



Comment on “Shiatsu as an Adjuvant Therapy for Depression in Patients With Alzheimer’s Disease: A Pilot Study”

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Abstract

Recently, there has been increasing interest toward nonpharmacological approaches for dementia and associated clinical manifestations, such as depression, with the common goal to improve health and quality of life of both patients and caregivers. In this scenario, the role of Shiatsu is of clinical and research interest, although to date a definitive recommendation on a systematic use in clinical practice cannot be made. To overcome the heterogeneity of the previous studies, we tested Shiatsu as an add-on treatment for late-life depression in a dedicated community of patients with mild-to-moderate Alzheimer’s disease. We found a significant adjuvant effect of Shiatsu for depression in these patients and hypothesized a neuroendocrine-mediated action on the neural circuits implicated in mood and affect regulation. However, this finding must be considered preliminary and requires confirmation in larger-scale controlled studies, possibly extending the range of outcome measures and including predictors of response. Future investigations should also include an objective assessment of the hypothalamus-pituitary-adrenocortical axis functioning. Nevertheless, starting from this pilot study, we suggest that a customized protocol applied for an adequate period in a controlled sample will represent a non-invasive and feasible advance for promoting patients’ mood and, possibly, slowing cognitive decline.

Keywords

alternative medicine, cognitive function, dementia, depression, health services

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More than 35 billion people worldwide have dementia and the number is rapidly rising with increased longevity. More than 90% of these subjects experience behavioral and psychological symptoms, including agitation, irritability, anxiety, apathy, and depression, particularly in the mid-to-late stage of the disease.¹ These symptoms significantly distress not only patients but also families and care staff.² Recently, mood disorders in cognitively impaired elderly people has generated considerable attention. Particularly, late-life depression is frequently associated with apathy and emotional lability, thus significantly worsening the burden of care.³ Management is traditionally based on pharmacological intervention. While antidepressant and antipsychotic medications may offer control of some symptoms, they have a number of potential side effects, mainly due to the hypersensitivity of the aging brain, the decreased hepatic and kidney drug metabolism, and the complex and often

unpredictable interactions with other drugs concomitantly taken. As such, doses require regular adjustments and different drugs are frequently changed.

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In recent years, there has been an increased interest toward the possibility of nonpharmacological approaches against dementia and associated clinical manifestations, with the common goal to improve cognition, mood, behavior, and, ultimately, quality of life.⁴ Regarding depression, an effective management of mood disorder means to improve the global health of patients and caregivers, reduce distress, avoid inappropriate medications, enable positive relationships and activities, delay institutionalization, and be cost-effective. In this scenario, the potential effect of Shiatsu, a popular technique of complementary and alternative medicine based on the principles of traditional Chinese medicine, is of increasing clinical interest. Basically, Shiatsu consists of pressure and scrubbing of the energy pathways in the body based on knowledge and application of traditional Chinese medicine to treat and relieve pain and a wide spectrum of pain-related symptoms. Although the most common indications are muscular-skeletal and psychological problems, Shiatsu is actually a holistic therapy and, as such, it also affects the patient's well-being, lifestyle, diet, sleep, and body-mind awareness.⁵

The working mechanism of Shiatsu and similar techniques (such as acupressure) are not fully known, but they can be explained by different theories. Traditional Chinese medicine speculates that acupressure stimulates the acupoints to enhance energy flowing along the meridians, achieving therapeutic outcomes by improving the functions of the body systems.⁶ Biochemical studies show that stimulation of the acupoints is able to induce complex neurohormonal responses; one of these may involve the hypothalamus-pituitary-adrenocortical axis in counteracting the overproduction of cortisol, thus promoting a relaxation response.⁷ Accordingly, similar manipulative therapies, such as massage and therapeutic touch, were shown to be useful in lowering patients' stress and cortisol after treatment.^{8,9} Finally, abnormal synaptic plasticity has been widely documented in depression and in both animal models and patients with Alzheimer's disease.¹⁰⁻¹⁵ In this context, the release of neuromodulators after Shiatsu might improve cortical plasticity and, consequently, mood and cognition.

Although previous studies regarding Shiatsu and acupressure stressed their effects in decreasing behavioral symptoms, few of these employed a rigorous study design. Of these investigations, two only used a standardized protocol and objective measurement of effectiveness.^{16,17} The other studies had a number of limitations, such as a subjective determination in deciding whether the treatment was effective, the small sample size, a non-double-blind design, and the lack of standardized protocols. Moreover, although only one study has recently proposed a standardized protocol,¹⁶ clinical experience has demonstrated that it is difficult for formal caregivers to adhere to a twice-a-day treatment schedule in long-term care facilities. In addition, despite the growing interest in its use, there is a need to examine Shiatsu in daily clinical practice and, where appropriate, to develop test protocols and specific training programs for the health care staff. Finally, to further increase the evidences for Shiatsu in dementia and late-life depression, the

available data should be carefully reviewed and the quality of the published studies critically analyzed.

To date, a definitive recommendation on a systematic use of Shiatsu in clinical practice cannot be made. In 2011, Robinson et al¹⁸ investigated the evidence of positive effects of Shiatsu and acupressure on behavior and psychological symptoms of dementia. The authors identified 40 randomized controlled clinical trials, 8 controlled clinical trials, 5 crossover trials, 6 within-participants studies, 1 observational study, 10 uncontrolled studies, and 1 prospective study. Overall, agitation, aggression, and nonaggressive behavior all declined significantly in demented patients, further supporting the clinical application of Shiatsu. However, a conclusive evidence of efficacy is still lacking, and while much of the research is of insufficient quality to translate into practice, the high-quality evidence for pain, postoperative nausea and vomiting, and sleep may be of use to Shiatsu or acupressure practitioners. On the other hand, the research on this topic is still very much in its infancy, and the practitioners need to work closely with both clinicians and researchers to build up a larger body of evidence. Given the prevalence of Shiatsu worldwide, the need for high quality research is imperative, and practitioners should be encouraged to engage in research using well-designed and reported studies, in particular with large and controlled samples.

