Action Potential Simulation Therapy (APS Therapy) for pain in people with MS; Report on a Two Year Pilot Study.

Emma Matthews RGN BSc., Miranda Olding RGN MSCN, Denise Kehoe, Heather Raisin, Emma Burgess, Rose Olding.

Abstract

People with MS commonly suffer from both nociceptive and neuropathic pain, and the latter is often resistant to treatment, or hard to resolve due to the unwanted side-effects of most of the appropriate drugs.

We carried out a two year pilot using the micro-current electrotherapy device, APS Therapy, to treat pain in people with MS, at a multi-disciplinary MS Therapy Centre, in Bedford, UK.

60 people completed an 8 week course of APS Therapy three times a week to treat 94 different pains.

Within 8 week periods, 47 people (78%) had a significant reduction in pain. Of the 94 pains, 75 (80%) had a reduction of at least one point on the Visual analogue Scale (VAS) for usual level of pain. The average reduction in points on the VAS was 3.04 for 'usual pain', and 4.87 for 'worst pain'. 31 'usual pain' scores (33%) were reduced to pain free. 33 people (57%) reduced or discontinued medications as a direct result of the effects of APS Therapy, and 33 (not necessarily the same) people went onto long term maintenance therapy.

Many participants reported other unexpected benefits of treatment, which impacted positively on their quality of life.

Robust research on APS Therapy is scant, but based on the outstanding results of this pilot is a very promising area for further research and clinical treatment.

Introduction

The problem of pain in the UK

Pain is defined as ‘An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage’ (1)

Chronic pain is defined as continuous, long-term pain of more than 12 weeks or after the time that healing would have been thought to have occurred in pain after trauma or surgery.(2)

Neuropathic pain is defined as pain resulting from a lesion or disease affecting the somatosensory system.(3)

Almost eight million people in the UK have chronic pain, or an estimated one in 5 Europeans. (4) As well as the human suffering, it also represents a significant burden to wider society and economies. Chronic pain accounts for 4.6 million GP appointments every year at a cost of £69 million. Expenditure is on referrals, appointments, prescribing, consequences of ineffective home prescribing and adverse events. (5)

Current medical treatment centres around medication, but drug treatments often cause unwanted side effects or other medical problems, and the costs of drugs for managing pain alone in England in 2009 amounted to £449 million. (6)

Access to pain management services in the UK is inconsistent, and available health services for pain differ markedly in the type of care they offer.(7)

Although in some chronic pain clinics, TENs, acupuncture, physical, psychological techniques, invasive treatments, and complementary therapies are offered, availability varies widely, rates of successful pain resolution are low, and 38% of people with chronic pain report inadequate pain management.(8, 9, 10)

The problem of pain in MS

Estimates vary as to the proportion of people with MS who suffer from pain, with some reports suggesting that up to 80% of people with MS may suffer from pain at some stage. (11,12,13)

People with MS commonly suffer from both types of pain; both nociceptive ('normal' type, after injury or with inflammation) and neuropathic. Neuropathic pain is often characterized as burning, severe shooting pains, and/or painful numbness or tingling. It is commonly a long term or chronic pain, and effective treatment is difficult as the classes of drugs to which it responds best are associated with various adverse effects. (sedation and weight gain most commonly) (14,15)

The aim of treatment is to minimise the level of pain and to develop coping strategies so that the individual can carry out normal day-to-day living. Treatment options include drugs and non-drug treatments such as physiotherapy, electrotherapy or a combination.

Electrical therapies

There are many modalities of electrical therapies currently in use within physical therapy for pain relief and injury repair, which have been categorised into 3 broad areas(16)

Electrical stimulation agents, including Transcutaneous Electrical Nerve stimulation (TENS), Action Potential Simulation Therapy (APS Therapy), Interferential Therapy (IFT), Functional Electrical Stimulation (FES), and Microcurrent therapy (MCT),

Thermal modalities, including Infra red Irradiation (IFR), Therapeutic Ultrasound and Laser Therapy, and

Non Thermal Modalities including Pulsed Ultrasound, Pulsed Electromagnetic Fields (PEMFs) and Microcurrent Therapy (MCT)

The most commonly used form of electrotherapy in healthcare is TENS. This uses an alternating current to affect pain gate mechanisms. A Cochrane review concludes that 'despite the widespread use of TENS machines, the analgesic effectiveness of TENS still remains uncertain'(17)

We heard about some exceptional case studies carried out in Hull using the electro-therapy Action Potential Stimulation (APS) Therapy showing effectiveness in reducing both pain and fatigue; drastically reducing the medication used, and increasing mobility, independence and quality of life in people with MS, (18) and decided to investigate.

APS Therapy

Action Potential Simulation (APS Therapy) is a type of micro-current therapy.
These therapies involve application of electric currents of similar form and magnitude to those produced naturally by the body and there is evidence that this can promote healing in a variety of damaged tissues. (19)

The APS Therapy device uses an electrical wave form that mimics, or 'simulates' the normal physiological action potential of nerve conduction. The device is said to produce action potentials that are four times stronger than those naturally occurring in the neuron. When swelling, inflammation, poor circulation and pain occur due to mechanical, chemical or electrical disturbances, by stimulating the body's natural regenerative processes (as in depolarisation), it is postulated that these conditions are encouraged to resolve. (19)

