective complementary and alternative therapies to see if the performance could be enhanced. Such would be of great potential and value to people with dementia. Among the various complementary therapies, acupressure, massage and aromatherapy are commonly used and seen as relatively non-invasive procedures for managing a variety of symptoms, especially agitation/aggression. The combination of aromatherapy and massage or acupressure (Fujii *et al.*, 2008; Smallwood *et al.*, 2001; Turten Kaymaz and Ozdemir, 2016; Yang *et al.*, 2015; Yang *et al.*, 2016) showed the greatest improvement in agitation and other behaviour disorders of BPSD compared with aromatherapy,massage, or acupressure treatment applied alone.

Limitations

Several limitations are acknowledged in this study. Due to time limitation, this systematic review did not include all the categories of complementary and alternative therapies. Only five interventions (Acupuncture/Acupressure, Aromatherapy, Massage, BLT, and TENS) were assessed for whether they had efficacy in reducing behaviour and psychological symptoms in patients with dementia. More complementary and

alternative therapies should be assessed in future research for their effectiveness and safety in relation to improvement of BPSD in people with dementia. Meanwhile, we have screened three major databases, with coverage of probably most relevant articles. However, manual search from the reference lists of selected articles is a very effective method to find other highly related studies. An additional limitation is that we did not discuss the safety of complementary and alternative medicines. Although few studies had reported side effects with use of CAM in persons with dementia, it is important to reduce or avoid any possible risks.

Conclusion

Dementia as a medical problem, which currently can not be cured, but the symptoms of dementia and the quality of life of patients with dementia can be improved by different therapies. Although not all studies demonstrated consist statistic significant improvement, there were obviously benefited evidences or positive trend from CAM. More research, however, is needed to provide definitive evidence about the benefits of CAM.

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References

Ancoli-Israel S, Gehrman P, Martin JL, Shochat T, Marler M, Corey-Bloom J, Levi L. 2003a. Increased light exposure consolidates sleep and strengthens circadian rhythms in severe Alzheimer's disease patients. *Behav Sleep Med*. **1**: 22-36.

Ancoli-Israel S, Martin JL, Gehrman P, Shochat T, Corey-Bloom J, Marler M, Nolan S, Levi L. 2003b. Effect of light on agitation in institutionalized patients with severe Alzheimer disease. *Am J Geriatr Psychiatry*. **11**: 194-203.

Aselage M, Amella E. 2010. An evolutionary analysis of mealtime difficulties in older adults with dementia. *J Clin Nurs*. **19**.

Ballard C, Corbett A, Chitramohan R, Aarsland D. 2009a. Management of agitation and aggression associated with Alzheimer's disease: controversies and possible solutions. *Curr Opin Psychiatry*. **22**: 532-540.

Ballard CG, Gauthier S, Cummings JL, Brodaty H, Grossberg GT, Robert P, Lyketsos CG. 2009b. Management of agitation and aggression associated with Alzheimer disease. *Nat Rev Neurol*. **5**: 245-255.

Ballard CG, O'Brien JT, Reichelt K, Perry EK. 2002a. Aromatherapy as a safe and effective treatment for the management of agitation in severe dementia: The results of a double-blind, placebo-controlled trial with Melissa. *J Clin Psychiatry*. **63**: 553-558.

Ballard CG, Aarsland D, McKeith I, O'Brien J, Gray A, Cormack F, Burn D, Cassidy T, Starfeldt R, Larsen JP *et al.*,. 2002b. Fluctuations in attention: PD dementia vs DLB with parkinsonism. *Neurology*. **59**: 1714-1720.

Banerjee S. 2009. *The use of antipsychotic medication for people with dementia: Time for action.* London: Department of Health.

Burns A, Allen H, Tomenson B, Duignan D, Byrne J. 2009. Bright light therapy for agitation in dementia: a randomized controlled trial. *Int Psychogeriatr*. **21**: 711-721.

Burns A, Perry E, Holmes C, Francis P, Morris J, Howes M-J, Chazot P, Lees G, Ballard C. 2011. A double-blind placebo-controlled randomized trial of Melissa officinalis oil and donepezil for the treatment of agitation in Alzheimer's disease. *Dement Geriatr Cogn Dis*. **31**: 158-164.

Cameron M, Lonergan E, Lee H. 2003. Transcutaneous electrical nerve stimulation (TENS) for dementia. *Cochrane Database Syst Rev*: Cd004032.

Chen M-L, Lin L-C, Wu S-C, Lin J-G. 1999. The effectiveness of acupressure in improving the quality of sleep of institutionalized residents. *J Gerontol A Biol Sci Med Sci*. **54**: M389-M394.

Chen RC, Liu CL, Lin MH, Peng LN, Chen LY, Liu LK, Chen LK. 2014. Non-pharmacological treatment reducing not only behavioral symptoms, but also psychotic symptoms of older adults with dementia: A prospective cohort study in Taiwan. *Geriatr Gerontol Int*. **14**: 440-446.

