Zenstant Painblock Neurosensory Algorithm

Method, development, and validation

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Pain is one of our most important survival signals. It tells us to protect an injured area so that it can heal. Unfortunately pain goes far beyond a simple evolutionary safety net and can be one of the most profoundly damaging challenges to a fulfilling life. From relatively simple yet common aspects such as fear of pain which prevent some people from seeking necessary medical or dental care, to the life-changing damage of chronic pain from fibromyalgia to cancer, pain ravages the intellect, keeping your attention locked onto trying to minimize the sensation, inducing long term stress responses which damage the immune system and changes behavior, not just from trying to limit the pain, but in narrowing one's ability to think beyond the pain, leaving a sufferer in an emotionally fragile and cognitively limited state (Rawl 2013).

The costs of pain goes far beyond personal ones. A study by health economists from Johns Hopkins estimated that the annual cost of chronic pain is $635 billion per year (Gaskin and Richard, 2012). And to compound the problem, pharmaceutical solutions tend to be self-perpetuating, leading not only to an estimated $16 billion spent per year in 2011 for legitimate pain-relief needs, but also keeping people who need pain relief from being able to obtain it because of an ever increasing level of regulatory and law enforcement problems trying to cope with those who obtain and redistribute pain killing drugs without proper medical oversight. Pain management is a problem that is not going to go away in our aging population (Pizzo et al., 2011).

New solutions are needed beyond stronger drugs or better regulatory oversight.

What is pain?

At a biological level, pain (nociceptive) receptors are free nerve endings, scattered throughout your body that send signals indicating tissue damage through two types of nerves, A- delta which carries faster-travelling “sharp” pain signals, and C-fibers which send signals much more slowly, usually triggering a more diffuse and “achy” type pain. For example, if you run at night, you will eventually hit the wrong patch of ground and sprain your ankle. The initial sensation is not one of pain, but that “uh oh” sensation that “this is *going* to hurt,” carried by stretch receptors at the ends of your muscles which respond very quickly. Almost immediately after this comes the A-delta signal indicating the actual signal for damage followed by the slow C-fiber signal. And while a sprain is a relatively straightforward injury, its interactions with inflammatory responses and potential for retriggering the injury can mean weeks of discomfort and limited mobility.

Pain is not a simple linear sensation. There are multiple categories of pain, each based on a specific type of condition or injury. Based on the specific nature of the condition, pain management requires different classes of analgesics with varying targets, duration and level of efficacy, such as morphine or codeine which block pain, or anesthetics which specifically target the physical sensation such as acetaminophen or NSAIDs. In addition, pain is mapped along a distorted sensory homunculus that defines how sensitive you are to touch across different parts of your body. This is why biting your tongue or a paper cut on a finger can bother you so much more than even a relatively serious injury to your foot. But pain receptors also innervate your internal organs through a poorly understood subset of your nervous system called the enteric nervous system and signals “visceral” pain. The enteric nervous system is only vaguely mapped in your brain, leading millions of kids to talk of a “tummy ache” which could be anything from appendicitis to just wanting to stay home from school, and drive doctors crazy with the inability of their patients to be more specific when asked “where does it hurt?”

What makes pain an even more problematic sense is how it interacts with attention and emotional states. One way to think of pain is as a mechanism for redirecting your attention internally, taking it away from looking around out there and focusing on a potential problem inside. The degree to which pain receptors can force your attentional pathways to disengage from the external world is a serious problem. Think about how easy it was to concentrate on anything the last time you had a toothache. At least that was a clear location for the problem, dealt with by a trip to the dentist. Now imagine pain in a place governed by your enteric nervous system, ill defined, hard to localize and, unfortunately really hard to get to. It might be triggered by a small, relatively harmless gall bladder stone which can mimic all the symptoms of a heart attack, to cancer, which can create creeping pain throughout your whole body, with nothing you can do about it without major medical intervention. Pain *grabs* your attention, drawing it to a problem you can't do anything about, which psychologically cuts down your ability to attend to anything outside the perceived damage to your own body. And as pain persists, it begins to induce long term stress responses at a physiological level such as raising blood pressure and increasing likelihood of heart attacks and strokes as well inducing severe emotional responses leading to depression and feelings of helplessness. This is the underlying problem of chronic pain – not so much the injury but how it ravages your cognitive resources.

A further complication is due to the body's way of dealing with changes in neurochemistry leading to drug tolerance. While anesthetics/analgesics may offer relief, over time, the body's neurochemistry tries to adapt to the presence of administered pain relievers by multiple mechanisms such as receptor down regulation or up regulation of receptor agonists. These effects lead to a need for increasing dosages of pharmaceutical pain relievers to achieve the same level of effectiveness. At a behavioral level, this causes pain sufferers to chase ever increasing amounts and types of pain relievers. This is not an indication of a drug-abusive or addictive personality, but rather an unfortunate and near-universal side effect of normal physiological feedback systems. Such drug seeking behaviors cause tremendous problems for both medical professionals and patients as the act of attempting to seek relief can run afoul of regulatory and law enforcement policies (Hansen, 2005).