Literature review for micro-current and APS Therapy

A literature review on over 70 papers on micro-current therapy in 2009 concluded that there was evidence for its use with non-uniting fractures, spinal fusions and skin ulcers, particularly where other forms of treatment had not been successful; that in vitro studies also suggest that there is unexplored potential for its use in musculoskeletal disorders. However, higher quality and more comprehensive research is needed. (20)

An assessment of APS Therapy on 285 Patients with chronic pain in 2002 reported a mean average VAS of 6.8 before treatment and 3.3 after treatment in the over 50s, and 6.3 and 2.2 re in the under 50s. Out of the 285 patients, 44 (15%) ended with a '0' VAS and 199 (69%) with a score of 5 or less. (21)

A trial of APS Therapy in patients awaiting or having neurosurgery for intractable spinal pain concluded that the number of patients treated was too low to reach a statistical conclusion, but recommended that patients waiting for destructive surgery should first be put on a thorough trial of APS Therapy as there appeared to be a promising trend.(22)

In a 1999 randomized, patient blinded, placebo-controlled study on 76 patients with chronic osteoporotic back pain, reported pretreatment baseline VAS value average of of 57.79, and post-treatment value after the sixth treatment of 9.7 (p= 0,0001); 6 patients maintained benefits 6 months post treatment.(23)

A 1999 study comparing APS therapy with TENS in 99 patients with osteoarthritis of the knee did not find a significant difference in VAS between the two treatment groups given just 6 treatments over a 2 week period. The APS group showed a significant improvement in measures of knee flexion and swelling that was still evident when reviewed 1 month after the last treatment. (24)

A 2015 randomised controlled trial comparing APS Therapy with Interferential (another micro-current therapy) found significant reductions in both VAS and WOMAC (arthritic symptoms)

in both groups using only 10 treatments; Timed Up and Go was also reduced in the APS Therapy group.(25)

Methods

Sample

People with MS who presented with pain in the MS Nurse's clinic were screened for suitability and contra-indications, and offered the chance to trial the therapy. Pain due to spasticity/muscle spasm, or pain whose origin was uncertain, where more investigations were needed, were excluded.

Contra-indications include having a Pacemaker, epilepsy, pregnancy, or active cancer, or in the past 3 months, stroke, heart attack, deep vein thrombosis or pulmonary embolus. One participant had a baclofen pump; after discussion with the manufacturers of both devices, this was allowed in this case. We also checked that participants felt able to drink the recommended litre and a half of water daily during therapy.

All the participants gave their informed consent to take part in the study; it was made clear that participation in the study was optional. 57 had MS, 3 did not. (2 were members of staff, and one a volunteer.)

An 8 week course of APS Therapy, with 3 x sessions a week ideally, but often 2 or even less in practice, was offered. This comprised of 4, back to back, 8 minute electrode placements, in a designated clinic room at the multi-disciplinary MS Therapy Centre in Bedford, UK. We had first one, and then 2 APS Therapy clinic machines. People who could apply the electrodes themselves had one teaching session and then self-treated, with minimal supervision from staff; about 30% of people needed assistance, which was given primarily by trained carers or volunteers.

During the 8 week course, 10 people dropped out. One had headache, and one, vomiting after 1st treatment, and decided not to proceed. Detoxification reactions (usually headache) are possible, although not common if drinking the recommended amount of water, and are self-limiting. One experienced flickering in her vision and decided not to proceed. Although there is no documented precendent for this, and the cause was uncertain, electrotherapies can trigger migraine in susceptible people. Three people became unwell, two with existing other conditions and one with an MS relapse since starting treatment and either unable or decided not to proceed. Four were discouraged after experiencing no benefit between 2 and 6 weeks.

60 people in this study went on to use APS Therapy to treat 94 different pains.

46 of the pains were neuropathic, including 4 sciatic type pains, and 48 were nociceptive, including back pain, joint pain and injury, fibromyalgia pain and headaches.

48 were women and 12 were men. The average age was 52 for women and 51 for men. 17 people had relapsing remitting MS, 40 had primary or secondary progressive, and 3 did not have MS.

In the first year we measured pain using the visual analogue pain scale (VAS), asking each participant to score for both for the usual, and the worst level of pain, and how much of the time the pain was average, how much of the time worse. Medication use was recorded. In the second year we also used the Brief Pain Inventory and Pittsburgh Sleep Scale; for the sake of coherence this study only examines data kept for the whole duration.

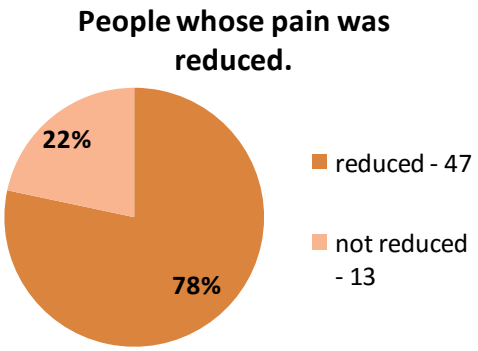
Results:

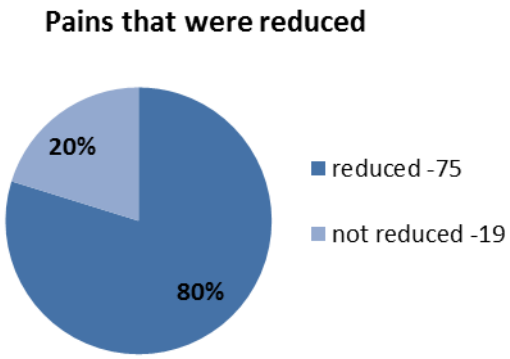
In consecutive 8 week periods;

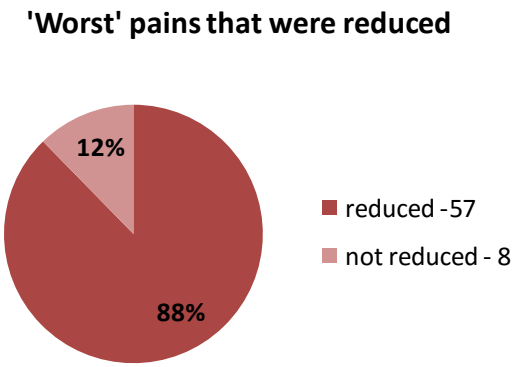
Of the 60 people, 47 (33%) had reduction in pain.

