Research Reviews

Research reviews

This section is designed to give a synopsis of some of the latest research published in Medline listed journals over the last year or so. It will concentrate on controlled trials and systematic reviews, but will also include other papers that may be of interest to the readership. Some papers will be reviewed in more detail than others. If summaries and comments are based on an abstract only, this will be indicated. The main reviewer in this section is Mike Cummings, London. Other reviewers are indicated after the relevant review.

RCTs

Acupuncture may increase the success rate of IVF (n=160)


Summary
The objective of this study was to evaluate the effect of acupuncture on the pregnancy rate in assisted reproduction therapy (ART) by comparing a group of patients receiving acupuncture treatment shortly before and after embryo transfer with a control group receiving no acupuncture. This was a prospective randomized study, performed within a fertility centre. After giving informed consent, 160 patients who were undergoing ART and who had good quality embryos were randomly divided into the following two groups: embryo transfer with acupuncture (n = 80) and embryo transfer without acupuncture (n = 80). Acupuncture was performed in 25 minutes before and after embryo transfer. In the control group, embryos were transferred without any additional therapy. The main outcome measure was clinical pregnancy – defined as the presence of a fetal sac during an ultrasound examination six weeks after embryo transfer. Clinical pregnancies were documented in 34 of 80 patients (42.5%) in the acupuncture group, and in 21 out of 80 patients (26.3%) in the control group. The authors concluded that acupuncture seems to be a useful tool for improving pregnancy rate after ART.

Comment
In this study the authors chose points that, according to TCM principles, ‘relax the uterus’. Before embryo transfer the points used were: CV6, SP8, LR3, GV20 and ST29. After embryo transfer the points used were: ST36, SP6, SP10 and LI4. In addition to these, four auricular points were used, two in the right and two in the left. The side used for individual points was changed after embryo transfer. CV6, SP6, SP8 and ST29 all stimulate myotomes that are segmentally relevant to the uterus - T11 to L1 and S2 to S4, although that was not the expressed intention of the authors.

This seems to be a straight-forward and positive study, however, the results should be interpreted with caution as the statistics for the fertility centre are not given, and the pregnancy rate in the control group appears to be lower than might be expected. The pregnancy rate for this sample, given the parameters of the IVF, would be expected in many western centres to be 35 to 40%, i.e. the rate in the acupuncture group. The lower rate observed in the control group could be a result of chance (a type 1 statistical error); or, as this study was open, the patients randomised to control may have suffered some degree of stress as a result of the disappointment at not getting acupuncture. It is highly speculative, but this minor level of stress may have caused suboptimal conditions for implantation in the control group.

Whilst the pregnancy rate at six weeks is important, the crucial outcome is the ‘take home baby rate’. It is hoped that the authors will publish this data. Following this the next step for the group might be to repeat the study with a non-penetrating sham control, and an adequate power calculation.
Electroacupuncture during oocyte aspiration is an adequate analgesic, but does not affect the pregnancy rate (n=286)


**Summary**

In a previous study on the effect of electroacupuncture (EA) in combination with a paracervical block (PCB) as an analgesic method during oocyte aspiration in IVF treatment, EA appeared to increase the pregnancy rate. This study was designed to test the hypothesis that EA as an analgesic during oocyte aspiration would result in: (i) a better IVF pregnancy rate than with alfentanil; (ii) peroperative analgesia that was as good as that produced by alfentanil; (iii) less postoperative abdominal pain, nausea and stress; and (iv) a reduction in the use of additional analgesics. Neuropeptide Y (NPY) concentrations in follicular fluid (FF) were analysed when possible. In this prospective, randomised, multicentre clinical trial, 286 women undergoing oocyte aspiration were randomly allocated to the EA group (EA plus a PCB) or to the alfentanil group (alfentanil plus a PCB). No significant differences were found between the EA and alfentanil groups in any of the IVF variables. NPY concentrations in FF were significantly higher in the EA group compared with the alfentanil group. No significant correlations between pregnancy rate and NPY concentrations were found in either analgesic group. Both EA plus a PCB and alfentanil plus a PCB induced adequate peroperative analgesia during oocyte aspiration evaluated using the visual analogue scale. After two hours, the EA group reported significantly less abdominal pain, other pain, nausea and stress than the alfentanil group. In addition, the EA group received significantly lower amounts of additional alfentanil than the alfentanil group. Conclusions: EA does not improve pregnancy rate in the clinical situation tested. The observation that NPY concentrations in FF were higher in the EA group may be important for human ovarian steroidogenesis. The analgesic effects produced by EA are as good as those produced by conventional analgesics, and the use of opiate analgesics with EA is lower than when conventional analgesics alone are used.