Cohen-Mansfield J. 2001. Nonpharmacologic interventions for inappropriate behaviors in dementia: a review, summary, and critique. *Am J Geriatr Psychiatry*. **9**: 361-381.

Cohen-Mansfield J. 2013. Nonpharmacologic treatment of behavioral disorders in dementia. *Curr Treat Options Neurol*. **15**: 765-785.

Department of Health. 2009. Living well with dementia: A national dementia strategy. Retrievedfrom https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/168220/dh_094051.pdf

Dowling GA, Burr RL, Van Someren EJ, Hubbard EM, Luxenberg JS, Mastick J, Cooper BA. 2008. Melatonin and Bright-Light Treatment for Rest-Activity

Disruption in Institutionalized Patients with Alzheimer's Disease. *J Am Geriatr Soc*. **56**: 239-246.

Dowling GA, Graf CL, Hubbard EM, Luxenberg JS. 2007. Light treatment for neuropsychiatric behaviors in Alzheimer's disease. *West J Nurs Res*. **29**: 961-975.

Ernst E, Pittler MH, Wider B. 2001. *The desktop guide to complementary and alternative medicine: an evidence-based approach*. Mosby: Hartcourt.

Finkel S. 2000. Introduction to behavioural and psychological symptoms of dementia (BPSD). *International Journal of Geriatric Psychiatry*. **15**: S2-S4.

Forrester LT, Maayan N, Orrell M, Spector AE, Buchan LD, Soares-Weiser K. 2014. Aromatherapy for dementia. *The Cochrane Library*.

Fu CY, Moyle W, Cooke M. 2013. A randomised controlled trial of the use of aromatherapy and hand massage to reduce disruptive behaviour in people with dementia. *BMC Complement Altern Med*. **13**: 165.

Fujii M, Hatakeyama R, Fukuoka Y, Yamamoto T, Sasaki R, Moriya M, Kanno M, Sasaki H. 2008. Lavender aroma therapy for behavioral and psychological symptoms in dementia patients. *Geriatr Gerontol Int*. **8**: 136-138.

Gill SS, Bronskill SE, Normand S-LT, Anderson GM, Sykora K, Lam K, Bell CM, Lee PE, Fischer HD, Herrmann N. 2007. Antipsychotic drug use and mortality in older adults with dementia. *Ann Intern Med*. **146**: 775-786.

Gould F. 2003. *Aromatherapy for holistic therapists*. Nelson: Thornes.

Graf A, Wallner C, Schubert V, Willeit M, Wlk W, Fischer P, Kasper S, Neumeister A. 2001. The effects of light therapy on mini-mental state examination scores in demented patients. *Biol Psychiatry*. **50**: 725-727.

Gray SG, Clair AA. 2002. Influence of aromatherapy on medication administration to residential-care residents with dementia and behavioral challenges. *Am J Alzheimers Dis Other Demen*. **17**: 169-174.

Herz RS. 2009. Aromatherapy facts and fictions: a scientific analysis of olfactory effects on mood, physiology and behavior. *Int J Neurosci*. **119**: 263-290.

Hickman SE, Barrick AL, Williams CS, Zimmerman S, Connell BR, Preisser JS, Mitchell C, Sloane PD. 2007. The effect of ambient bright light therapy on depressive symptoms in persons with dementia. *J Am Geriatr Soc*. **55**: 1817-1824.

Hicks-Moore SL, Robinson BA. 2008. Favorite music and hand massage: Two interventions to decrease agitation in residents with dementia. *Dementia.* **7**: 95-108.

Holmes C, Hopkins V, Hensford C, MacLaughlin V, Wilkinson D, Rosenvinge H. 2002. Lavender oil as a treatment for agitated behaviour in severe dementia: a placebo controlled study. *Int J Geriatr Psychiatry*. **17**: 305-308.

Holt FE, Birks TP, Thorgrimsen LM, Spector AE, Wiles A, Orrell M. 2003. Aroma therapy for dementia. *Cochrane Database Syst Rev*. **3**.

Hozumi S, Hori H, Okawa M, Hishikawa Y, Sato K. 1996. Favorable effect of transcranial electrostimulation on behavior disorders in elderly patients with dementia: a double-blind study. *Int J Neurosci*. **88**: 1-10.

Lin LC, Yang MH, Kao CC, Wu SC, Tang SH, Lin JG. 2009. Using acupressure and Montessori-based activities to decrease agitation for residents with dementia: A Cross-over trial. *J Am Geriatr Soc*. **57**: 1022-1029.

Lin PW, Chan WC, Ng BF, Lam LC. 2007. Efficacy of aromatherapy (Lavandula angustifolia) as an intervention for agitated behaviours in Chinese older persons with dementia: a cross-over randomized trial. *Int J Geriatr Psychiatry*. **22**: 405-410.