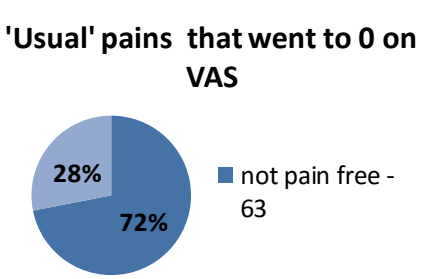
Of the 94 ‘usual pains’, 75 (80%) had reduction.

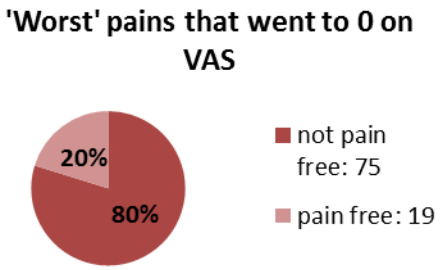
Of the 65 recorded ‘worst pains’, 57 (88%) were reduced.











31 ‘usual’ pains (33%) went down to 0/10, or pain free.

19 ‘worst’ pains (20%) went down to pain free.

‘Reduction’ was quantified as 1 or more whole points on the VAS for pain.

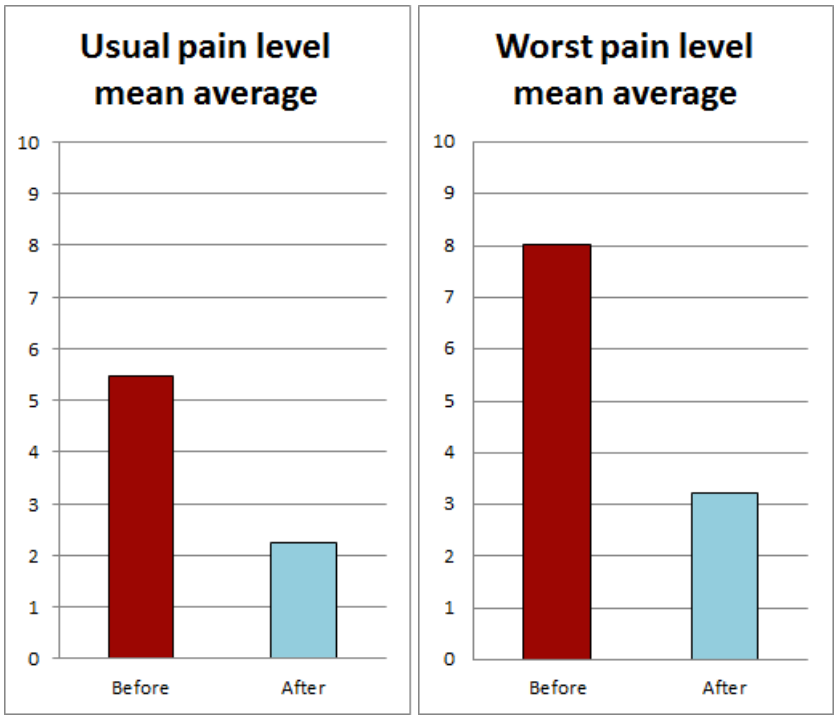
Neuropathic pains appeared to respond almost as well as nociceptive pains to the treatment

33 people reduced or discontinued medication as a direct result of the results of the APS Therapy, on reflection, with more supervision, we feel that this could have been more.

The mean pre-treatment score on the VAS for ‘Usual level of pain’ overall was 5.46. Mean reduction in pain was 3.22 points, to a mean post-treatment VAS of 2.24

Mean pre-treatment score for ‘worst pain’ was 8.01. Mean reduction in pain was 4.78 Average to a post-treatment VAS of 3.23.

Mean averages tend to flatten the results, which were in fact quite polarized, with some cases having no response to treatment, and many, dramatic responses.



To examine the response, we broke the results down into pains with typical neuropathic features, (described as 'pins and needles, burning, tingling, shooting, stabbing, sunburn-like', and with no known tissue damage or musculoskeletal cause) and those more likely to be nociceptive (aching, throbbing, or due to injury, low back pain etc) and also into the main painful areas, for both 'usual' level and 'worst' level of pain.