**Comment**

This was a well conducted and reported trial. The electroacupuncture used was a high frequency (80Hz) segmental stimulus to ST29 bilaterally, and a low frequency (2Hz) heterosegmental stimulus to LI4 and TE5. Additionally, ST36 bilaterally and GV20 were manually stimulated every minute.

Based on a suitable calculation, this was an adequately powered trial, but, unlike Paulus et al, it did not show any difference between the groups in terms of pregnancy rate. The equivalent figure for the outcome used in Paulus et al (gestational sac present at six weeks), in this trial, was between 31-34% (ongoing pregnancy rate) and 43-49% (initial pregnancy rate).

In terms of acupuncture the key difference may have been the timing of course. In this trial the acupuncture was performed once immediately before and during oocyte aspiration. Embryo transfer is performed some three to five days after this, and in Paulus et al the acupuncture was given before and after the latter procedure.

Stener-Victorin et al are now planning further research to investigate the effects of a course of treatment leading up to the IVF treatment procedures.
Preoperative electroacupuncture reduces postoperative analgesic requirements (n=100)


**Summary**

This study examined the effects of preoperative electroacupuncture (EA) at classical bilateral acupuncture points (Zusanli, ST36) on postoperative pain and opioid-related side effects. One hundred healthy consenting women undergoing lower abdominal surgery were randomly assigned to four treatment regimens: group I (n=25), control; group II (n=25), sham-EA (needle insertion without electrical stimulation); group III (n=25), low-EA (2Hz EA); and group IV (n=25), high-EA (100Hz EA). EA groups received needle insertion with or without electrical stimulation 20 minutes prior to anaesthesia. All patients received patient-controlled analgesia (PCA) of morphine post-operatively. Postoperative pain was evaluated by recording (1) the time of the first required analgesic, (2) the number of PCA demands, (3) the total amount of morphine required by PCA, and (4) patients' VAS pain score.

The authors found that the time of first analgesic requested was 10, 18, 28, and 28 minutes in the control, sham-, low-, and high-EA groups, respectively. During the first 24 hours, the total amount of morphine required was decreased by 21, 43 and 61% in the sham-, low- and high-EA groups, respectively. The incidence of nausea and dizziness during the first 24 hours after surgery was significantly reduced in both the low-EA and high-EA groups compared with the control and sham-EA groups. They also found that sham-EA exerted a beneficial effect with respect to its pain relieving quality but not the side effect profiles. They concluded that their findings demonstrate that preoperative treatment with low-EA and high-EA can reduce postoperative analgesic requirements and associated side effects in patients undergoing lower abdominal surgery.

**Comment**

This is an interesting study for two reasons. First, 100Hz electroacupuncture (EA) was more effective than 2Hz in reducing postoperative analgesic requirements. Second, sham EA had some effect on analgesic requirements, but no significant effect on nausea or dizziness.

The authors explain the first observation here purely in terms of the number of conditioning stimuli applied. Over the 20 minute period of conditioning stimuli, the authors estimated that the 100Hz EA group received about 20 times the number of electrical pulses as the 2Hz EA group. This is presumably based on the fact that the relevant afferents cannot respond to every impulse at 100Hz because of their latency.

The authors describe the acupuncture treatment as follows:

Two 30 gauge stainless steel acupuncture needles were inserted at the Zusanli point on both legs, with a distance between the needles of approximately 3cm, i.e. one needle serving as the positive pole, and the other as the negative pole to allow electrical stimulation of the selected point.

Electricity was generated as an output of constant current of 0.5mA, 1 ms square pulse, at a maximum tolerable intensity (a strong, but not painful sensation as reported by the patient), and at 2 or 100Hz depending on the group assignment.

This is slightly unclear because if the intensity was adjusted for individual tolerance (as would be expected), then the current output used would not be the same for all patients.