Lyketsos CG, Veiel LL, Baker A, Steele C. 1999. A randomized, controlled trial of bright light therapy for agitated behaviors in dementia patients residing in long-term care. *Int J Geriatr Psychiatry*. **14**: 520-525.

Manthorpe J, Watson R. 2003. Poorly served? Eating and dementia. *J Adv Nurs*. **41**.

Melnyk BM, Fineout-Overholt E. 2011. *Evidence-based practice in nursing & healthcare: A guide to best practice*. Lippincott Williams & Wilkins.

Mishima K, Okawa M, Hishikawa Y, Hozumi S, Hori H, Takahashi K. 1994. Morning bright light therapy for sleep and behavior disorders in elderly patients with dementia. *Acta Psychiatr Scand*. **89**: 1-7.

Moyle W, Cooke ML, Beattie E, Shum DH, O'Dwyer ST, Barrett S. 2014. Foot massage versus quiet presence on agitation and mood in people with dementia: a randomised controlled trial. *Int J Nurs Stud*. **51**: 856-864.

National Institutes of Health. 2016. National Center for Complementary and Alternative Medicine. Retrived from http://nccam.nih.gov.

O'Connor DW, Eppingstall B, Taffe J, van der Ploeg ES. 2013. A randomized, controlled cross-over trial of dermally-applied lavender (Lavandula angustifolia) oil as a treatment of agitated behaviour in dementia. *BMC Complement Altern Med*. **13**: 315.

Oliveira AMD, Radanovic M, Mello PCHD, Buchain PC, Vizzotto ADB, Celestino DL, Stella F, Piersol CV, Forlenza OV. 2015. Nonpharmacological interventions to reduce behavioral and psychological symptoms of dementia: A systematic review. *BioMed Res Int*. **2015**.

Posadzki P, Ernst E, Lee MS. 2012. Complementary and alternative medicine for Alzheimer's disease: an overview of systematic reviews. *Focus Altern Complement Ther*. **17**: 186-191.

Remington R. 2002. Calming music and hand massage with agitated elderly. *Nurs Res*. **51**: 317-323.

Rodriguez-Mansilla J, Gonzalez-Lopez-Arza MV, Varela-Donoso E, Montanero-Fernandez J, Jimenez-Palomares M, Garrido-Ardila EM. 2013. Ear therapy and massage therapy in the elderly with dementia: a pilot study. *J Tradit Chin Med*. **33**: 461-467.

Salzman C, Jeste D, Meyer RE, Cohen-Mansfield J, Cummings J, Grossberg G, Jarvik L, Kraemer H, Lebowitz B, Maslow K. 2008. Elderly patients with dementia-related symptoms of severe agitation and aggression: consensus statement on treatment options, clinical trials methodology, and policy. *J Clin Psychiatry*. **69**: 889.

Scherder E, Bouma A, Steen L. 1995. Effects of simultaneously applied short-term transcutaneous electrical nerve stimulation and tactile stimulation on memory and affective behaviour of patients with probable Alzheimer's disease. *Behavioural Neurology*. **8**: 3-13.

Scherder EJA, Bouma A. 1999. Effects of transcutaneous electrical nerve stimulation on memory and behavior in Alzheimer's disease may be stage-dependent. *Biol Psychiatry*. **45**: 743-749.

Scherder EJA, Bouma A, Steen LM. 1998. Effects of 'isolated' transcutaneous electrical nerve stimulation on memory and affective behavior in patients with probable Alzheimer's disease. *Biol Psychiatry*. **43**: 417-424.

Scherder EJA, Van Someren EJW, Swaab DF. 1999. Transcutaneous electrical nerve stimulation (TENS) improves the rest–activity rhythm in midstage Alzheimer's disease. *Beh Brain Res*. **101**: 105-107.

Schneider LS, Dagerman K, Insel PS. 2006. Efficacy and adverse effects of atypical antipsychotics for dementia: meta-analysis of randomized, placebo-controlled trials. *Am J Geriatr Psychiatry*. **14**: 191-210.

Selbæk G, Aarsland D, Ballard C, Engedal K, Langballe EM, Benth JŠ, Bergh S. 2016. Antipsychotic Drug Use Is Not Associated With Long-Term Mortality Risk in Norwegian Nursing Home Patients. *J Am Med Dirs Assoc*. **17**: 464. e461-464. e467.

Shi GX, Li QQ, Yang BF, Liu Y, Guan LP, Wu MM, Wang LP, Liu CZ. 2015. Acupuncture for Vascular Dementia: A Pragmatic Randomized Clinical Trial. *ScientificWorldJournal*. **2015**: 161439.

Sierpina VS, Sierpina M, Loera JA, Grumbles L. 2005. Complementary and integrative approaches to dementia. *South Med J*. **98**: 636-645.