To overcome the heterogeneity of the previous studies and some of the aforementioned limitations, we first tested Shiatsu as an add-on treatment for late-life depression in a dedicated community of patients with mild-to-moderate Alzheimer's disease.¹⁹ In a group of 12 participants, in addition to standard pharmacological and physical interventions, once-weekly Shiatsu treatment for 10 months produced a significant improvement of a mood score scale in 6 subjects randomly selected. Although we found a within-group improvement of all the outcome measures considered (cognition, mood, and functional status), the analysis of differences before and after the interventions showed a statistically significant amelioration only of depression in patients undergoing Shiatsu + physical activity compared with those practicing physical activity alone.¹⁹ We concluded for an adjuvant effect of Shiatsu for depression in patients with Alzheimer's disease and hypothesize that the underlying pathomechanism might involve the neuroendocrine-mediated action of Shiatsu on neural circuits implicated in mood and affect regulation. We also provided experimental evidence that an integrated approach based on drug therapy, physical activity, and Shiatsu may be a feasible way to slow down affective decline in patients with Alzheimer's disease and to alleviate the caregivers' burden of care.¹⁹ However, such a complex approach cannot easily allow to "quantify" how much improvement was due to Shiatsu itself or to the stimulation provided by the interactions among these components.

Overall, this was a pilot study that should be viewed in lights of a number of limitations, including the very small sample size, the unbalanced sex distribution, the limited number of psychopathological tests used, the lack of double blinding, and

the absence of a follow-up after the end of the protocol.¹⁹ Moreover, given that participants came from the same community, contamination between the 2 groups cannot be ruled out, although narrow differences between experimental and control group outcomes would be expected. Finally, as usual in similar studies, the improvement produced by Shiatsu might, at least in part, be due to a placebo effect provided by the caring attention of dedicated therapist who induces a sense of calm and positive anticipation. For these reasons, the finding must be considered preliminary given that it requires confirmation and cross-validation in larger-scale controlled studies, possibly extending the range of outcome measures and predictors of response. Moreover, exploring the mechanisms behind the effect of Shiatsu by including the measurement of other variables (such as pain, agitation, diet, and sleep) appears worthy of investigation in future studies and predictive of useful additional data. Future studies should also elucidate whether Shiatsu and acupuncture reduce depression in people with dementia through an objective assessment of hypothalamus-pituitary-adrenocortical axis functioning.

Despite the limitations, however, some counterarguments should be considered. First, the recruitment of cohorts of suitable sample size is inherently difficult in the case of these patients given the need for proxy consent, the occurrence of complex comorbidities, and the high rate of hospitalization, thus reducing the opportunity to recruit or retain participants in complex controlled trials. Second, blinding is always a challenge in the assessment of all kinds of nonpharmacologic therapeutic interventions, where the comparison treatment must somehow mimic the study treatment while maintaining blindness.²⁰ Yet without the rigorous methodology of a carefully randomized and placebo-controlled double-blinded study, the suspicion will remain that the apparent therapeutic effect obtained by Shiatsu (or by other forms of alternative/complementary medicine) is actually a nonspecific or placebo effect produced by cultivating the patient's optimistic expectations in the context of a good therapeutic relationship.^{21,22} Third, longitudinal studies are recommended to investigate the long-term effects of Shiatsu on cognitive and psychological variables. In this frame, findings from our study provide references for future clinical trials in terms of sample size estimation and recruitment strategies, optimal protocol dosage to be used, outcome measurement and timing to be considered, as well as strategies of data collection and intervention implementation.

Based on our study and literature review, we can propose some key recommendations for practitioners. First, the limited evidence currently available suggests the strong need for a more rigorous research. Second, investigators using a randomized controlled trial design need to ensure that they strictly adhere to the principles of randomized controlled trial design itself, namely the random assignment of participants to treatment or control groups and the blinding of data collectors; after randomization, the 2 groups need to be followed up in exactly the same way, and the only difference should be the treatment being compared. Third, because symptoms, severity, and course of depression differ from person to person, it is

important to consider the individual responses to the intervention. Finally, Shiatsu or other nonpharmacological options should be compared with pharmacological therapies in order to prioritize treatments.

In conclusion, the finding from our study¹⁹ suggests that Shiatsu may play a role in promoting psychological well-being of dementing patients. Further investigations with large-scale and methodologically robust design are recommended to produce stronger evidence for application of cost-effective interventions. The high prevalence of both depression and dementia in the elderly highlights the treatment gap currently present among these patients. As known, mood and other psychological symptoms in patients with dementia are influenced by many pathophysiological and biopsychosocial factors, so that Shiatsu, integrated with other therapeutic options, might reveal even greater effectiveness. Promoting psychophysical wellness will increase patients' compliance to cognitive rehabilitation, improve quality of life, and reduce the negative outcomes related to disease complications and distress. Starting from this study,¹⁹ we suggest that a customized Shiatsu protocol applied for an adequate period of time in a large controlled sample will represent a useful and noninvasive advance for promoting not only an improvement of patients' mood but, possibly, also a slowing of cognitive decline.

Author Contributions

GL and SSC conceptualized the study. MP and RB performed the literature review. GL and VV were involved with writing the original draft. GD and DC were involved in the writing, review, and editing of the article. MB supervised the study. All authors approved the final version of the paper.

Declaration of Conflicting Interests

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Ethical Approval

Not applicable.

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