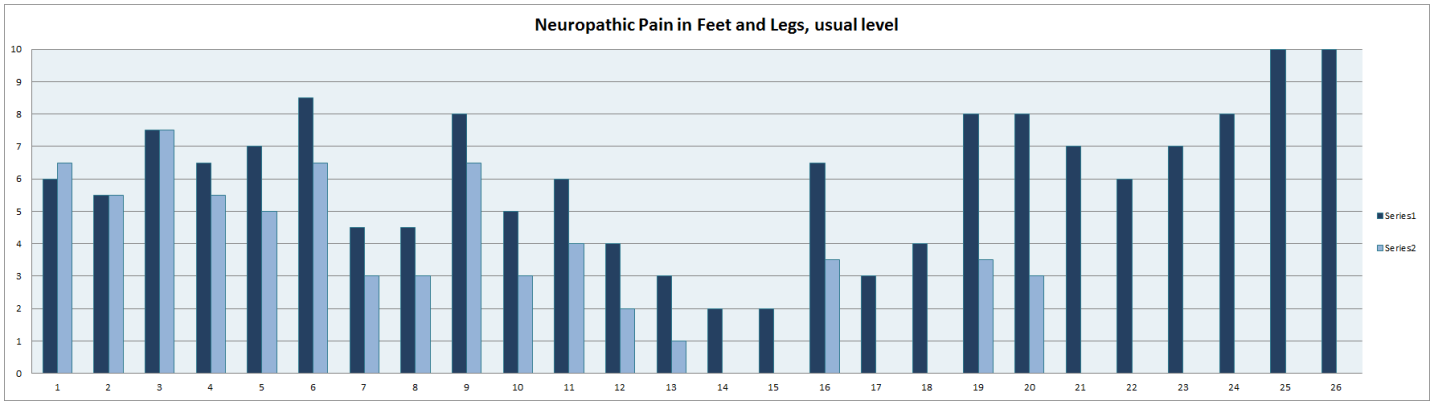
Neuropathic pain in feet and legs

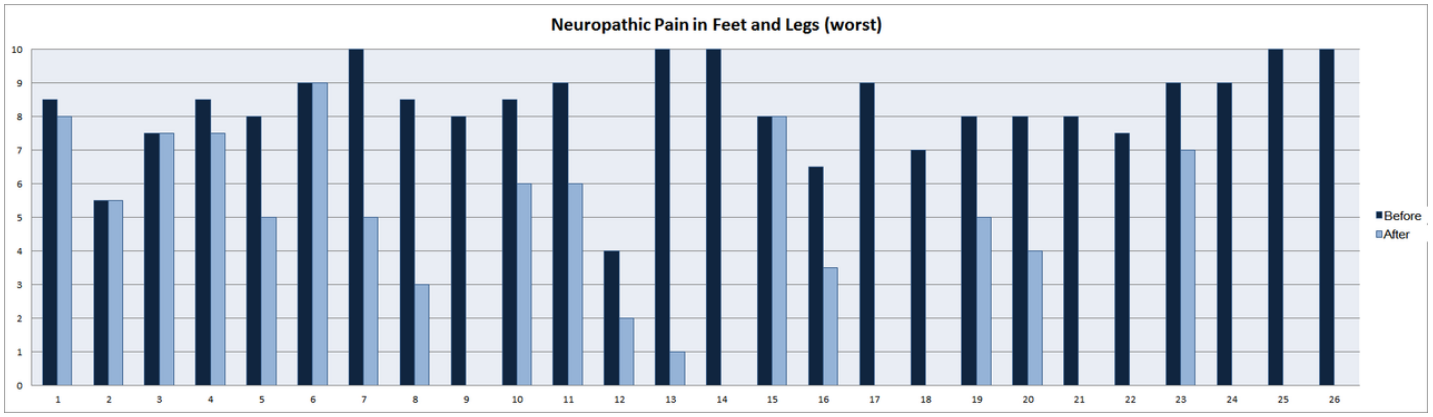
There were 26 cases of neuropathic type pain in the feet and legs.

Participants' mean pain score before treatment program was 6.06 (SD =2.22), and their mean pain score after the program was 2.65 (SD = 2.58). A repeated measures t-test showed this difference was statistically significant: t(25) = 5.905, p=0.001, two-tailed.

‘Worst pain’ for neuropathic feet and legs was a pre-treatment mean of 8.3, and reduced by 4.7 on the VAS on average, to a post treatment mean of 3.6.

3 individual’s pain did not respond at all, 23 people experienced a drop of 1 or more points, and of these, 10 people went to pain free.