Smallwood J, Brown R, Coutler F, Irvine E, Copland C. 2001. Aromatherapy and behaviour disturbances in dementia: A randomized controlled trial. *Int J Geriatr Psychiatry*. **16**: 1010-1013.

Snow LA, Hovanec L, Brandt J. 2004. A controlled trial of aromatherapy for agitation in nursing home patients with dementia. *J Altern Complement Med*. **10**: 431-437.

Suzuki M, Tatsumi A, Otsuka T, Kikuchi K, Mizuta A, Makino K, Kimoto A, Fujiwara K, Abe T, Nakagomi T *et al.*,. 2010. Physical and psychological effects of 6-week tactile massage on elderly patients with severe dementia. *Am J Alzheimers Dis Other Demen*. **25**: 680-686.

Taguchi T, Yano M, Kido Y. 2007. Influence of bright light therapy on postoperative patients: a pilot study. *Intensive Crit Care Nurs*. **23**: 289-297.

Testad I, Corbett A, Aarsland D, Lexow KO, Fossey J, Woods B, Ballard C. 2014. The value of personalized psychosocial interventions to address behavioral and psychological symptoms in people with dementia living in care home settings: a systematic review. *Int Psychogeriatr*. **26**: 1083-1098.

Turten Kaymaz T, Ozdemir L. 2016. Effects of aromatherapy on agitation and related caregiver burden in patients with moderate to severe dementia: A pilot study. *Geriatr Nurs*.

Van Someren EJ, Scherder EJ, Swaab DF. 1998. Transcutaneous electrical nerve stimulation (TENS) improves circadian rhythm disturbances in Alzheimer disease. *Alzheimer Dis Assoc Disord*. **12**: 114-118.

Vickers A, Zollman C. 1999. ABC of complementary medicine: Massage therapies. *Br Med J*. **319**: 1254.

Wang PS, Schneeweiss S, Avorn J, Fischer MA, Mogun H, Solomon DH, Brookhart MA. 2005. Risk of death in elderly users of conventional vs. atypical antipsychotic medications. *N Engl J Med*. **353**: 2335-2341.

Weaver MT. 1985. Acupressure: an overview of theory and application. *Nurse Pract*. **10**: 38-42.

Wood-Mitchell A, James IA, Waterworth A, Swann A, Ballard C. 2008. Factors influencing the prescribing of medications by old age psychiatrists for behavioural and psychological symptoms of dementia: a qualitative study. *Age and ageing*. **37**: 547-552.

Yang M-H, Wu S-C, Lin J-G, Lin L-C. 2007. The efficacy of acupressure for decreasing agitated behaviour in dementia: A pilot study. *J Clin Nurs*. **16**: 308-315.

Yang MH, Lin LC, Wu SC, Chiu JH, Wang PN, Lin JG. 2015. Comparison of the efficacy of aroma-acupressure and aromatherapy for the treatment of dementia-associated agitation. *BMC Complement Altern Med*. **15 (1)**.

Yang YP, Lee FP, Chao HC, Hsu FY, Wang JJ. 2016. Comparing the Effects of Cognitive Stimulation, Reminiscence, and Aroma-Massage on Agitation and Depressive Mood in People With Dementia. *J Am Med Dir Assoc*. **17**: 719-724.

Zhao M, Haley DR, Nolin JM, Dunning K, Wang J, Sun Q. 2009. Utilization, cost, payment, and patient satisfaction of rehabilitative services in Shandong, China. *Health policy*. **93**: 21-26.

