



Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration

ISSN: 2167-8421 (Print) 2167-9223 (Online) Journal homepage: informahealthcare.com/journals/iafd20

ALSUntangled No. 28: Acupuncture

The ALSUntangled Group

To cite this article: The ALSUntangled Group (2015) ALSUntangled No. 28: Acupuncture, Amyotrophic Lateral Sclerosis and Frontotemporal Degeneration, 16:3-4, 286-289, DOI: [10.3109/21678421.2015.1039240](https://doi.org/10.3109/21678421.2015.1039240)

To link to this article: <https://doi.org/10.3109/21678421.2015.1039240>



Published online: 11 May 2015.



Submit your article to this journal [↗](#)



Article views: 6677



View related articles [↗](#)



View Crossmark data [↗](#)

ALS-UNTANGLED

ALSUntangled No. 28: Acupuncture

The ALSUntangled Group

ALSUntangled reviews alternative therapies on behalf of patients with ALS (PALS). Here we review the use of acupuncture for ALS, for which we have had more than 200 requests (1).

Overview

Acupuncture is a technique from ancient China in which thin needles are inserted into specific locations along the skin to produce a therapeutic effect (2). Variations have arisen, including the additions of pressure, heat, laser light, shock waves, electricity or medications (2,3); for the purposes of this review we consider all these variations under the term ‘acupuncture’. Acupuncture has been advertised to improve pain, spasticity, cramps and anxiety in patients with ALS, and to slow, stop, and sometimes even reverse their muscle weakness (4–6). In Shanghai China, more than 50% of PALS use it to treat their illness (7). This review does not address symptomatic benefits, but focuses on purported effects on ALS disease progression.

Mechanism(s)

There are at least two mechanisms by which acupuncture has been suggested to exert its therapeutic effects.

Traditional Chinese Medicine (TCM) holds that body functions are regulated by an energy called ‘qi’ which flows along specific paths or meridians (2,3). Disruptions or blockages in the flow of this energy are thought to be responsible for disease, and insertion of needles into specific locations (acupoints) restores energy flow and ameliorates disease (2,3). No convincing scientific evidence for qi, meridians or acupoints has yet been found (3,8,9).

More modern concepts start with needle insertions activating the endogenous opioid neuropeptides enkephalin, beta-endorphin, and dynorphin (3,10). These in turn are purported to have downstream effects on brain areas involved in pain perception. Opioids can also modulate the immune system

(11–13); in so doing, they could theoretically alter the progression of diseases where the immune system plays a pathogenic role, including ALS (14,15). Some studies find elevated beta-endorphin levels (10), altered functional MRI patterns (16–20), and even altered inflammatory markers (21,22) including in ALS animal models (23,24), following acupuncture. Some studies find that opioid antagonists such as naloxone or genetic down-regulation of opioid receptors can block the beneficial effects of acupuncture (10). ALSUntangled assigns a TOE ‘Mechanism’ grade of B based on this information (Table I).

However, there are some problems with these modern theories. They do not explain acupoints; in some studies, ‘sham’ acupuncture utilizing telescoping needles that do not break the skin works as well as ‘real’ acupuncture, raising the possibility that acupuncture works via a placebo effect (3). The data are not consistent across investigators (3,25). Many of the ‘positive’ studies on acupuncture mechanisms originate in China (3,8), and the percentage of ‘negative’ studies published by Chinese investigators has been found to be unusually low (3,26), meaning there may exist a publication bias.

Pre-clinical data

Two papers by the same group have examined the effects of acupuncture in the SOD1 mutant mouse model of ALS (23,24). Both papers showed that acupuncture was associated with reduced inflammatory markers compared to mice not receiving acupuncture (23,24). One paper showed that acupuncture was associated with improved motor neuron survival and delayed loss of motor performance compared to mice not receiving acupuncture (23). There are multiple methodological flaws in these papers according to published guidelines (27), including incomplete sample characterizations, small animal numbers, and failure to blind raters. These findings have not been independently confirmed. ALSUntangled assigns a TOE ‘Pre-Clinical’ grade of C based on this information (Table I).

Table I. TOE Grades (2) for acupuncture as an ALS treatment.

	Grade	Explanation
Mechanism	B	Acupuncture can alter inflammatory markers in an animal model of ALS
Pre-Clinical	C	Multiple flawed peer-reviewed publications report benefits of acupuncture in ALS models
Cases	A	One or more peer reviewed publications report benefits of acupuncture in PALS
Trials	D	One peer reviewed publication reports benefits from acupuncture in a flawed ALS trial
Risks	D	More than 0% but less than 5% of patients treated with acupuncture experienced death or hospitalizations

Data in PALS

There is one small pilot trial of acupuncture in PALS (28). Eighteen patients were treated twice daily for five days, with before and after measurements of oxygen saturation, end-tidal carbon dioxide, respiratory rate, pulse rate and ALSFRS-R. Statistically significant improvements were seen only in oxygen saturation and pulse rate after acupuncture. There are several problems with this study including small numbers, short duration, lack of a control group, and lack of blinding. The findings have never been replicated. The sizes of the observed improvements in mean oxygen saturation (from 95.42% to 95.58%) and in mean pulse rate (82.49 to 80.08) are of dubious clinical significance. ALSUntangled assigns a TOE 'Trials' grade of D based on this information (Table I).