Apart from the above details, this is a well reported paper, and adds to the positive literature on the preemptive use of acupuncture to reduce postoperative analgesic requirements.
Acupuncture anaesthesia in inguinal hernia repair (n=12)


**Summary**

This study was undertaken to evaluate the efficacy of acupuncture anaesthesia in inguinal hernia repair. Twelve patients with non-recurrent inguinal hernia had Lichtenstein mesh repair under acupuncture anaesthesia. Selected acupuncture loci were stimulated with fine needles connected to low frequency current. Supplementary local anaesthetic was given when required. Four (33%) patients reported satisfactory analgesic effect throughout the operation without need for additional medication, eight (67%) patients experienced mild discomfort during the operation requiring 1-4 mL of 1% lignocaine injection. Blood pressure and heart rate were stable during the procedure. All patients were able to sit up and resume their diet immediately post-operatively. All but one of the patients were discharged on day one after the procedure, with no early or late complications reported. Most patients were satisfied with the analgesic effect of acupuncture anaesthesia. The authors concluded that acupuncture anaesthesia is a feasible anaesthetic option. It reduces the amount of local anaesthetic required, and thus the associated potential complications. It is effective in pain relief and inhibiting gastrointestinal upset. Postoperative recovery was rapid and complication free.

**Comment**

This is a small case series of acupuncture used for acute surgical analgesia. When acupuncture is used as the sole or principal agent for surgical analgesia in an awake patient, the technique is often referred to as acupuncture anaesthesia. Even though acupuncture does not act as an anaesthetic agent, it is sometimes used, as in this case series, to take the place of an anaesthetic.

Patients were premedicated with a small dose of pethidine (25mg) and diazepam (5mg). Electroacupuncture (EA) at 4Hz was performed on the side of the hernia for 15 minutes prior to the surgery. The pairs of points used were ST36 and SP6, GB27 and 28, KI13 and 14, and paraincisional points. The latter points were needled using 3cm needles, but all the rest were needled using 1cm needles. With the exception of ST36 and SP6, all the needles were removed just before surgery. Four of the patients required no local anaesthetic and were pain free throughout the procedure. The average quantity of lignocaine used was only 1.4ml of 1%. It is not clear whether this was the mean requirement of all 12, or whether it was only those eight who required it. Either way, it is a very small quantity compared with the usual volume used in this type of surgery.

The doses of premedication were unlikely to result in sufficient analgesia alone to perform surgery. There are no details of the patients' weights in the paper, but it is unlikely that they were so small that 25mg of pethadine and 5mg of diazepam would have been sufficient to cover surgery.

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**Other Clinical Papers**

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**Electrical acupuncture therapy** for patients with spinal cord injuries (n=100)


**Summary**

The objective of this study was to examine whether electrical acupuncture therapy through adhesive surface electrodes and concomitant auricular acupuncture therapy could improve the neurologic or functional recovery in acute traumatic spinal cord injury patients. A total of 100 acute traumatic spinal cord injury patients with American Spinal Injury Association (ASIA) impairment grading of A and B were recruited into this study. They were randomly divided into acupuncture and control groups. In the acupuncture group, electrical acupuncture therapy...
via the adhesive surface electrodes was applied to bilateral Hou Hsi (SI3) and Shen Mo (BL62) acupoints. In auricular acupuncture, four acupoints related to the spinal cord were selected for stimulation at the antihelix, helix, and lower portion of the ear-back areas. Acupuncture therapy was initiated early in the emergency room setting or soon after spinal surgical intervention. Rehabilitation therapy was also provided to the patients during acupuncture therapy. In the control group, only rehabilitation therapy was provided to the patients. Neurologic and functional scores were assessed during the time of admission, hospital discharge, and one year post injury. There were significant improvements in neurologic (sensory and motor), and functional scores in the acupuncture group compared with the initial admission period when assessed during the time of hospital discharge and one year post injury. A greater percentage of patients in the acupuncture group recovered to a higher ASIA impairment grading. The authors concluded that the use of concomitant auricular and electrical acupuncture therapies, when implemented early in acute spinal cord injury, can contribute to significant neurologic and functional recoveries.