Figure 1 Flow chart of trial selection process for this review

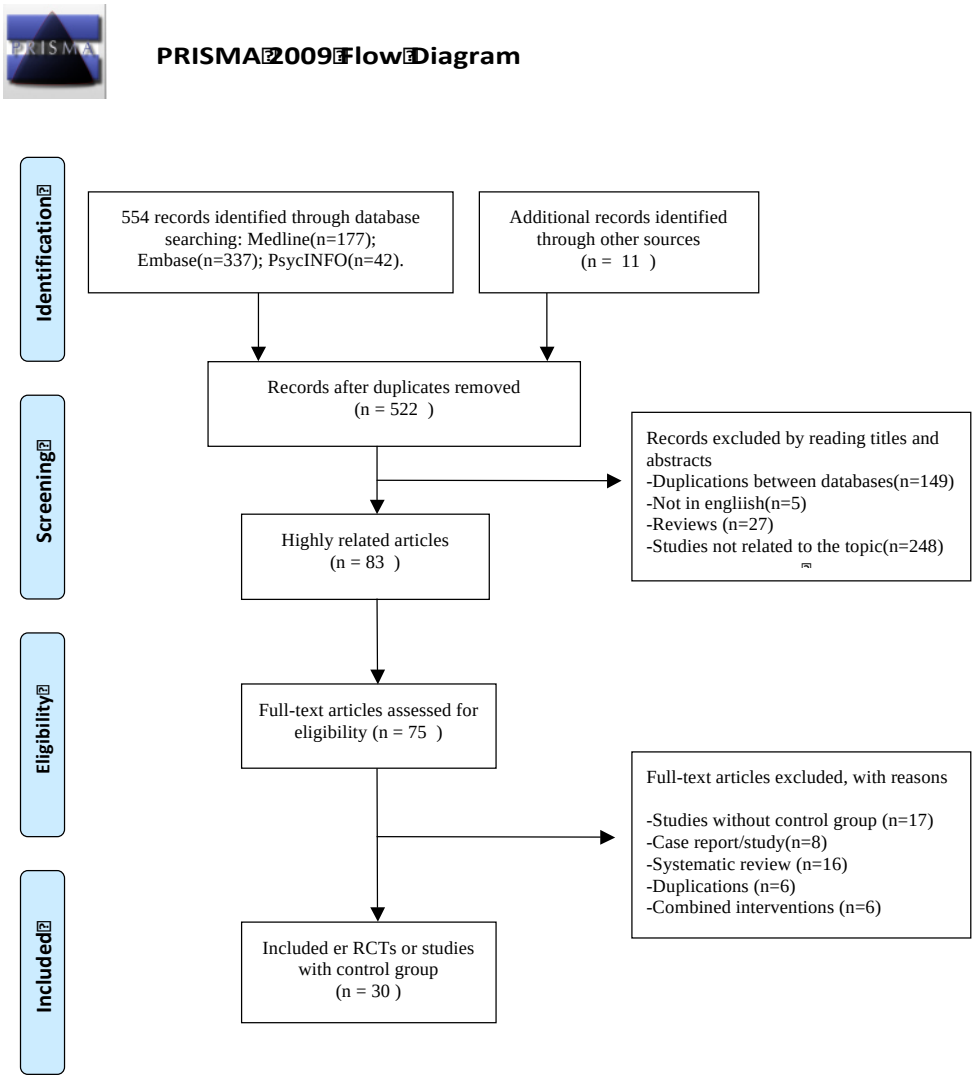

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Figure 2 The Melynk`s level of evidence