Two groups have published case series describing the effects of acupuncture in PALS (29–32). The first group published in Chinese (29,30); we reviewed an available translation (31). Between 1980 and 1996 this group reportedly treated 46 PALS for six to 24 months. In addition to acupuncture, treatment included Chinese herbs and exercises (31). Six of the patients were said to have achieved 'clinical remission, where atrophic muscles were largely restored, the patient then being able to survive with the disease more than 10 years after the diagnosis' (31). In 11 of the patients, the treatments were said to be 'markedly effective, where the ability of managing daily activities was enhanced somewhat, or being able to survive more than five years after diagnosis' (31). For 24 patients, treatments were said to be 'fairly effective, muscular atrophy slows down, with survival over three years' (31). In the remainder, treatments were 'ineffective, symptoms do not improve significantly, with survival less than three years' (31). Criticisms of this work include a lack of detail regarding the ALS diagnoses, lack of a control group, lack of blinding and failure to use validated ALS outcome measures.

The second group reported on two PALS treated with acupuncture five days per week for four weeks and a 'detoxification' supplement regimen (32). From the information provided, patient 1 would have been classified as 'clinically probable ALS'

(EEC). Patient 2 had no documented upper motor neuron findings and thus may have had 'progressive muscular atrophy' (33) or 'lower motor neuron predominant ALS' (34,35). Subjective measurement of speech intelligibility and manual muscle testing improved in both patients over the study period. Problems with this study include an incomplete work-up for ALS mimic syndromes in patient 2 (testing to exclude atypical myasthenia gravis or multi-focal motor neuropathy should have been performed (36)). Also, outcome measures were subjective with no apparent blinding of the raters, the concomitant 'detoxification' regimen is not well described, and the follow-up duration was short.

Within the online community PatientsLikeMe, 72 members reported trying acupuncture for ALS and 19 of these completed evaluations of it. In terms of effectiveness, three reported it to be 'moderate', seven 'slight', six 'none' and three 'unknown' (37). Google search identified no additional case reports. ALSUntangled assigns a TOE 'Cases' grade of A based on this information (Table I).

Risks and costs

Large series suggest that acupuncture is generally safe but not entirely without risk (3). Mild adverse events such as pain or bleeding occur in 7–11% of patients (3,38–40), and serious adverse events have occasionally occurred including cardiac tamponade (3,41), pneumothorax (3,42), and transmission of infections (3,43). ALSUntangled assigns a TOE 'Risks' grade of D based on this information (Table I).

Costs of acupuncture vary greatly depending on the specific type and frequency. PALS on Patients-LikeMe report a range of costs from less than \$25 to more than \$200 per month.

Conclusions

Acupuncture is reasonably safe, and has potential mechanisms of action, pre-clinical studies and case reports suggesting that it could be a useful treatment for ALS. However, before it can be endorsed even as a candidate for a phase II trial, the studies described above need to be independently replicated using more clearly verified diagnoses and more rigorous

designs, including appropriate controls and validated ALS outcome measures.

Acknowledgements

ALSUntangled is sponsored by the ALS Association and the Motor Neurone Disease Association.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