Comment
The ‘electrical acupuncture’ used in this study was really TENS at 75Hz, 200µsec (pulse width) and 10mA. It was applied five times per week, presumably until discharge from the unit. Auricular acupuncture involved the placement of indwelling needles that were replaced weekly. This is an encouraging trial, however, as there was no sham intervention, it is not possible to determine which aspects of the intervention were responsible for the observed effects. The latter may have derived entirely from the extra attention devoted to the patients in the acupuncture group. It probably would have been fairly easy to design a credible sham, and, in view of the results of Johansson et al., a sham control ought to be used in any further trials of this nature. Johansson et al. found that sham TENS was as effective as real TENS or electroacupuncture in the rehabilitation after hemiplegic stroke. It is notable that this trial is not referred to in this paper, whereas there is a reference to a positive trial of ‘electrical acupuncture therapy’ in stroke rehabilitation by the first author. This could be interpreted as selective citation.

Reference

Percutaneous tibial nerve stimulation in chronic pelvic pain (n=33)


Summary
Neuromodulative therapies have been used with moderate success in patients with chronic pelvic pain. Intermittent Percutaneous Tibial Nerve Stimulation (PTNS) is a ‘new’ [according to the authors] minimally invasive treatment option, which has been shown to significantly decrease accompanying pain complaints in patients with lower urinary tract dysfunction, such as urge incontinence or urgency/frequency. In this study, the authors evaluated the objective results of PTNS in patients with chronic pelvic pain as their main complaint. In a prospective multicentre trial PTNS was evaluated in 33 patients with chronic pelvic pain. Effects were recorded by worst visual analogue score (VAS) for pain in daily diaries, the McGill pain questionnaire and the SF-36 general quality of life questionnaire at baseline and after 12 weeks of treatment. Subjective (patients’ request to continue chronic treatment to keep the obtained success) and objective responses (decrease in mean VAS >50% and VAS <3 after treatment) were evaluated. A subjective response was seen in 42% of all patients. In seven patients (21%) mean VAS decreased >50%, in six cases (18%) the decrease was >25%. After 12 weeks of treatment, seven patients (21%) ended up with a mean VAS <3. In all patients quality of life (SF-36) significantly improved, as did the total pain rate intensity (McGill). Despite very modest
overall success rates and the need for placebo-controlled studies, the authors concluded that PTNS may have a place in the treatment of patients with chronic pelvic pain who have already tried many other therapies and are left with no further option.

Comment
This is a small cohort study using a form of electrical stimulation of the lower leg that is virtually indistinguishable from electroacupuncture at SP6. A needle is placed posterior to the medial edge of the tibia, 3 to 4 cm above the medial malleolus, and stimulated electrically (20 Hz, 200 µsec, 0-10 mA). Rather than a second needle, a TENS pad is used as the other electrode. The pad is placed near the arch of the foot. The intensity is adjusted until there is flexion of the hallux or flaring of the toes. In this study treatment was performed weekly for 12 weeks.

The result is encouraging, but further research using a suitable control will be needed to determine whether the observed effect is specific.

Unfortunately, the authors do not use either of the terms acupuncture or electroacupuncture in the abstract or keywords, so the paper would not necessarily show up on a database search for acupuncture.

Acupuncture appears to reduce symptoms in chronic prostatitis/chronic pelvic pain syndrome (n=12)

Summary
The objective of this pilot study was to determine whether acupuncture improved pain, voiding symptoms, and the quality of life of men with chronic prostatitis/chronic pelvic pain syndrome. Men diagnosed with chronic prostatitis/chronic pelvic pain syndrome (National Institutes of Health [NIH] criteria) who were refractory to standard therapy (antibiotics, alpha-blockers, anti-inflammatories, phytotherapy) were referred for acupuncture treatment. The treatment protocol involved three sets of acupuncture points totalling 30 points (eight points were electrically stimulated) given alternatively twice weekly for six weeks. The patients completed the NIH Chronic Prostatitis Symptom Index (CPSI) at baseline and the CPSI and subjective global assessment at six weeks (end of treatment), 12 weeks, and at least six months after the baseline assessment. Twelve men underwent a minimum of six weeks of acupuncture treatment. The average follow-up (from baseline) was 33 weeks (range 24 to 52). A significant decrease occurred in total NIH-CPSI (28.2 to 8.5), NIH-CPSI pain (14.1 to 4.8), NIH-CPSI urinary (5.2 to 1.3), and NIH-CPSI quality-of-life (8.8 to 2.3) scores after an average of 33 weeks of follow-up. Ten patients (83%) had a sustained greater than 50% decrease in NIH-CPSI at final visit (average 33 weeks). Ten patients (83%) reported marked improvement on the subjective global assessment at 12 weeks. At an average of 33 weeks, eight patients (67%) had sustained marked improvement on subjective global assessment evaluation. No adverse events were reported in this pilot study. The authors concluded that acupuncture appeared to be a safe, effective, and durable treatment in improving symptoms in, and the quality of life of, men with chronic prostatitis/chronic pelvic pain syndrome refractory to treatment. A larger controlled study is required to confirm these encouraging initial results.

