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Latest Publications You Should Not Miss

Hsieh C, Kong J, Kirsch I, Edwards RR, Jensen KB, Kaptchuk TJ, Gollub RL: Well-loved music robustly relieves pain: a randomized, controlled trial. PLoS One 2014;9:e107390.

Music has pain-relieving effects, but its mechanisms remain unclear. We sought to verify previously studied analgesic components and further elucidate the underpinnings of music analgesia. Using a well-characterized conditioning-enhanced placebo model, we examined whether boosting expectations would enhance or interfere with analgesia from strongly preferred music. A two-session experiment was performed with 48 healthy, pain experiment-naïve participants. In a first cohort, 36 were randomized into 3 treatment groups, including music enhanced with positive expectancy, non-musical sound enhanced with positive expectancy, and no expectancy enhancement. A separate replication cohort of 12 participants received only expectancy-enhanced music following the main experiment to verify the results of expectancy-manipulation on music. Primary outcome measures included the change in subjective pain ratings to calibrated experimental noxious heat stimuli, as well as changes in treatment expectations. Without conditioning, expectations were strongly in favor of music compared to non-musical sound. While measured expectations were enhanced by conditioning, this failed to affect either music or sound analgesia significantly. Strongly preferred music on its own was as pain relieving as conditioning-enhanced strongly preferred music, and more analgesic than enhanced sound. Our results demonstrate the pain-relieving power of personal music even over enhanced expectations.

Trial Information: Clinicaltrials.gov NCT01835275.

Lee J, Napadow V, Kim J, Lee S, Choi W, Kaptchuk TJ, Park K: Phantom acupuncture: dissociating somatosensory and cognitive/affective components of acupuncture stimulation with a novel form of placebo acupuncture. PLoS One 2014;9:e104582.

In a clinical setting, acupuncture treatment consists of multiple components including somatosensory stimulation, treatment context, and attention to needle-based procedures. In order to dissociate somatosensory versus contextual and attentional aspects of acupuncture, we devised a novel form of placebo acupuncture, a visual manipulation dubbed phantom acupuncture, which reproduces the acupuncture needling ritual without somatosensory tactile stimulation. Subjects ($N = 20$) received both real (REAL) and phantom (PHNT) acupuncture. Subjects were retrospectively classified into two groups based on PHNT credibility (PHNTc, who found phantom acupuncture credible; and PHNTnc, who did not). Autonomic and psychophysical responses were monitored. We found that PHNT can be delivered in a credible manner. Acupuncture needling, a complex, ritualistic somatosensory intervention, induces sympathetic activation (phasic skin conductance (SC) response), which may be specific to the somatosensory component of acupuncture. In contrast, contextual effects, such as needling credibility, are instead associated with a shift toward relative cardiovagal activation (decreased heart rate) during needling and sympathetic inhibition (decreased SC) and parasympathetic activation (decreased pupil size) following acupuncture needling. Visual stimulation characterizing the needling ritual is an important factor for phasic autonomic responses to acupuncture and may underlie the needling orienting response. Our study suggests that phantom acupuncture can be a viable sham control for acupuncture as it completely excludes the somatosensory component of real needling while maintaining the credibility of the acupuncture treatment context in many subjects.

**Sundberg T, Petzold M, Kohls N, Falkenberg T:
Opposite drug prescription and cost trajectories
following integrative and conventional care for pain –
a case-control study. PLoS One 2014;9:e96717.**

Objectives: Pharmacotherapy may have a limited role in long-term pain management. Comparative trajectories of drug prescriptions and costs, two quality-of-care indicators for pain conditions, are largely unknown subsequent to conventional or integrative care (IC) management. The objectives of this study were to compare prescribed defined daily doses (DDD) and cost of first line drugs for pain patients referred to conventional or anthroposophic IC in Stockholm County, Sweden.

Methods: In this retrospective high quality registry case-control study, IC and conventional care patients were identified through inpatient care registries and matched on pain diagnosis (ICD-10: M79), age, gender and socio-demographics. National drug registry data was used to investigate changes in DDD and costs from 90/180 days before, to 90/180 days after, index visits to IC and conventional care. The primary selected drug category was analgesics, complemented by musculo-skeletal system drugs (e.g. anti-inflammatories, muscle relaxants) and psycholeptics (e.g. hypnotics, sedatives).

Results: After index care visits, conventional care pain patients (n = 1,050) compared to IC patients (n = 213), were prescribed significantly more analgesics. The average (95% CI) group difference was 15.2 (6.0 to 24.3), $p = 0.001$, DDD/patient after 90 days; and 21.5 (7.4 to 35.6), $p = 0.003$, DDD/patient after 180 days. The cost of the prescribed and sold analgesics was significantly higher for conventional care after 90 days: euro/patient 10.7 (1.3 to 20.0), $p = 0.025$. Changes in drug prescription and costs for the other drug categories were not significantly different between groups.

Conclusions: Drug prescriptions and costs of analgesics increased following conventional care and decreased following IC, indicating potentially fewer adverse drug events and beneficial societal cost savings with IC.

**Cramer H, Haller H, Lauche R, Steckhan N,
Michalsen A, Dobos G: A systematic review and meta-
analysis of yoga for hypertension. Am J Hypertens
2014;27:1146–1151.**

Background: The aim of this systematic review and meta-analysis was to evaluate the quality of evidence and the strength of recommendation for yoga as a therapeutic means in the management of prehypertension and hypertension.