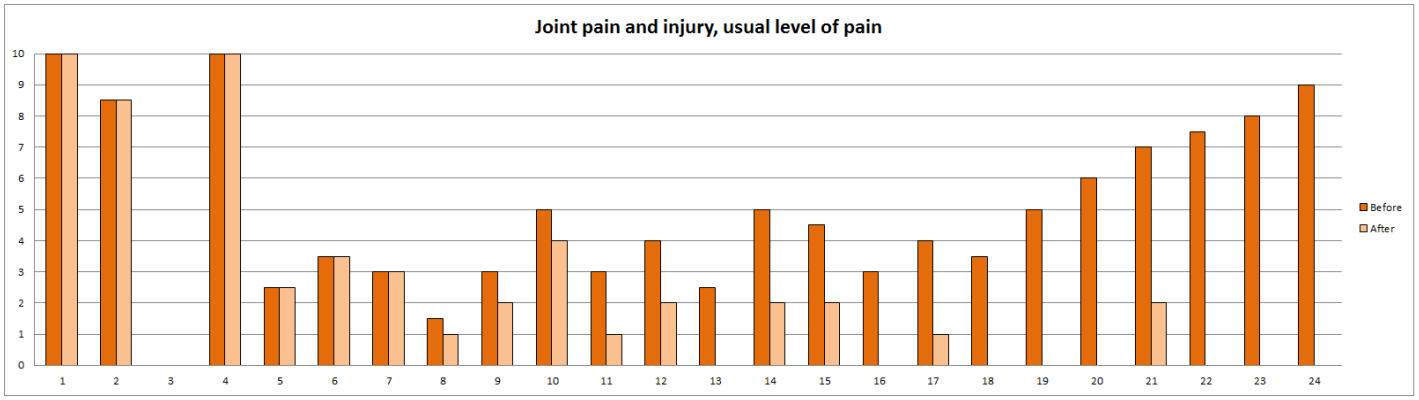


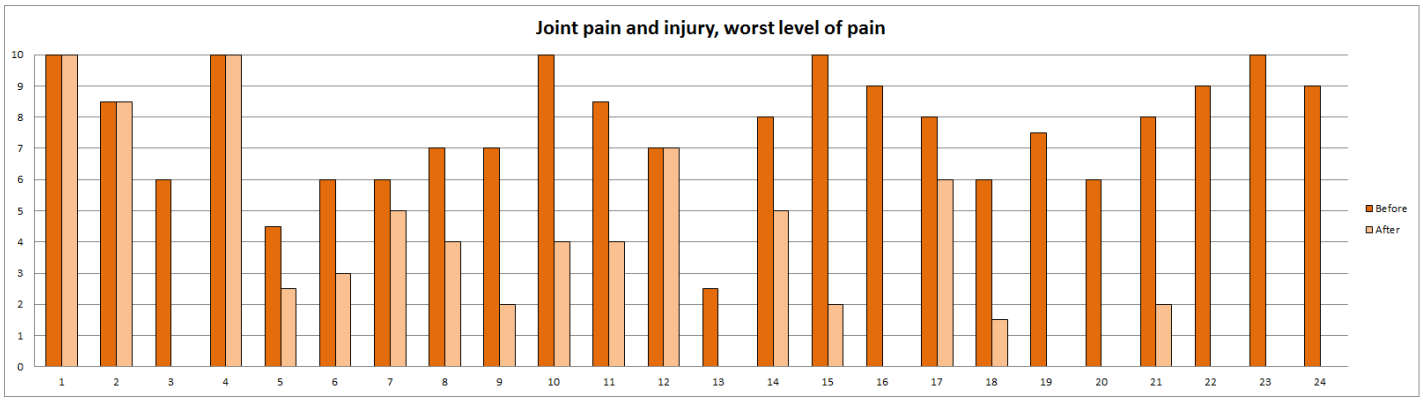
Joint pain or injury

There were 24 cases of joint pain or injury. Participants' mean pain score before the treatment programme was 4.95 (SD =2.73), and their mean pain score after the programme was 2.27 (SD = 3.06). A repeated measures t-test showed this difference was statistically significant: t(23) = 4.761, p=0.001, two-tailed

'Worst pain' for the 16 joint type pains had a pre-treatment mean of 7.6 points on the VAS, and fell by an average 4.5 points on the VAS to a mean of 3.2.

Actual results were quite polarised, with 6 people having no response, and 8 going to pain free.

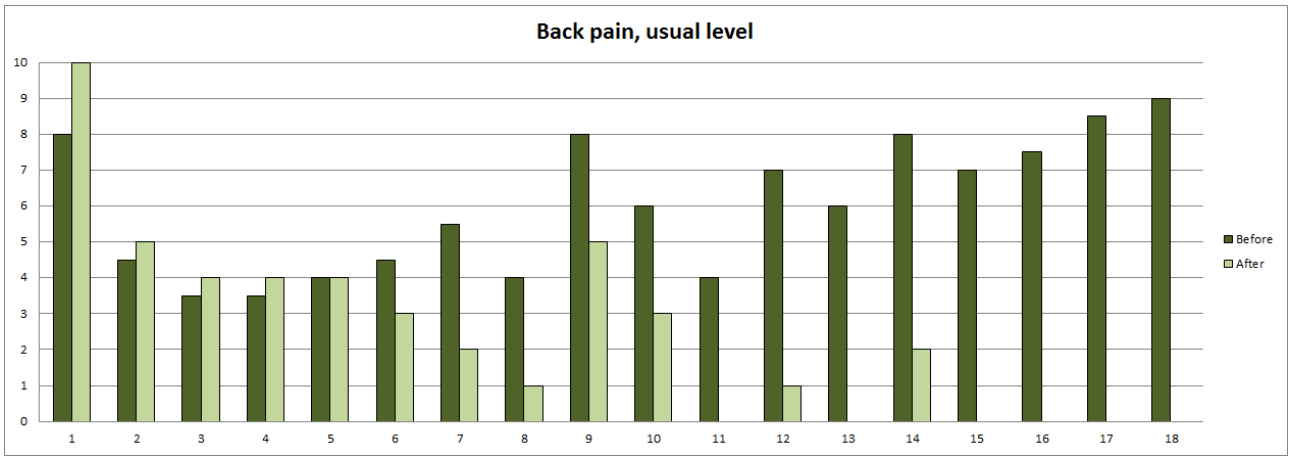




Back pain

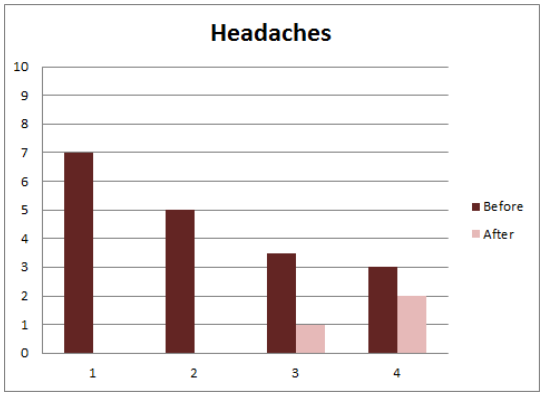
There were 18 cases of back pain. Participants' mean pain score before going on the programme was 6.03 (SD =1.89), and their mean pain score after the programme was 2.44 (SD = 2.64). A repeated measures t-test showed this difference was statistically significant: t(17) = 4.459, p=0.001, two-tailedPeople struggled to score back pain on 'usual' or 'worst', scoring it just for 'usual' for when it occurred.