1. <http://www.alsuntangled.com/open.php>. Accessed March 8, 2015.
2. <http://en.wikipedia.org/wiki/Acupuncture>. Accessed March 3, 2015.
3. Ernst E. Acupuncture: a critical analysis. *J Int Med*. 2006;259:125–37.
4. <http://www.drmihtaly-acupuncture.com/chinese-scalp-acupuncture-als.html>. Accessed March 7, 2015.
5. <http://www.hughscupuncture.com/als-treatment-by-acupuncture-and-traditional-chinese-medicine/>. Accessed March 7, 2015.
6. <http://www.taoiststudy.com/content/use-qigong-herbal-medicine-achieve-cure-als>. Accessed March 7, 2015.
7. Pan W, Chen X, Bao J, Bai Y, Lu H, Wang Q, et al. The use of integrative therapies in patients with amyotrophic lateral sclerosis in Shanghai, China. *Evidence-Based Complementary and Alternative Medicine*. 2013;2013:1–6.
8. Ramey D. Acupuncture points and meridians do not exist. *Scientific Review of Alternative Medicine*. 2001;5:143–8.
9. Gorski D. Integrative oncology: really the best of both worlds? *Nature Reviews Cancer*. 2014;2014:692–700.
10. Han J-S. Acupuncture and endorphins. *Neurosci Lett*. 2004;361:236–40.
11. Eisenstein T. Opioids and the immune system: what is their role? *Br J Pharmacol*. 2011;16:1826–8.
12. Panerai AE, Radulovic J, Monastera G, Manfredi B, Locatelli L, Sacerdote P. Beta-endorphin concentrations in brain areas and peritoneal macrophages in rats susceptible and resistant to experimental allergic encephalomyelitis: a possible relationship between tumour necrosis factor alpha and opioids in the disease. *J Neuroimmunol*. 1994;51:169–76.
13. McCarthy L, Wetzel M, Sliker JK, Eisenstein TK, Rogers TJ. Opioids, opioid receptors and the immune response. *Drug Alcohol Depend*. 2001;62:111–23.
14. Murdock BJ, Bender DE, Segal BM, Feldman EL. The dual roles of immunity and ALS: injury overrides protection. *Neurobiol Dis*. 2015;77:1–12.
15. Hooten KG, Beers DR, Zhao W, Appel SH. Protective and toxic neuroinflammation in amyotrophic lateral sclerosis. *Neurotherapeutics*. 2015; Jan 8 [Epub ahead of print].
16. Napadow V, Makris N, Liu J, Kettner NW, Kwong KK, Hui KKS. Effects of electroacupuncture versus manual acupuncture on the human brain as measured by fMRI. *Hum Brain Map*. 2005;24:193–205.
17. Wu MT, Sheen JM, Chuang KH, Yang P, Chin SL, Tsai CY et al. Neuronal specificity of acupuncture response: an fMRI study with electroacupuncture. *Neuroimage*. 2002;16:1028–37.
18. Fang JL, Krings T, Weidemann J, Meister IG, Thron A. Functional MRI in healthy subjects during acupuncture; different effects of needle rotation in real and false acupoints. *Neuroradiology*. 2004;46:359–62.
19. Cho ZH, Chung SC, Jones JP, Park JB, Park HJ, Lee HJ, et al. New findings of the correlation between acupoints and corresponding brain cortices using functional MRI. *Proc Nat Acad Sci U S A*. 1998;95:2670–3.
20. *Acupoint-specific fMRI patterns in human brain. *Neurosci Lett*. 2005;383:236–40.
21. Zillstra F, van den Berg-de-Lange I, Huygen F, Klein J. Anti-inflammatory actions of acupuncture. *Mediators of Inflammation*. 2003;12:59–69.
22. Kim ST, Doo AR, Kim SRN, Kim SY, Kim YY, Kim JH, et al. Acupuncture suppresses kainic acid-induced neuronal death and inflammatory events in mouse hippocampus. *J Physiol Sci*. 2012;62:377–83.
23. Yang E, Jiang J, Lee S, Hwang H, Lee M, Choi S. Electroacupuncture reduces neuroinflammatory responses in symptomatic amyotrophic lateral sclerosis model. *J Neuroimmun*. 2010;223:84–91.
24. Jiang J, Yang E, Baek M, Kim S, Lee S, Choi S. Anti-inflammatory effects of electroacupuncture in the respiratory system of a symptomatic amyotrophic lateral sclerosis model. *Neurodegenerative Dis*. 2011;8:504–14.
25. Chapman C, Benedetti C, Colpitts Y, Gerlach R. Naloxone fails to reverse pain thresholds elevated by acupuncture. *Pain*. 1983;16:13–31.
26. Vickers A, Goyal N, Harland R, Rees R. Do certain countries produce only positive results? A systematic review of controlled trials. *Control Clin Trials*. 1998;19:159–66.
27. Ludolph A, Bendotti C, Blaugrund E, Chio A, Greensmith L, Loeffler J, et al. Guidelines for preclinical animal research in ALS/MND: a consensus meeting. *Amyotroph Lateral Scler*. 2010;11:38–45.
28. Lee S, Kim S. The effects of sa-am acupuncture treatment on respiratory parameters in amyotrophic lateral sclerosis. *Evidence Based Complementary and Alternative Medicine*. 2013;2013:506317.
29. Yongde C. Formulating a therapeutic program with the governing vessel in treating 46 cases of ALS. *Shanghai Journal of Moxibustion*. 1998;17:43.
30. Yongde C. Clinical observation on 46 cases of ALS in consideration of the treatment principle breaking through the Dumai. *Zhejiang Journal of Integrating Traditional Chinese and Western Medicine*. 1999;9:16–7.
31. <http://www.itmonline.org/arts/als.htm>. Accessed March 19, 2015.
32. Liang S, Christner D, DuLaux S, Laurent D. Significant neurological improvement in two patients with amyotrophic lateral sclerosis after four weeks of treatment with acupuncture injection point therapy using enercel. *J Acupunct Meridian Stud*. 2011;4:257–61.
33. Rowland L. Progressive muscular atrophy and other lower motor neuron syndromes of adults. *Muscle Nerve*. 2010;41:161–5.
34. Ince P, Evans J, Knopp M, Forster G, Hamdalla HH, Wharton SB, et al. Corticospinal tract dysfunction in the progressive muscular atrophy variant of ALS. *Neurology*. 2003;60:1252.
35. Kim W, Liu X, Sandner J, Pasmantier M, Andrews J, Rowland L, et al. Study of 962 patients indicates progressive muscular atrophy is a form of ALS. *Neurology*. 2009;73:1686.
36. Visser J, van den Berg-Vos M, Franssen H, van den Berg L, Vogels J, Wokke J, et al. Mimic syndromes in cases of progressive spinal muscular atrophy. *Neurology*. 2002;58:1593–6.
37. http://www.patientslikeme.com/treatment_evaluations/browse?brand=f&condition_id=9&id=213-acupuncture-side-effects-and-efficacy. Accessed March 21, 2015.
38. White A, Hayhoe S, Hart A, Ernst E. Adverse events following acupuncture: a prospective survey of 32,000 consultations with doctors and physiotherapists. *Br Med J*. 2001;323:485–6.