Comment
This is a small uncontrolled study but the results are encouraging. The subjects underwent quite intense treatment - 12 sessions over six weeks, which included electroacupuncture. Much of the needling was segmental.

As the authors and an editorial comment suggest, these results need to be followed up with a controlled trial. If they decide on an efficacy trial, this reviewer hopes that the sham intervention does not miss the point, i.e. that they do not use needling off-point as a control.
Posterior tibial nerve stimulation in the treatment of idiopathic nonobstructive voiding dysfunction (n=39)


**Summary**

The objective of this study was to evaluate the effect of stimulation of the posterior tibial nerve in the treatment of voiding dysfunction. Thirty-nine patients with chronic voiding dysfunction necessitating clean intermittent catheterisation were enrolled in a prospective multicentre trial in the Netherlands (n=19) and Italy (n=20). They underwent 12 weekly sessions of posterior tibial nerve stimulation. Frequency/volume charts, an incontinence quality-of-life instrument, and the MOS 36-item Short-Form Health Survey were completed at 0 and 12 weeks. Subjective success was defined by the patient’s positive response resulting in a request to continue treatment. Efficacy was based on analysis of the frequency/volume charts comparing the baseline values with the data at 12 weeks. A reduction of 50% or more in total catheterised volume was considered as an objective success (primary outcome measurement). Of the 39 patients, 23 (59%) chose to continue treatment. The frequency/volume charts showed a 50% decrease in total catheterised volume in 16 (41%) of 39 patients. Additionally, 10 patients (26%) noted a reduction of 25% to 50% in their total catheterised volume. For all patients, the total catheterised volume decreased by a mean of 228mL (range 49 to 528). The incontinence quality-of-life instrument and Short-Form Health Survey parameters improved significantly. The authors concluded that percutaneous stimulation of the posterior tibial nerve seems to be an effective, minimally invasive option worth trying in patients with idiopathic voiding dysfunction. Improvement was seen in objective micturition parameters, as well as in subjective quality-of-life data.

**Comment**

This is another trial of a type of electro-acupuncture at SP6 for a form of bladder dysfunction. The results appear encouraging, but again controlled trials are needed to confirm the efficacy of this intervention.

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**Experimental Studies (humans)**

Auricular acupuncture reduces the anaesthetic requirement of desflurane (n=10)


**Summary**

In most acupuncture studies it is difficult or even impossible to conduct a truly double-blind trial. However, this is possible when treatments are carried out on anaesthetised patients. Since acupuncture provides analgesia, this team tested the hypothesis that needle stimulation of a combination of four ear acupoints would significantly reduce anaesthetic requirement. Ten healthy volunteers were anaesthetised with desflurane and randomly assigned to no treatment or acupuncture; the alternative treatment was given on a subsequent study day. Auricular acupuncture was performed with needles placed at the Shenmen, Thalamus, Tranquiliser and Master Cerebral points on the right ear. Anaesthetic requirement, determined by the Dixon up-and-down method, was defined by the average desflurane concentration that prevented purposeful movement of the extremities in response to noxious electrical stimulation. Volunteers required a greater desflurane concentration to prevent movement on the control than on the acupuncture day: 4.9 (0.7; SD) vs. 4.4 (0.8) vol. %, (p=0.003). Acupuncture thus reduced anaesthetic requirement by 8.5 (7)%.