4 people's pain got worse, one was unchanged, 13 benefitted, and of these, 6 went to pain free.



Headaches

4 people were treated for headaches. The mean pre-treatment VAS was 4.6, dropping by an average of 3.9 points to a post-treatment average of 0.8. Severity scores did not capture the reduction in frequency, which was very dramatic.

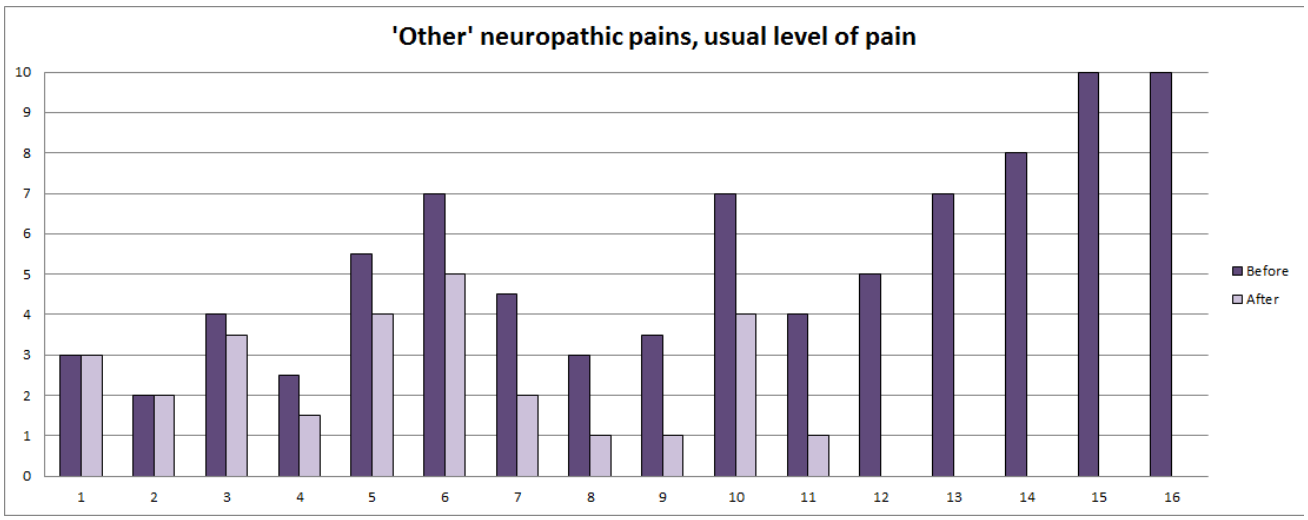


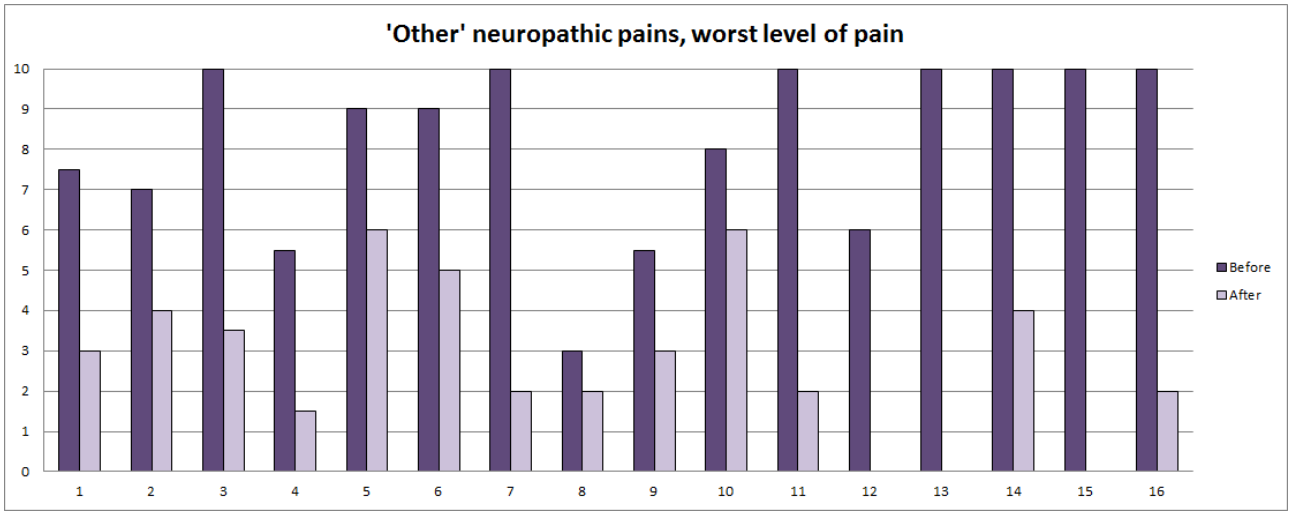
Other neuropathic or nerve pain

There were 16 cases of neuropathic pain of the trunk, arms, hands and face.