39. Melchart D, Weidenhammer W, Streng A, Reitmayr S, Hoppe A, Ernst E, et al. Prospective investigation of adverse effects of acupuncture in 97733 patients. *Arch Intern Med.* 2004;164:104–5.
40. MacPherson H, Scullion A, Thomas KJ, Walters S. Patient reports of adverse events associated with acupuncture treatment: a prospective national survey. *Qual Saf Health Care.* 2004;13:349–55.
41. Ernst E, Zhang J. Cardiac tamponade caused by acupuncture: a review of the literature. *Int J Cardiol.* 2011;149:287–9.
42. Demir M, Oruc M, Dalli A, Kaya H, Karadeniz G. A rare complication of acupuncture: pneumothorax. *Tuberk Toraks.* 2014;62:316–8.
43. Ernst E, Sherman KJ. Is acupuncture a risk factor for hepatitis? Systematic review of epidemiological studies. *J Gastroenterol Hepatol.* 2003;18:1231–6.

The ALSUntangled Group currently consists of the following members: Richard Bedlack, Colin Quinn, Chafic Karam, Alex Sherman, Lyle Ostrow, Orla Hardiman, Terry Heiman-Patterson, Laurie Gutmann, Mark Bromberg, Gregory Carter, Edor Kabashi, Tulio Bertorini, Tahseen Mozaffar, Peter Andersen, Jeff Dietz, Josep Gamez, Mazen Dimachkie, Yunxia Wang, Paul Wicks, James Heywood, Steven Novella, L. P. Rowland, Erik Pioro, Lisa Kinsley, Kathy Mitchell, Jonathan Glass, Sith Sathornsumtee, Hubert Kwiecinski, Jon Baker, Nazem Atassi, Dallas Forshew, John Ravits, Robin Conwit, Carlayne Jackson, Kate Dalton, Katherine Tindall, Ginna Gonzalez, Janice Robertson, Larry Phillips, Michael Benatar, Eric Sorenson, Christen Shoesmith, Steven Nash, Nicholas Maragakis, Dan Moore, James Caress, Kevin Boylan, Carmel Armon, Megan Grosso, Bonnie Gerecke, Jim Wymer, Bjorn Oskarsson, Robert Bowser, Vivian Drory, Jeremy Shefner,

Noah Lechtzin, Melanie Leitner, Robert Miller, Hiroshi Mitsumoto, Todd Levine, James Russell, Khema Sharma, David Saperstein, Leo McClusky, Daniel MacGowan, Jonathan Licht, Ashok Verma, Michael Strong, Catherine Lomen-Hoerth, Rup Tandan, Michael Rivner, Steve Kolb, Meraida Polak, Stacy Rudnicki, Pamela Kittrell, Muddasir Quereshi, George Sachs, Gary Pattee, Michael Weiss, John Kissel, Jonathan Goldstein, Jeffrey Rothstein, Dan Pastula, Gleb Levitsky, Mieko Ogino, Jeffrey Rosenfeld, Efrat Carmi, Merit Cudkowicz, Christina Fournier, Paul Barkhaus, Brett Morrison, Lorne Zinman, Eric Valor.

Note: this paper represents a consensus of those weighing in. The opinions expressed in this paper are not necessarily shared by every investigator in this group.