**Comment**

This is the third trial of this type published in the last two years. Each one has used a different group.bmj.com on September 6, 2017 - Published by group.bmj.com
treatment method, but the same outcome measure. The first tested a TENS stimulus just anterior to
the ears,1 and gave a result similar to this study. The second tested electroacupuncture in the legs,2
and showed no effect. The latter study used an intervention very similar to that in Lin et al
(reviewed above),3 which showed a positive effect on postoperative analgesic requirements. It seems
that there is quite a way to go to determine the optimum parameters for stimulation in different
circumstances.

Reference list
1. Greif R, Laciny S, Mokhtarani M, Doufas AG,
Bakhshandeh M, Derfer L et al. Transcutaneous electrical
stimulation of an auricular acupuncture point decreases

2. Morioka N, Akca O, Doufas AG, Chernyak G, Sessler DI.
Electro-acupuncture at the Zusanli, Yanglingquan, and
Kunlun points does not reduce anesthetic requirement.

3. Lin JG, Lo MW, Wex YR, Hsieh CL, Tsai SK, Sun WZ.
The effect of high and low frequency electroacupuncture

Experimental Studies (animals)

Acupuncture modulates the sympathetic nerve
activity to the ovaries in a rat PCO model
(n=56)
Stener-Victorin E, Lundeberg T, Cajander S, Aloe
L, Manni L, Waldenstrom U et al. Steroid-induced
polycystic ovaries in rats: effect of electro-
acupuncture on concentrations of endothelin-1
and nerve growth factor (NGF), and expression of
NGF mRNA in the ovaries, the adrenal glands,
and the central nervous system. Reprod Biol

Summary
Previous studies on the effect of repeated
electroacupuncture (EA) treatments in rats with
steroid-induced polycystic ovaries (PCO), EA has
been shown to modulate nerve growth factor
(NGF) concentration in the ovaries as well as
corticotropin releasing factor (CRF) in the median
eminence (ME). In this study the authors tested
the hypothesis that repeated EA treatments
modulate sympathetic nerve activity in rats with
PCO. This was done by analysing endothelin-1
(ET-1), a potent vasoconstrictor involved in
ovarian functions, as well as NGF and NGF mRNA
expression involved in the pathophysiological
process underlying steroid-induced PCO. The
main result in this study was that concentrations
of ET-1 in the ovaries were significantly lower in
the PCO group receiving EA compared with the
healthy control group (p<0.05). In the hypothalamus, however, ET-1 concentrations were
found to be significantly higher in the PCO group
receiving EA than in the healthy control group
(p<0.05). Concentrations of ovarian NGF protein
were significantly higher in the PCO control
group compared with the healthy control group
(p<0.001), and these concentrations decreased
significantly after repeated EA treatments
compared with those in the PCO control group
(p<0.05) and were found to be the same as those
in the healthy control group. The authors conclude
that their results indicate that EA modulates the
neuroendocrinological state of the ovaries, most
likely by modulating the sympathetic nerve
activity in the ovaries, which may be a factor in
the maintenance of steroid-induced PCO.

Comment
This appears to be a high quality experimental
study, as would be expected of this group. This
reviewer is not qualified to give an indepth
commentary of the work, but if readers are
interested in more details, the full text is available
online at Biomed Central. The specific web
address for this paper is: http://www.rbej.com/
content/1/1/33.
Sacral acupuncture effects on bladder activity and the EEG (n=27)


**Summary**

Using urethane-anaesthetized rats, the effects of acupuncture stimulation to the sacral segment on the urinary bladder activity and cortical electroencephalogram (EEG) were examined. The acupuncture suppressed urinary bladder activity in 36 of 68 trials. On many occasions (22/36 trials), suppression was accompanied by an increase in EEG amplitude. In such cases, the EEG power increased in all frequency bands after stimulation. The same EEG changes could be induced when the bladder was empty with no contraction. The results suggest that acupuncture stimulation affects both the bladder activity and sleep-arousal system.

**Comment**

In this study the EEG changes associated with acupuncture were not those expected with painful stimuli (tail or foot pinch). The latter tend to cause a shift to smaller and faster waves. A change in EEG activity was only observed when acupuncture stimulation suppressed bladder activity. When the stimulation site was shifted to the lumbar area the effect was hardly observed (six trials in three rats). This reviewer is not familiar enough with EEGs to comment on the authors’ conclusions, however, this is an interesting study, and may be an area worthy of further investigation.