Participants' mean pain score before the programme was 5.38 (SD =2.54), and their mean pain score after the programme was 1.75 (SD = 1.68). A repeated measures t-test showed this difference was statistically significant: $t(15) = 4.310$, $p=0.001$, two-tailed.

Mean average for 'worst pain' was 8.2, reducing by 5.4 points to a mean of 2.8 post-treatment

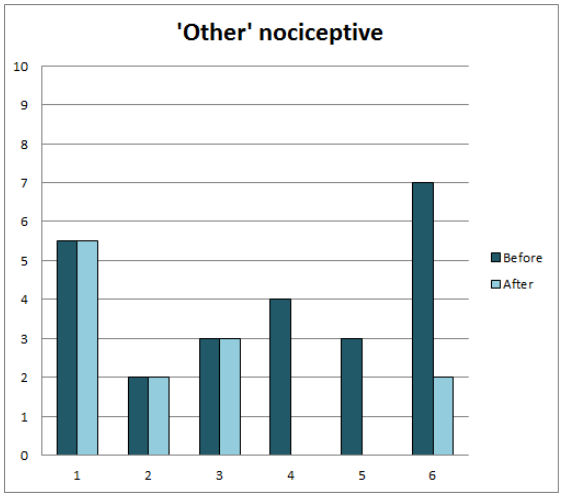

'Other' neuropathic pains, usual level of pain
10
9
8
7
6
5
4
3
2
1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
Before
After


'Other' neuropathic pains, worst level of pain
10
9
8
7
6
5
4
3
2
1
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
Before
After

‘Other’ nociceptive pains

There were 6 cases of ‘other’ nociceptive pain.

Participants’ mean pain score before the programme was 4.09 (SD =1.86), and their mean pain score after the programme was 2.08 (SD = 2.06). A repeated measures t-test showed this difference was not statistically significant: t(5) = 2.148, p=0.085, two-tailed, probably due to the small sample size. 2 cases of muscle fatigue type pain and one pain from metalwork post pin and plate, did not respond to treatment. 1 psoriasis pain and 1 varicose vein pain, and 1 case of aching arms, had a significant reduction in pain, 2 went to 0 points on the VAS.



‘Other benefits’

In our study’s population of people with MS, there were many self-reported ‘other benefits’ perceived to be a result of the therapy, which we had not kept outcome measures for. These included:

- Improvement in mobility x 11 (some in hand dexterity, some walking)
- Increase in energy, reduction in fatigue x 4
- Reduction in swollen/discoloured legs & ankles x 3
- Alleviation of life-long insomnia x 2
- Cessation of recurrent UTIs during treatment x 4
- Disappearance of swollen glands on neck x 1
- Cessation of ‘fluid on skull’ sensation x 1
- Reduction in dizziness X 2
- Reduced ‘cognitive fog’ x 2
- Reduction in stiffness/spasm x 7
- Improvement in bowel function x 1
- Improvement in sleep quality and quantity

Improvements in sleep quality and quantity occurred on such a regular basis that after one year we began to record using the Pittsburgh sleep scale, along with outcome measures on the effect of pain on everyday life and mood, which will be analysed in another paper.

Discussion

For this exploratory pilot study, there was no control group, and many possible variables. Data was collected in the course of a working clinic, by the clinicians and staff on the treatment team, which can introduce bias to the results.

The introduction of other new therapies or treatments (eg physiotherapy, changes to medication regimes) was avoided where possible during the trial period, (except for the reduction or withdrawal of analgesics), but not banned.

Our sample, as typical in MS, often had to cancel appointments due to health problems, transport or general difficulties, but still achieved significant results.

It was interesting to note that effectiveness was similar between the neuropathic and nociceptive type pains when using APS Therapy in MS.

The mode of action of APS Therapy is not fully understood. In nociceptive pain, injury or disease can cause oedema, inflammation, neuronal dysfunction, circulatory disturbance and lack of oxygen supply to the tissues or organ systems. Inflammation in tissue also promotes the build-up of chemicals, known as the “inflammatory soup” which may interfere with neural transmission.

If there is poor transmission or even cessation of activity along the neuron, as a result of injury, inflammation, or disease process, the system cannot conduct its action potentials, and the homeostatic and regenerative mechanisms are disturbed. In MS, the normal conduction of action potentials is detrimentally affected by the loss of myelin, and this may explain way some, although not all, people with MS experience additional benefits with APS Therapy.

It has been postulated by Papendorp (25) that introducing external action potentials through the use of APS Therapy may result in the metabolic catabolism and subsequent excretion from the body of inflammatory substances. As inflammatory metabolites may be a major cause of pain,

removing the cause allows for pain reduction. Circulation is also improved and thus antibodies, enzymes, neurotransmitters and hormones are conveyed at an increased rate to the treated area, stimulating the body's own healing mechanisms.

In our study, people with nociceptive pain or injury were far more likely to obtain a lasting or curative effect on their pain.

In cases of neuropathic pain, the model of enhanced removal of inflammatory compounds is not so viable. It is well known that the release of neurotransmitters, including the body's own pain regulating agents, is stimulated by the electrical discharge of action potentials along nerve cells, and voltage gated ion channels remain a key research priority for the pharmaceutical industry. Recent research by Cho et al, (27) suggests that stimulation of action potentials creates an increase in spontaneous neurotransmitter release by pre-synaptic neurons that stays elevated well after the stimulation has ended. This mechanism would correspond with the effects we have seen in neuropathic pain, which tend to respond well, with a waning effect necessitating treatment every 7^{th} day to retain pain relief.