Non-pharmaceutical pain management

Because of the widespread problem of managing pain, numerous non-pharmaceutical techniques are often applied to try and manage intractable or chronic pain with varying scientific basis and success. The fact that pain is a system that has evolved to grab and hold your attention provides an opportunity to weaken its hold by learning to deliberately change your attentional state (Chan et al, 2012). This has allowed the development of therapies which change people's ability to redirect their attention through meditation, mindfulness practices and even talk therapy, although as these techniques are almost never used in isolation it is difficult to gauge their individual effectiveness. In addition, all of these techniques require substantial dedication and effort on both the part of the person in pain as well as their support group and for many people in pain, relief is needed faster than many of these techniques can provide. What is needed is a rapidly effective technique capable of affecting the patient's attentional and emotional state, thus limiting the need for broader ranging pharmaceutical treatment.

Hearing, as the fastest sense, is one of the best mechanisms for changing attention and emotion, which may be why music or other sonic therapies are often effective in dealing with stress and chronic pain (Bradshaw et al, 2011). It's also why meditation and mindfulness, usually with a strong sonic component such as chanting or verbal guidance can shift attention onto a single feature or idea to the exclusion of other input and yielding a significant impact on pain, chronic and otherwise. Changing the way your brain pays attention and responds emotionally can short circuit the devastating cognitive and emotional loops that pain can cause, without having to delve into a pharmaceutical blockade of the pain signals themselves. Furthermore because of the deep seated neural connections between auditory input and subconscious networks underlying basic sensory, emotional, attentional and cognitive processing, properly structured sound can have direct measurable effects on nociceptive systems. This explains why one of the most popular alternative treatments is music therapy or musically-guided meditation. Many musical forms – their key, their beat – activate and reinforce proper brain activity, making music effective for treating psychological and physiological conditions where something has gotten out of synch. From depression to Parkinsons, from anxiety disorders to insomnia, from ADHD to autism, properly structured music can effectively treat many conditions without pharmaceuticals or drastic changes in lifestyle.

But traditional music therapy's "top-down" structure is one of its most serious limitations. A musical piece is selected or composed based on what has worked before or what matches a series of parameters that seems to help for conditions. This can be effective, but it often ignores what makes music and sound a fast and effective mode. Hearing is a "bottom-up" sense, operating at least ten times faster than vision and our other senses. Sound gets into the subconscious and preconscious realms where emotion, physiology, memory and pre-decision making functions take place. This is why the use of music-independent, properly structured sound that targets specific behaviors will prove more effective than musical selections which may be limited by the cognitive biases of the provider, requiring relatively long time spans to achieve effectiveness for the patient. For example, an early foray into this area showed that exposing surgical patients to sounds that induce synchronized responding between cortical lobes of the brain reduced the need for surgical and post-operative anaesthesia (Dabu-Bondac et al, 2010). This demonstrates that the use of properly structured sound can have significant positive effects on pain relief at a physiological level.

Painblock and Neurosensory Algorithms:

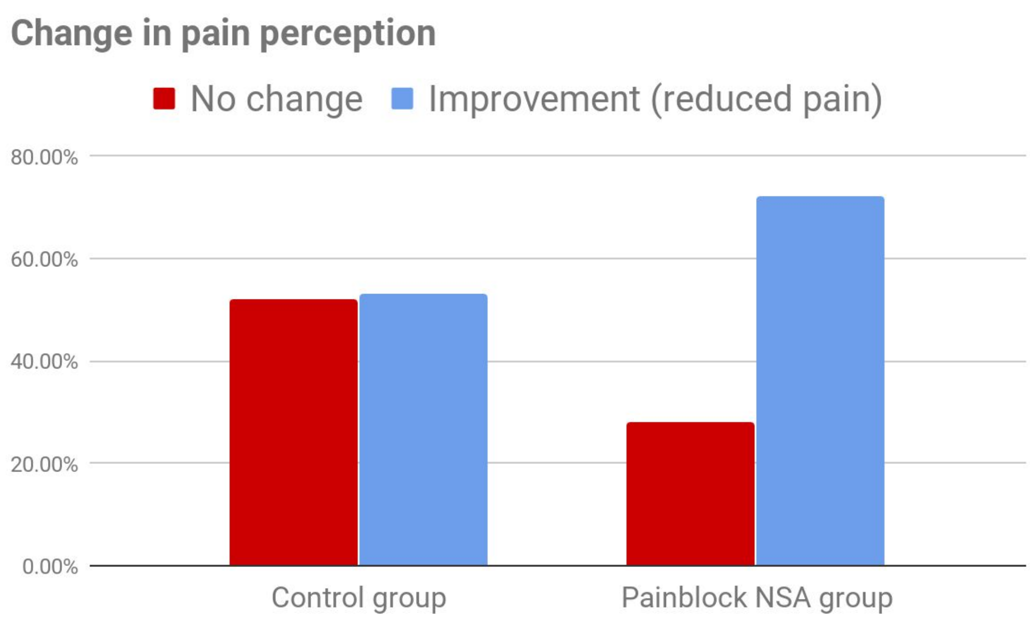
Painblock is the new auditory based treatment for relief of transient and chronic pain using Zenstant's Neurosensory Algorithm technology. Neurosensory Algorithms (NSAs) are digitally designed acoustic modulators that can stimulate regions of the human brain responsible for processing sensory localization, attention, memory, emotional or physiological state. NSAs are derived from best frequency and best temporal neural response characteristics of sound- sensitive and auditory processing regions of the brain. These regions have been partially mapped by studies using such diverse techniques as behavioral/psychophysical tests, electroencephalography (EEG), magnetoencephalography (MEG), neural imaging by Positron Emission Tomography (PET) and functional Magnetic Resonance Imaging (fMRI). The unique feature of NSAs is their derivations from overlap of sound sensitive areas of the brain with regions of the brain involved in specific emotional, attentional, and physiological states. By using NSAs to change an existing soundtrack, we use sound in the same way that radio uses a carrier wave - to get the specific features of the sound to affect the listener's brain in a controlled fashion. NSA technology has been used in numerous sound-based applications, most recently as the driving principle behind the extremely popular and effective sleep induction app "Sleep Genius."

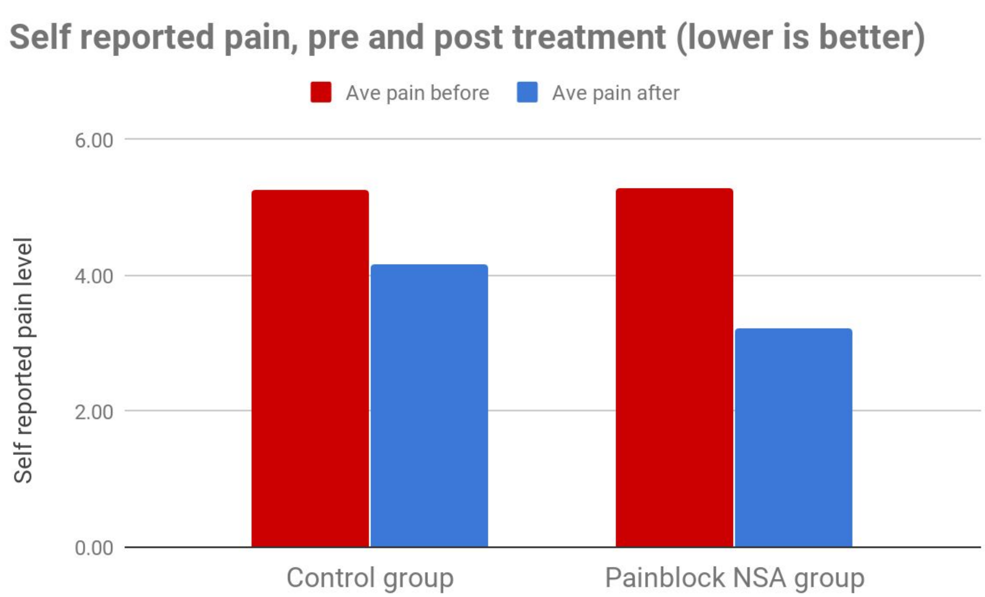
Painblock uses NSA modulation to carry out two basic tasks: interfere with the user's ability to pay attention to pain, and block negative emotional engagement with the painful experience. The Painblock NSAs do not cause direct anesthetic effects. Rather they interfere with the listener's ability to extend their reaction to the painful signal beyond the domain of the actual injury or condition. This is beneficial to the listener by:

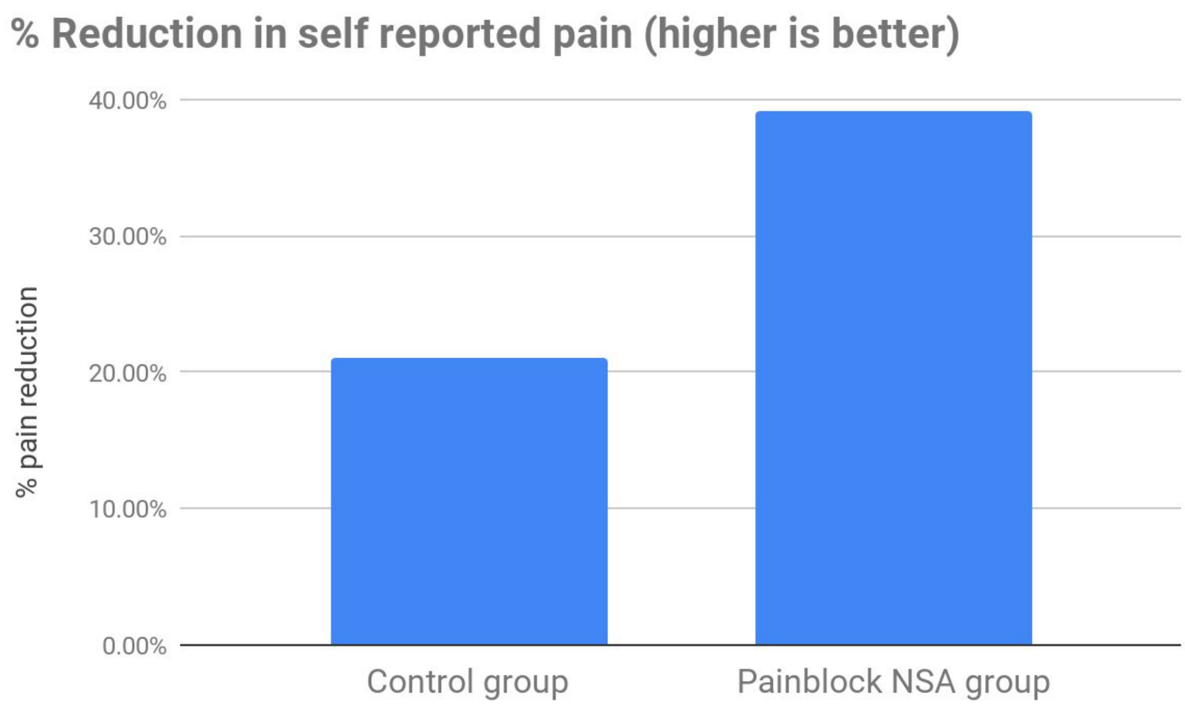
- Limiting the degree and amount of pain perceived by reducing attentional targeting
- Reducing associated anxiety and fear, preventing irrational escalation of pain-avoidance behavior such as required by uncomfortable medical procedures
- Increasing cognitive strength and available resources that would otherwise be bound up in pain-related states.

Data from Trials

Initial individual trials of Painblock showed high levels of efficacy and requests for repeat access in invasive vocal cord pulsed KTP laser treatment, chronic lower-middle back pain and migraine headaches as well as painful aesthetic procedures (tattooing and waxing). Subsequently, Painblock was tested as a double blind on-line version and in limited trial form in collaboration with a clinic in a New England rheumatology clinic. Online testing of 50 subjects demonstrated a highly statistically significant effect (t-test, $p < 0.01$) of pain reduction.







The clinical trial demonstrated non-statistically significant but suggestive reduction of stress and pain, particularly in fibromyalgia patients. Results from both datasets are being used to design improvements in the algorithms for different conditions. Zenstant is currently working to establish full scale clinical trials in dental and surgical offices in the United States.

Delivery

Because NSAs use audio modulation to achieve their results, standard musical file formats (AAC, WAV, MP3) are usable for delivery of most channel content. Musical carrier content is provided either by in-house compositions, algorithmic generation or royalty free catalog content. NSAs are generated and mixed using proprietary techniques on commercially available sound and mathematical software and subject to rigorous analysis before release to a pre-selected testing group.

The Painblock algorithm can be used to modulate any type of music. Initial studies will be carried out using simple complex “drone” type ambient music sufficient to carry the required modulations. It will be possible, however, to modulate music of the patient’s choice with similar efficacy, allowing patients to use their own favorite songs and playlists as treatment platforms.

Delivery to the patient will be via a small tablet with noise suppressing headphones. Initial testing will be carried out by providing test subjects with the tablet, presenting them with a brief standardized questionnaire about their demographics, condition, current medications and treatments and level of pain. The patient will then listen to the Painblock tracks for a set period of time, typically 15-30 minutes with volume, repetition and playback under their own control. At the end of the session, patients will be presented with another screen presenting them with a pain assessment scale and allowing them to log off. All data will be anonymized with the patient represented as an ID code.

Long term goal

The long term goal of Painblock is to provide short term or chronic pain management patients with a non-pharmaceutical, non-habit forming technique that can give them control over their pain issues. Painblock users should see a significant reduction in both their pain symptoms and their need for pharmaceutical or other pain-management procedures, and all under their own control.

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