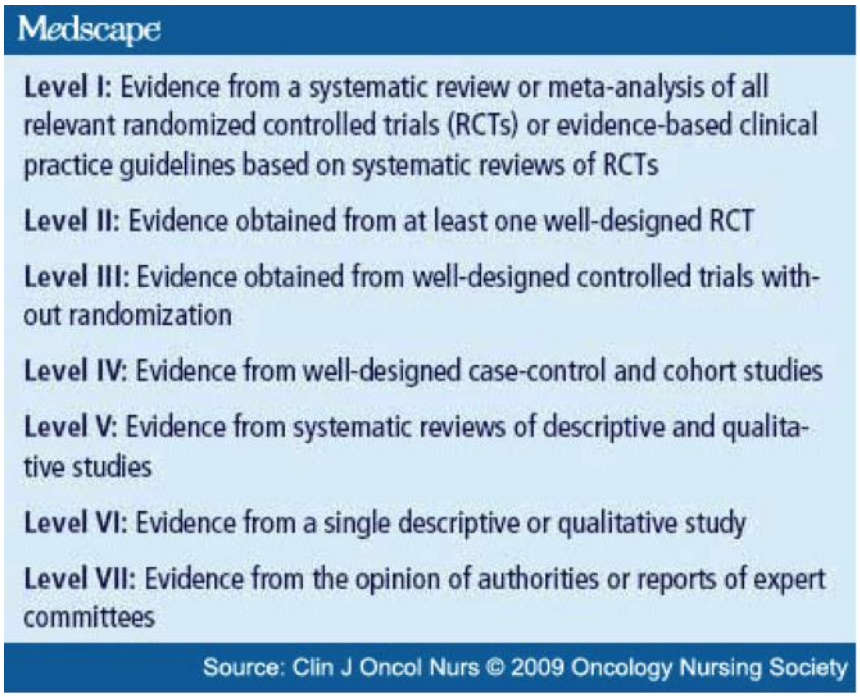

Table 1 Descriptions of different therapies

Complementary and Alternative Medicine	**Descriptions**
General	**Complementary and Alternative Medicine (CAM)** was defined as "diagnosis, treatment and/or prevention which complements mainstream medicine by contributing to a common whole, satisfying a demand not met by orthodoxy, or diversifying the conceptual frameworkof medicine" (Ernst *et al.*, 2001).
Acupuncture/Acupressure	**Acupuncture** is one of the foremost forms of treatment in Chinese medicine. It involves the use of sharp, thin needles that are inserted into the body at very specific points. This process is believed to adjust and alter the body's energy flow into healthier patterns, and is used to treat a wide variety of illnesses and health conditions (Zhao *et al.*, 2009). **Acupressure** is a non-invasive variation of acupuncture involving constant pressure to stimulate meridians or acupoints of the human body to balance energy, thus promoting individual well-being (Lin *et al.*, 2009).
Aromatherapy	**Aromatherapy** is the use of pure essential oils from fragrant plants to help relieve health problems and improve the quality of life in general (Forrester *et al.*, 2014).
Massage	**Massage therapy**, defined as manipulation of soft tissue areas of the body, is offered in clinical settings to assist relaxation, facilitate sleep, and relieve muscular aches and pains (Vickers and Zollman, 1999).
Bright Light Therapy (BLT)	**BLT** is a method of maintaining or restoring the natural circadian rhythm by assisting daytime awakening using bright lights (Taguchi *et al.*, 2007).
Transcutaneous Electrical Nerve Stimulation (TENS)	**TENS**, a type of peripheral nerve stimulation, is the application of an electrical current through electrodes attached to the skin. The most common clinical application of TENS is for pain management. TENS is also used occasionally for the treatment of a range of neurological and psychiatric conditions (Cameron *et al.*, 2003).

Table 2 Studies meeting criteria for this systematic review

Study (setting)	Intervention type	Attention control	Study design	Length	Number of times (W)	Length of each session	Sample Population	Outcome focus	Outcome measures	Impact	Level of evidence
Acupuncture/Acupressure*											
Lin et al., 2009 (Taiwan)	1)Acupressure 2)Montessori	15minutes subject's companion	RCT (Double-blinded)	4 wk	5 days a week	15 minutes	133, Dementia	Agitation Function quality of life Emotional express and response	CMAI; Ease-of-care; AARS	Sig.decrease in agitation. Ease-of-care improved sig. P<0.001. Apparent affect sig. better.	**II**
Shi et al., 2015 (China)	Acupuncture	Care as usual	RCT (Single-blinded)	6 wk	once every other day	30 minutes	120, VsD	Cogntive status Activities of daily living Health-related quality of life	MMSE; ADL; DEMQOL	NS, but MMSE(p=0.014), ADL(p=0.003) scores sig.diff between pooled-acupuncture and control group	**II**
Rodriguez-Mansilla et al.,2013 (Spain)	1)Ear acupuncture 2)massage	Care as usual	RCT (Double-blinded)	12 wk	every 15 days	NA	120, Dementia	Behavior alterations, sleep disturbances, and participation in therapy and in eating	MMSE; ADL	Sig.positive effect of massage and ear acupuncture compared with control group(p<0.001)	**II**
Yang et al.,2007 (Taiwan)	Acupressure	Companion-ship and conversation	Quasi-experimental study	6 wk	twice a day;5 days a week	15 minutes	31, Dementia	Agitation	CMAI; Daily records; Ease-of-care inventory	Sig. Diff between two groups.(p<0.001) CMAI sig. reduction	**III**
Aromatherapy											
Ballard et al, 2002 (U.K.)	Melissa Aromatherapy	Sunflower oil	RCT (Double-blinded)	4 wk	twice a day	1-2 minutes(Rubbed on the face or both arms)	72, Severe Dementia	Agitation Quality of life	CMAI; NPI	CMAI sig. Reduction(p<0.0001); Quality of life indices improved(p=0.005)	**II**

(Continues)

Table 2. (Continued)

Study (setting)	Intervention type	Attention control	Study design	Length	Number of times (W)	Length of each session	Sample Population	Outcome focus	Outcome measures	Impact	Level of evidence
Burns et al.,2011(UK)	Melissa Aromatherapy 1)AP2)AM	Sunflower oil	RCT (Double-blinded)	12 wk	twice per day, daily	1h(massaged into hands and arms)	114, AD	Agitation	PAS; NPI; QOL	NS	**II**
Fu et al.,2013 (Australia)	1)Aromatherapy and hand massage 2) Aromatherapy	water spray	RCT (Single-blinded)	6 wk	twice daily, every day	4h	67, Dementia	Agitation	CMAI; MMSE	NS(some effect)	**II**
Gray et al.,2002 (US)	1)Lavender vera 2)Sweet orange 3)tea tree	No aroma	Quasi-experimental study	NA	10- second interval	20 minutes	13	Combative behavior	Videotapes	NS difference between two groups.	**III**
Holmes et al.,2002 (UK)	Aromatherapy(2 % lavender oil)	Water spray	Quasi-experimental study	2 wk	every other day	2h(4p.m.-6p.m.)	15, Severe Dementia	Agitation	PAS	Sig. Improvement in PAS scores(p=0.016)	**III**
Lin et al., 2007 (Hong Kong)	Aromatherapy(Lavender oil)	Care as usual	RCT (Cross-over design)	3 wk	once at night, daily	1h(sprayed)	70, Dementia	Agitation	CCMAI; CNPI	CCMAI and CNPI decreased sig.(p<0.001)	**II**
Smallwood et al., 2001 (U.K.)	1)Aromatherapy 2)Massage	All patients in 3 groups;AM, CA and M	RCT (Single-blinded)	4 wk	Four times daily,twice weekly	15 minutes(10-11 a.m.,11-12 non,2-3 p.m. and 3-4 p.m.)	21, Severe Dementia	Disordered behaviour	Video recording Behavior categories	AM showed greatest reduction, compared with CA(P=0.05).Sig. Diff between the hours of 3 or 4 pm(p<0.05)	**II**
Yang et al.,2015 (Taiwan)	1)Aroma-acupressure 2)Aromatherapy	Care as usual	RCT (Single-blinded)	4 wk	5	15 minutes	276, Dementia	Agitation	CMAI; HRV	CMAI sig. lower in the post-test and post-3-week(p<0.01). HRV sig. higher from second to fourth week (p<0.01)	**II**

