Published in final edited form as:
Fam Community Health. 2008 ; 31(3): 240–246. doi:10.1097/01.FCH.0000324481.40459.69.

Cranial Electrical Stimulation Potential Use in Reducing Sleep and Mood Disturbances in Persons With Dementia and Their Family Caregivers

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Abstract

Family caregivers of persons with dementia and their care recipients frequently experience sleep and mood disturbances throughout their caregiving and disease trajectories. Because conventional pharmacologic treatments of sleep and mood disturbances pose numerous risks and adverse effects to elderly persons, the investigation of other interventions is warranted. As older adults use complementary and alternative medicine interventions for the relief of sleep and mood disturbances, cranial electrical stimulation, an energy-based complementary and alternative medicine, may be a viable intervention. The proposed mechanism of action and studies that support cranial electrical stimulation as a modality to reduce distressing symptoms are reviewed. Directions for research are proposed.

Keywords

complementary and alternative medicine; cranial electrical stimulation; caregiver; dementia

Alzheimer's disease (AD) is a chronic, progressive, brain disorder resulting in a loss of memory, reasoning, language skills, and the ability to care for one's self.[1] AD is the seventh leading cause of death in the United States.2 Currently, the number of persons with AD living in the United States is estimated at approximately 4 to 6 million, most of whom are older than 65 years.3 A conservative estimate of the growing number of persons likely to develop AD by the year 2050 is projected to be between 14 and 17 million.4 These figures represent a possible 300% increase in the prevalence of AD over the next 4 decades.

Family caregivers are the foundation of support to persons with dementia. Because the duration of dementia is often between 3 and 20 years, their caregivers often maintain these roles for an extended period of time. More than 30% of caregivers for the elderly are themselves aged 65 or older.[5] Elderly spousal caregivers of persons with dementia are at risk for many negative health outcomes, including sleep disturbances, depressive symptoms, immune system dysfunction, and an increased risk for morbidity and mortality in comparison with noncaregivers.[6–8]

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As many as 68% of community-dwelling, elderly caregivers of persons with dementia experience some form of sleep disturbance 3 or more times a week,[9] with 20% of them taking prescription for sleep medication.[10] Sleep disturbances in caregivers of persons with dementia are reported as being the result of common behavioral disturbances that occur in persons with dementia, including wandering and nighttime awakenings.[9,11] Greater use of healthcare services, increased use of hypnotics, and impairments in quality of life are also associated with sleep disturbances.[12–14] In addition, several studies indicate that insomnia may be predictive of psychiatric disorders, including depression, although the physiological mechanisms for this are not well understood.[15,16] Care recipient sleep disturbances, coupled with the potentially negative perceived stress involved in providing care to a loved one for a period of time spanning years, may result in sleep disturbances in the caregiver.[17]

Studies estimate that between 19% and 44% of persons with AD suffer from some form of sleep disruption.11,[18] The etiologies of sleep disruptions in AD are multifaceted. Degradation of neuronal pathways that initiate and maintain sleep, changes in the hypothalamic suprachiasmatic nucleus (the circadian “pacemaker” of the body), and other modifications in brainstem regions and pathways that regulate sleep–wake cycles have been implicated in the sleep disturbances observed in AD patients.[19] Frequent manifestations of sleep disturbances in persons with AD include day–night sleep pattern reversals, frequent nighttime awakenings, increases in daytime sleep, and decreases in slow-wave sleep and rapid eye movement sleep. 20 Postmortem findings on persons with AD have been reported to have similar neuroendocrine findings as are found in persons with depressive symptoms without dementia, suggesting that depression in nondemented adults and in AD share, at least partly, a common pathophysiology. 21

Numerous studies support the finding that AD caregivers and care recipients (dementia–care dyad) share mutual affective states.[22,23] Despite the decades of research of AD caregivers, few intervention studies have been reported that measured the outcomes of research on the dementia–care dyad. However, there is an increasing understanding in the scientific community that a move toward interventions and appropriate analyses of both members of the dementia–care dyad need to be undertaken.