One of our concerns when starting this project was the provision of long term maintenance therapy, should this be required. In face we found that people in need of maintenance were able to reduce the frequency of their treatment to once a week, or in one case once fortnightly, and still retain the effect, and we have been able to continue to provide a maintenance service. 33 participants, predominately with neuropathic pain, have continued with long term maintenance of APS Therapy.

Conclusion

APS Therapy seemed to be a safe and effective therapy to try in cases of both neuropathic and nociceptive pain. Statistical testing proposed effectiveness in all but the smallest sample ('other nociceptive pain') Participants in this study, most of whom had MS, had a significant reduction in pain using APS Therapy in 78% of cases. The therapy was safe, and in the main, people were extremely happy with this mode of treatment, preferring it to drug therapy, and in some cases reducing and discontinuing analgesic drugs as a result.

We hope that by presenting our pilot study of an APS Therapy service in the context of available research on the subject, we can stimulate further clinical use and research.

References

1) H. Merskey and N. Bogduk, Eds,.*Classification of Chronic Pain, Second Edition,* IASP Task Force on Taxonomy, IASP Press, Seattle, 1994.

2) British Pain society 2014 For media, FAQs http://www.britishpainsociety.org/media_faq.htm (accessed 3/2/2014)

3)) International Association for the Study of Pain, 2011 www.iasp-pain.org/AM/Template.cfm?Section=Pain_Definitions (Accessed 3/2/2014)

IASP 2011 http://www.iasp-pain.org/GlobalYear/NeuropathicPain

4) Breivik H, Collett B, et al. Survey of chronic pain in Europe: prevalence, impact on daily life, and treatment. *Eur J Pain* 2006 **10**(4):pp 287-333

5) Belsey J. Primary care workload in the management of chronic pain: A retrospective cohort study using a GP database to identify resource implications for UK primary care. *Journal of Medical Economics* 2002 **. 5,** (1-4) pp 39-50

6) NHS Information Centre. Prescription Cost Analysis for England 2009. Available at: http://www.ic.nhs.uk

7) Harris M, Spence A, et al. (2000) Clinical Standards Advisory Group (CSAG): Services for patients with pain

8) Breaking through the Barrier', Chief Medical Officer 2008 Annual Report, March 2000

9) InSites Consulting. Pain Proposal Patient and PCP Surveys. July – September 2010

10) Collett, B. Betteridge, N., Semmons, I , Trueman, P. Pain Proposal, Improving the current and future management of chronic pain 2010 www.arthritiscare.org.uk/.../main.../**PainProposal**UKSnapshotFinal.pdf

11) Ehde DM, et al.The scope and nature of pain in persons with multiple sclerosis. *Multiple Sclerosis* 2006;**12**(5):pp 629-638.

12) Hirsh AT, et al. Prevalence and impact of pain in multiple sclerosis: physical and psychologic contributors. *Archives of Physical Medicine and Rehabilitation* 2009;**90(**4):pp 646-651.

13) Archibald CJ, et al.Pain prevalence, severity and impact in a clinic sample of multiple sclerosis patients. *Pain* 1994;**58**(1):89-93.

14) **IASP** 2011 http://www.iasp-pain.org/GlobalYear/NeuropathicPain

15) Neuropathic pain – pharmacological management: the pharmacological management of neuropathic pain in adults in non-specialist settings. National Institute for Clinical Excellence November 2013

16) Watson, T. Narrative Review : Key concepts with electrophysical agents Physical Therapy Reviews 2010. **15**(4): 351-359.

17) Cochrane Database Syst Rev. 2008 Jul 16;(3)

18) Van der Plaat, L. unpublished case studies using APS Therapy on people with MS in a day hospice setting. 2013

19) Berger P. Electrical pain modulation for the chronic pain patient. *South African Journal of Anaesthesiologyand Analgesia*. 1999;**5**:14-19.

20) Van Papendorp DH, Kruger MC, Maritz C, Dippenaar NG.
Medical Hypotheses- 2002 Elsevier

21) Papendorp DH van. (2002). Assessment of Pain Relief on 285 patients with chronic pain. *Biomedical Research* 2002; **26:** 249-253.

22) Du Preez, J. Neurosurgical Pain Conditions University of Pretoria

23) Odendaal & Joubert APS Therapy- a new way of treating chronic backache, a pilot study *South African Journal of Anaesthesiology and Analgesia.*1999; **5** 1

24) Berger, P. Matzner, L Study on 99 patients with osteoarthritis (OA) of the knee to investigate the effectiveness of low frequency electrical currents on mobility and pain: Action

Potential Simulation therapy (APS) current compared with transcutaneous electrical nerve stimulation (TENS) and placebo.*South Africa Journal of Anaesthesiology and Analgesia* 1999 **5**: 2

25) Eftekharasadat, B, Babaei-Ghazani, A., Habibzadeh,A.,Kolahi,B.(2015) Efficacy of action potential simulation and interferential therapy in the rehabilitation of patients with knee osteoarthritis.*Therapeutic Advances in MusculoSkeletal disease 7(3): 67–75.*

26)) Papendorp DH van. (2002). Assessment of Pain Relief on 285 patients with chronic pain. *Biomedical Research* 2002; **26:** 249-253.

27) Cho, R.W., Buhl, L.K., Volfson,D. Tran, A.. Li, F. Akbergenova,Y. Littleton, J.T. *Neuron*. 2015 doi:10.1016/j.neuron.2015.10.011