(Continues)

Table 2. (Continued)

Study (setting)	Intervention type	Attention control	Study design	Length	Number of times (W)	Length of each session	Sample Population	Outcome focus	Outcome measures	Impact	Level of evidence
O`Connor et al.,2013 (Australia)	Aromatherapy (30% lavender oil)	Inactive control oil	RCT (Single-blinded)	3 wk	3 times per day	2 minutes (Rubbed into arms)	64, Mild til Severe Dementia	Agitation	PGCAR MMSE CMAI	NS(some effects)	**II**
Massage											
Hicks-Moore et al., 2008 (Canada)	1)HM 2)FM 3)FMHM	Care as usual	RCT	NA	NA	10 minutes	41, Mild to Moderate Dementia	Agitation	CMAI	Sig. Decreased agitation in the three inventions	**II**
Moyle et al., 2014 (Australia)	Foot Massage	Quiet presence	RCT (Double-blinded, Cross-over design)	3 wk	every weekday	10 minutes	55, moderate to severe dementia	Agitation aggression and depressed mood	CMAI OERS	CMAI sig. diff. between the two groups($p=0.03$) OERS with a positive change in alertness in foot massage group	**II**
Suzuki et al., 2010 (Japan)	Tactile Massage	Participated in regular activities	Quasi-experimental study	6 wk	5 times a week	20 minutes(16.00-17.00)	40, Severe Dementia	BPSD	MMSE GBS BEHAVE-AD CgA	Scores of "Intellectual", "emotional function"and "aggressiveness" decreased sig.($p<0.05$)	**III**
Remington., 2002	1)HM2)CM 3)HMCM	Care as usual	RCT (Single-blinded)	2 wk	NA	10 minutes	68, Dementia	Agitation	CMAI	Physically nonaggressive behaviors decreased sig.($p<0.01$)Verbally agitated behavior improved at one hour following intervention.	**II**

(Continues)

Table 2. (Continued)

Study (setting)	Intervention type	Attention control	Study design	Length	Number of times (W)	Length of each session	Sample Population	Outcome focus	Outcome measures	Impact	Level of evidence
BLT											
Ancoli-Israel et al.,2003a	BLT(>2500lux) 1)MBL 2)EBL	DRL	RCT	10 d	every other day	2h	92, Severe AD	Agitation	CMAI ABRS	NS, but Posthoc analysis showed sig. decreased in that Physical Agitation ratings(p=0.001) and Total Agitation (p= 0.0004).	**II**
Ancoli-Israel et al.,2003b	BLT(2500lux) 1)MBL 2)EBL	DRL(<300lux)	RCT	10 d	NA	2h	92, AD	Sleep and Circadian activity rhythms	MMSE Actigraphy	NS (Some effects:consolidated sleep and strengthened circadian rhythms)	**II**
Graf et al., 2009 (Australia)	BLT(3000 lux)	DLT(100lux)	RCT (Single-blinded)	10 d	daily	2h (Evening)	23, AD/VD	Cognitive functions	MMSE BTR	Sig increased in MMSE with BLT(p=0.0012). Sig. Phase delay of 56 min on BTR(p=0.025).	**II**
Burns et al., 2009 (U.K.)	Full spectrum BLT(10000 lux)	Normal Light	RCT (Single-blinded)	8 wk	daily	2h(Morning)	48, Dementia	Agitation	MMSE CSDD CRBRS CMAI Actigraphy	Limited reduction in agitation, sleep was improved and efficacy in the winter months.	**II**
Dowling et al., 2008	BLT (≥2,500lux) 1)LM 2) LP 3)Control	Indoor Light (150-200lux)	RCT	10 wk	every weekday	1h(Morning)	50, AD	Rest-Activity Rhythm	Actigraphy	NS, LM group showed sig. improvement in daytime somnolence.	**II**
Dowling et al., 2007	BLT(>2,500 lux)	Usual Indoor Light	RCT	10 wk	every weekday	1h (Morning /Evening)	70, AD	Neuropsychiatric behaviors	NPI-NH	Sig. diff between groups on agitation/ aggression, depression/dysphoria,aberrant motor behavior, appetite/eating disorders (p<0.05)	**II**