INADEQUACIES OF CONVENTIONAL TREATMENTS FOR SLEEP AND DEPRESSIVE SYMPTOMS

Hypnotics are the most common therapy for insomnia in older adults.24 Age-related differences seen in the elderly related to changes in pharmacokinetics and pharmacodynamics may alter the effects of these medications. In addition, long-acting hypnotics may cause adverse daytime effects such as excessive daytime sleepiness, poor motor coordination, and visuospatial problems, which may lead to falls and injury. In a recent meta-analysis, findings indicate that hypnotics do more harm than good in the elderly.25 It is noteworthy that the incidence of falling is a strong predictor of placement in skilled nursing facilities among the elderly otherwise capable of living in the community.[26] Other disadvantages related to the use of hypnotics in older patients include (1) alteration of sleep architecture with a reduction in slow-wave sleep and rapid eye movement sleep; (2) development of tolerance when used continuously, resulting in reoccurrence of insomnia symptoms unless the dosage is increased; (3) rebound insomnia and anxiety caused by withdrawal; and (4) exacerbation of coexisting medical conditions.[24] Elderly caregivers of persons with AD and their care recipients may be placed at great risk for adverse events when either the elderly caregiver or the person with AD is taking hypnotics for the relief of symptoms related to insomnia.

Conventional treatment of depressive symptoms in older adults is generally limited to the administration of antidepressant medications, with few persons receiving specialized mental

healthcare.[5] When older adults were referred for a mental health consultation, approximately 50% of those referred never made one mental health visit.[27] Despite the proven efficacy of antidepressant medications, studies have shown that about 40% of adult patients stop taking newly prescribed antidepressant medications within 4 to 6 weeks, and less than 40% of patients in primary care stay on antidepressants for 180 days or longer.[28] It is believed that this proportion may be higher in older adults as a result of increased sensitivity to adverse effects. Disturbed sleep and mood of both members of the dementia–care dyad initiate a vicious cycle that can have deleterious health effects and detriments in quality of life for both and can lead to institutionalization of the person with AD. Given the complexities and inadequacies that exist in the treatment of sleep disturbances and depressive symptoms in the elderly, the need for other treatment modalities that minimize the disadvantages and adverse effects seen in conventional therapy of these disorders is timely.

USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE PRACTICES BY OLDER ADULTS

Complementary and alternative medicine (CAM) is defined as "a group of diverse medical and healthcare systems, practices, and products that are not presently considered to be part of conventional medicine."[29] CAM is generally categorized into four major classifications: (1) mind–body medicine (eg, meditation, prayer); (2) biologically based practices (eg, dietary supplements, herbs); (3) manipulative and body-based therapies (eg, chiropractic medicine, massage); and (4) energy medicine (eg, pulsed fields, including cranial electrical stimulation, and magnetic fields).

Use of CAM products and practices by all persons, including older adults, in the United States is rising. Specific data regarding the prevalence and use of CAM for treatment of sleep or mood disorders are intriguing. Using data obtained during the 2002 National Health Interview Survey,[30] 18.9% of all adults reported having insomnia during the past year, with 7% of these adults using a CAM practice for treatment of the insomnia. Reasons given for use of a CAM intervention include that a conventional treatment was not helpful (40.7%), conventional treatment was too expensive (24.8%), and thoughts that a CAM practicewould be interesting to try (66.6%).[30] Another study,31 based on the 2002 National Health Interview Survey including the Alternative Health Supplement additional questions, found that 81.7% of persons who self-reported anxiety of depressive symptoms had used CAM in the past year, in comparison with 64.9% of those surveyed without self-report of anxiety or depressive symptoms who had used CAM within the past year for reasons other than for mental health. Thus, CAM interventions to treat sleep and mood disorders are worthy of further study.