Methods: MEDLINE/Pubmed, Scopus, CENTRAL, and IndMED were screened through February 2014 for randomized controlled trials (RCTs) on the effects of yoga interventions (≥ 8 weeks) compared with usual care or any active control intervention on blood pressure in patients with prehypertension (120–139/80–89 mm Hg) or hypertension ($\geq 140/\geq 90$ mm Hg). Risk of bias was assessed using the Cochrane risk of bias tool; quality of evidence was assessed according to the GRADE recommendations.

Results: Seven RCTs with a total of 452 patients were included. Compared with usual care, very low-quality evidence was found for effects of yoga on systolic (6 RCTs, $n = 278$; mean difference (MD) = -9.65 mm Hg, 95% confidence interval (CI) = -17.23 to -2.06 , $P = 0.01$; heterogeneity: $I^2(2) = 90\%$, $\chi^2(2) = 48.21$, $P < 0.01$) and diastolic blood pressure (6 RCTs, $n = 278$; MD = -7.22 mm Hg, 95% CI = -12.83 to -1.62 , $P = 0.01$; heterogeneity: $I^2(2) = 92\%$, $\chi^2(2) = 64.84$, $P < 0.01$). Subgroup analyses revealed effects for RCTs that included hypertensive patients but not for RCTs that included both hypertensive and prehypertensive patients, as well as for RCTs that allowed antihypertensive comedication but not for those that

did not. More adverse events occurred during yoga than during usual care. Compared with exercise, no evidence was found for effects of yoga on systolic or diastolic blood pressure.

Conclusions: Larger studies are required to confirm the emerging but low-quality evidence that yoga may be a useful adjunct intervention in the management of hypertension.

**Schützler L, Witt CM: Internal health locus of
control in users of complementary and alternative
medicine: a cross-sectional survey. BMC Complement
Altern Med 2014;30:320.**

Background: Complementary and alternative medicine (CAM) is widely used in Germany, with some treatments eligible for health insurance reimbursements. CAM encourages patients to play an active role in their healing process. The belief that a person's own behavior influences health is assessed as the internal health locus of control (IHLOC). Studies on the association between IHLOC and CAM use yield inconsistent results. Using various indicators of CAM use, we evaluated whether there were differences in IHLOC between different groups of CAM users.

Methods: A cross-sectional online survey was conducted. IHLOC was compared between participants with high and low appraisal of CAM, between participants who used different types of medications (none, CAM, conventional, both), and who consulted with different health care professionals (none, CAM, conventional, both). Independent samples t-tests and ANOVAs were conducted for the total group and for subgroups of chronically ill and healthy participants. Post-hoc, we conducted a multivariate linear regression evaluating which indicators of CAM use or other characteristics showed the strongest association with IHLOC.

Results: A total of 1,054 undergraduate students completed the survey. Participants with high CAM appraisal showed higher IHLOC than those with low CAM appraisal, regardless of whether they were chronically ill ($p < 0.001$). Participants without chronic conditions showed higher IHLOC when only using CAM medications than when using either conventional medications alone or both conventional and CAM medications ($p < 0.05$). All participants showed higher IHLOC when visiting only CAM practitioners than when visiting either only conventional or both conventional and CAM practitioners ($p < 0.05$). CAM appraisal was associated the strongest with IHLOC in the linear regression model.

Conclusions: Generally, participants using CAM more or exclusively, and participants with higher appraisal of CAM showed higher IHLOC than those with less CAM use or lower CAM appraisal. Because of the cross-sectional design, it is not possible to determine whether differences in IHLOC are reasons for or consequences of CAM use. Research using a longitudinal design is needed. The sample, though more representative than most student samples, might not represent the general population. Studies evaluating clinical populations might add to the findings.

**MacPherson H, Vertosick E, Lewith G, Linde K,
Sherman KJ, Witt CM, Vickers AJ; Acupuncture
Trialists' Collaboration: Influence of control group
on effect size in trials of acupuncture for chronic
pain: a secondary analysis of an individual patient
data meta-analysis. PLoS One 2014;9:e93739.**

Background: In a recent individual patient data meta-analysis, acupuncture was found to be superior to both sham and non-sham controls in patients with chronic pain. In this paper we identify variations in types of sham and non-sham controls used and analyze their impact on the effect size of acupuncture.

Methods: Based on literature searches of acupuncture trials involving patients with headache and migraine, osteoarthritis, and back, neck and shoulder pain, 29 trials met inclusion criteria, 20 involving sham controls (n = 5,230) and 18 non-sham controls (n = 14,597). For sham controls, we analysed non-needle sham, penetrating sham needles and non-penetrating sham needles. For non-sham controls, we analysed non-specified routine care and protocol-guided care. Using meta-regression we explored impact of choice of control on effect of acupuncture.

Findings: Acupuncture was significantly superior to all categories of control group. For trials that used penetrating needles for sham control, acupuncture had smaller effect sizes than for trials with non-penetrating sham or sham control without needles. The difference in effect size was

−0.45 (95% C.I. −0.78, −0.12; p = 0.007), or −0.19 (95% C.I. −0.39, 0.01; p = 0.058) after exclusion of outlying studies showing very large effects of acupuncture. In trials with non-sham controls, larger effect sizes associated with acupuncture vs. non-specified routine care than vs. protocol-guided care. Although the difference in effect size was large (0.26), it was not significant with a wide confidence interval (95% C.I. −0.05, 0.57, p = 0.1).

Conclusion: Acupuncture is significantly superior to control irrespective of the subtype of control. While the choice of control should be driven by the study question, our findings can help inform study design in acupuncture, particularly with respect to sample size. Penetrating needles appear to have important physiologic activity. We recommend that this type of sham be avoided.