(Continues)

Table 2. (Continued)

Study (setting)	Intervention type	Attention control	Study design	Length	Number of times (W)	Length of each session	Sample Population	Outcome focus	Outcome measures	Impact	Level of evidence
Lyketsos et al.,1999	BLT(10,000 lux)	Dim Light	RCT (Single-blinded, Cross-over design)	4 wk	daily	1h (Morning)	15, AD/ VsD	Agitation	Behave-AD,CSDD, sleeping hours	Sig. Improvement in nocturnal sleep($p<0.05$)	**II**
Mishima et al.,1994 (Japan)	BLT(3,000-5,000 lx)	Same Daily Schedule	Quasi-experimental study	4 wk	daily	2 h (Morning)	14, Moderate to Severe Dementia	sleep and behavior disorders	TST NST DST	Sig. Increased total and nocturnal sleep time	**III**
TENS											
Hozumi et al., 1996 (Japan)	TENS (6-80Hz/256-530μA)	Sham stimulation	RCT (Double-blinded)	4 wk	daily	20 minutes (Morning)	27, Multi-infarct Dementia	Sleep-wake and Behavior disorder	Neuropsychological tests; Waking Ees	Sig. Improvements in motivation ($p<0.01$), behavior disorders($p<0.05$), sleep disorder ($p<0.01$) and subjective complaints($p<0.01$).	**II**
Scherder et al., 1999b (The Netherlands)	TENS (160Hz/100μs)	Sham stimulation	RCT	6 wk	5 days a week	30 minutes a day	16, Midstage AD	Memory Behavior	WMS-R 8 Words Test RBMT BOP scale	Sig. effect for Visual Memory Span($p<0.004$). NS effects in physical, social and affective functioning.	**II**
Scherder et al., 1999a (The Netherlands)	TENS(burst)	Sham stimulation	RCT	6 wk	5 days a week	30 minutes a day	16, Midstage AD	Rest-activity rhythm	Actigraphy	Increased the coupling between the rest-activity rhythm	**II**

(Continues)

Table 2. (Continued)

Study (setting)	Intervention type	Attention control	Study design	Length	Number of times (W)	Length of each session	Sample Population	Outcome focus	Outcome measures	Impact	Level of evidence
Scherder et al., 1998 (The Netherlands)	"Isolated" TENS (160Hz/100μs)	Sham stimulation	RCT (Double-blinded)	6 wk	5 days a week	30 minutes a day	18,AD	Memory Affective Behavior	WMS-R, 8 Words Test, RBMT, Word Fluency, BOP scale	Sig. Effect on nonverbal short-term, long-term memory, word fluency and less need of help, while no improve in affective behavior	**II**
Van et al., 1998 (The Netherlands)	TENS(burst) (160Hz/100μs)	Sham stimulation	RCT	6 wk	5 days a week	30 minutes a day	14, Early Stage AD	Memory Affective Behavior	WMS-R, 8 Words Test, RBMT, Word Fluency, BOP scale	Positive effet on verbal long-term memory,visual short-term and long-term memory.	**II**

AARS: Apparent Affect Rating Scale, ABRS: the Agitated Behavior Rating Scale, ADL: Activity of Daily Living, BEHAVE-AD: Behave Alzheimer`s Disease, BTR: Body temperature rhythm, BOP-scale: the Stockton Geriatric Rating Scale of Beoordelingsschaal voor Oudere Patienten, CCMAI: Chinese versions of Cohen-Mansfield Agitation, CgA:Salivary chromogranin A, CMAI: Cohen-Mansfield Agitation Inventory, CNPI: Chinese versions of Neuropsychiatric Inventory, CRBRS: Crichton Royal Behavior Rating Scale, CSDD: Cornell Scale for Depression in Dementia, DEMQOL: Dementia quality of life, DST: Day Sleep Time, GBS: The Gottfries-Brane-Steen scale,GIT: Groninger Intelligence Test, HRV:heart rate variability.HF,parasympathetic nervous activity, MMSE: the Mini–Mental State Examination, NPI: The Neuropsychiatric Inventory, NPI-NH: The Neuropsychiatric Inventory-Nursing Home, NST: Nocturnal Sleep Time, OERS: Observed Emotion Rating Scale, PAS: the Pittsburgh Agitation Scale,PGCAR: the Philadelphia Geriatric Center Affect Rating Scale, RBMT:the Revermead Behavioral Memory Test for Face and Picture Recognition, TST:Total Sleep Time, WMS: the Wechesler Memory Scale-Revised, NA: not available

VEDLEGG 1

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