CRANIAL ELECTRICAL STIMULATION

Cranial electrical stimulation (CES) therapy involves the use of a small, battery-operated device that delivers low levels of alternating electrical current to the head via clips that are attached to the earlobes. CES devices are relatively small and compact (3.9 inches long, 3 inches wide, and 0.9 inches thick). CES therapy has had positive effects on the treatment of sleep disturbances, depressive symptoms, perceived stress, and other disorders in a variety of patient populations.32,33 CES intervention, a type of energy medicine, has been reported to increase blood and cerebrospinal fluid levels of serotonin, norepinephrine, and β-endorphin in depressed patients and in patients with no known medical illnesses.34,35 The changes in increased levels of serotonin, norepinephrine, and β-endorphin levels may result in the alleviation of sleep disturbances and depressive symptoms. Recent findings from functional magnetic resonance imaging (fMRI) after 4 weeks of CES use resulted in increased activation of the cingulate cortex. Activation in the cingulate has also been reported after taking selective serotonin reuptake inhibitors, a commonly prescribed classification of drugs used for the

treatment of depression (C. Bourguignon, A. G. Taylor, R. H. Gracely, J. Lewis, unpublished data, 2007).

Many types of electrical stimulation have been used to reduce depressive symptoms, sleep disturbances, and pain. Electroconvulsive therapy uses extremely strong current (around 110 V) and must be performed in highly controlled settings. Transcutaneous electrical stimulation frequencies usually are in the 50- to 200-Hz range, with 60 to 100 milliamperes (mA). This is a stronger current and different waveform in comparison with microcurrent CES devices. In addition, transcutaneous electrical stimulation is not cranial stimulation. Microcurrent CES devices usually have modified square-wave biphasic stimulation and frequencies between 0.3 and 3 Hz with 100 microamperes (μA). The Alpha-Stim device (Mineral Wells, Tex) that is commonly used for CES interventions delivers modified square-wave biphasic stimulation at 0.5 Hz and 100 μA and is approved by the Food and Drug Administration.

Although the mechanisms of CES stimulation are not conclusive, several theories attempt to explain the clinical effectiveness and empirical findings related to CES. It is generally believed that the effects are primarily mediated through a direct action on the brain at the limbic system (including the cingulated cortex), hypothalamus, thalamus, and/or reticular activating system (C. Bourguignon, A. G. Taylor, R. H. Gracely, J. Lewis, unpublished data, 2007).[32,36] CES is thought to influence ion and amino acid transport across cell membranes in the nervous system where these substances are used in the metabolism and production of neurotransmitters and peptides. Lower currents, consisting of 500 μA or less, increased ATP; however, higher currents, over 5 mA, showed a decrease in ATP to levels below baseline.37 In a rat study, findings demonstrated as much as a 3-fold increase in endorphin concentration after only one CES treatment.38 Although there is little biologic data on neurotransmitters specific to the Alpha-Stim device, in preliminary studies using the LISS Cranial Stimulator (a device with a similar waveform and strength as the CES device), participants had increases in plasma serotonin, norepinephrine, and β-endorphin.[39] The changes in increased levels of serotonin, norepinephrine, and β-endorphin may result in the alleviation of sleep disturbances and depressive symptoms.

In human studies, CES intervention has shown positive effects on the treatment of sleep disturbances, depressive symptoms, stress, anxiety disorder, headaches, pain, and fibromyalgia.[32,33,40–48] Only 1 study investigated the use of CES in a group of community-dwelling AD caregivers.[48] This randomized, placebo-controlled clinical study used a 2-group design to test the efficacy of the CES intervention. Study participants ($N = 38$) were randomly assigned to either the active CES treatment group or the sham CES treatment group. Participants wore the CES device for 60 minutes each day for 4 weeks. Outcome measures of sleep disturbances and depressive symptoms were collected via self-report measures at baseline and at 2 and 4 weeks. Results of this study included a trend toward statistical significance in the reduction of sleep disturbances, specifically daytime disturbances in the active CES intervention group in comparison with the sham intervention group ($P = 0.09$). Clinically meaningful reductions were found in sleep onset latency (time taken to fall asleep) in the active intervention group in comparison with the sham intervention group. Improvements in depressive symptoms were found in both the intervention and the control groups. Confirmation of the feasibility of the study protocol was obtained by robust recruitment of participants and by a low attrition rate. Because of the low level of electrical stimulation used in this study, adequate blinding of participants and investigators was possible. A limitation of this study arose from the self-report measurement of study outcomes and by not intervening or controlling for care recipient sleep and mood disturbances.

Effects of CES on sleep disturbances have been studied in small samples of persons with advanced AD with varying results.[49,50] One study of institutionalized, elderly persons ($N =$

27) with multi-infarct dementia showed improvements in nurses' reports of behavioral disorders and in sleep disturbances after 2 weeks of CES use.[49] In a study of 16 community-dwelling persons ($n = 8$ in experimental group; $n = 8$ in control group) with midstage AD, CES was applied for 30 minutes each day (5 days each week) for 6 weeks to test the effects of the intervention on the rest-activity periods and salivary cortisol levels. Effectiveness of the CES intervention in comparison to the results achieved in the control group were insignificant, both in measurement of rest-activity levels as measured by actigraphy and in salivary cortisol levels. Small sample sizes, varying intervention time periods, and nonstandardized CES settings limit the generalizability of these results. In addition, both studies enrolled persons with moderate to severe stages of dementia, when extensive physiological alterations to brain structure are present. Thus, studying the effects of CES in persons with early-stage dementia may yield more promising results.

Studies using the Alpha-Stim CES device have reported no adverse effects. A postmarketing survey originally conducted for the Food and Drug Administration sought healthcare practitioners' feedback on their patients' experiences using the CES device. Results from this survey revealed that 472 participants (94.4%) reported no negative adverse effects from the therapy. Six participants (1.2%) reported vertigo as an adverse effect and 2 (0.4%) reported nausea, whereas 3 (0.6%) reported skin irritation, and 1 (0.2%) reported anger, a metallic taste, a heavy feeling, or intensified tinnitus.[51] On the basis of published studies, use of CES is not associated with the deleterious adverse effects often reported in use of hypnotic medications in the elderly.

CES therapy in both animal and human models reportedly affects the neurotransmitters, namely, serotonin, norepinephrine, and dopamine, which have been shown to influence the development of sleep disturbances and depressive symptoms. Thus, CES therapy is a viable intervention to test in dementia–care dyads as an aid in reducing sleep disturbances and depressive symptoms and improving quality of life.

SUMMARY AND FUTURE WORK

Sleep disturbances and depressive symptoms pose threats to caregivers of persons with AD in terms of their own physical and psychological well-being and their ability to provide adequate care to the care recipient. These same distressing symptoms in persons with AD add to the burden experienced by the caregiver and may ultimately result in institutionalization of the care recipient. CES therapy has been shown to affect the neurotransmitters, which contribute to the development of sleep disturbances and depressive symptoms. CES may have fewer adverse effects for both caregivers and care recipients than medications. Because the CES intervention can be done in participants' home environments, this relieves caregivers from seeking respite care that would be needed if they were to go to a clinic for treatment.

Future work in studying the effects of CES should target both members of the dementia–care dyad because of the overlap of symptoms in the caregiver and care recipient. Enrolling community-dwelling persons with early stage dementia into research studies of CES is warranted. Longer intervention time periods of 6 to 8 weeks, objective measurements of sleep, namely actigraphy, to permit measurement of a variety of sleep outcomes while allowing for data collection in the participant's natural home environments, and measurement of other related indices of sleep (daytime sleepiness and fatigue) would enhance our understanding of the potential benefits of CES interventions in this population.

Acknowledgments

This publication was supported in part by a scholarship provided by the John A. Hartford Foundation Building Academic Geriatric Nursing Capacity Scholarship Program and by grant nos. 5-T32-AT000052 and 5-K30-AT000060

from the National Center for Complementary and Alternative Medicine. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the National Center for Complementary and Alternative Medicine or the National Institutes of Health.

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