

Migraine Trigger Site Surgery is All Placebo

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Background.—Over the last decade surgical treatments for migraine involving proposed trigger sites have been described and popularized by plastic surgeons in particular. Various related techniques aim to free up “trigger sites” by removal of small facial muscles or “decompressing” small facial nerves.

Discussion.—The basis for migraine trigger site surgery is without merit. There is one positive placebo controlled study with many limitations. Natural history and placebo mechanisms explain the outcomes from migraine surgery. The American Headache Society recommends that the migraine surgery not be performed outside of a clinical trial.

Conclusion.—Migraine trigger site surgery should not be performed.

Key words: migraine, migraine surgery, trigger site, placebo

INTRODUCTION

The late Louis Lasagna, one of the first placebo researchers, wrote in 1955 that sham injections are expected to be more effective than placebo pills.¹ It has since been demonstrated that placebo responses are larger with injections and, in particular, surgery.^{2,3} Subjective outcomes like pain are tremendously vulnerable to expectations and conditioning that comprise the placebo effect, which with natural history and biases on the part of physicians and patients are summated to constitute a clinical outcome. There is tremendous meaning surrounding the complex ritualized behavior that is surgery.⁴ The scope and extent of these influences is underappreciated.⁵ There is no better example of how placebo can flourish than in the characteristic fluctuating symptoms over short- and long-time periods that constitute migraine.

It is perhaps peculiar that migraine trigger site deactivation/decompression surgery was developed and is promulgated by those for the most part without formal Headache Medicine training, not boarded in Headache Medicine, those who do not generally manage patients with migraine, who do not contribute to the basic science of migraine, and for which this disorder is wholly outside their area of expertise, that is, surgeons. This situation is exacerbated by the very large number of frustrated,

impaired, and refractory migraine patients managed by Headache Medicine specialists.

NEW TREATMENT FOR MIGRAINE AND UNDERSTANDING MIGRAINE GENESIS

A new treatment for migraine must have at least a reasonable biological rationale, and this surgery does not. We are all smart enough to wax lyrical about possible mechanisms of action for anything. It remains that migraine is a central nervous system disorder. At no time were facial muscles or peripheral facial nerves implicated in migraine in a material way, and neuroscientists familiar with migraine pathophysiology disregard such hyperbole.⁶ Reengineering our understanding of migraine to include nerve entrapment or facial muscle trigger points is pure folly. Unschooled comparisons of well accepted nerve entrapments (carpal tunnel syndrome) or more controversial focal nerve lesions (trigeminal neuralgia) with the central brain disorder that is migraine are appealing only to those most peripheral to the science of migraine. Such prattle is a common false rationalization for migraine surgery.⁷

Practitioners skeptical of such migraine surgery have only one real case to answer, the one positive placebo controlled study of surgical deactivation of peripheral migraine headache trigger sites in those with frequent moderate to severe migraine by Guyuron and colleagues published in *Plastic and Reconstructive Surgery* in 2009.⁸ Placebo-controlled randomized clinical trials of surgical interventions remain uncommon, and the absence of an observational or nontreatment control group in most studies precludes any evaluation of the magnitude of the placebo effect separate from natural history. Surgical procedures do not lend themselves easily to blinded control, and for this reason we must be even more careful about the biological underpinnings of the proposed rationale. Professionals are often too uncritical of positive clinical trials, when practically all positive clinical studies of improbable events are wrong, due to a mixture of biases and random effects.⁹ All statistical results should be interpreted in the context of the totality of evidence, including the biological rationale, which for migraine surgery is very poor. All clinical studies have shortcomings, and this study was awash with concerns leading to publication not in a neurology or headache medicine journal but in a plastic surgery journal, the refuge for most of the published work on migraine surgery.

Limitations of the migraine trigger site deactivation study have been detailed elsewhere and include omission of selection criteria, subject gender absent, no data on prior treatments,

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medication overuse or relevant comorbidities, statistical problems including underpowering (no power calculation presented), concerns about incomplete blinding, and the primary endpoint did not follow International Headache Society guidelines.^{7,10,11} Further, using response of a single injection of onabotulinumtoxinA (onabot) to select those for surgery in reality selects placebo responders. Onabot is an ineffective treatment for episodic migraine, and effectiveness for chronic migraine with 31 injection sites is slim and possibly all placebo as well.^{12,13} Hence this migraine surgery study should not foster cautious optimism, but healthy skepticism, and migraine surgery should not be described as potentially useful.

Those unaccustomed to powerful surgical placebo responses should familiarize themselves with examples in the literature, including the classical ligation of the internal mammary artery, popular in the United States in the 1950s.¹⁴ Two blinded sham surgery controlled trials demonstrated robust improvements in both active and sham groups, with no significant difference.^{15,16} Sham surgery demonstrated decreased need for nitroglycerin and increased exercise tolerance, even complete pain relief and outcomes sustained for many months. One sham subject had improved electrocardiographic results after exercise. Such positive outcomes are more compelling than the migraine surgery outcomes!

Guyuron and colleagues also published a 5-year follow-up postmigraine surgery, without comparative controls, as controls were not followed for 5 years, claiming that “there is strong evidence that surgical manipulation of one or more trigger sites can successfully eliminate or reduce the frequency, duration, and intensity of migraine headache in a lasting manner.”¹⁷ Authors willfully omit other interpretations of improved outcome and even suggest elimination of migraine with surgery! Follow-up studies should be performed to explore longer term side effects of surgery. Failure to appreciate that response to an ineffective surgery can be due to regression to the mean, natural history (especially as the average age was 44 years), or other medical treatments separate to the expectancies and conditioning that is the placebo effect leads to bewilderment at how long a placebo response lasts. Recently, the same physicians published a randomized clinical trial comparing two techniques – neurectomy or decompression of the zygomaticotemporal branch of the trigeminal nerve for “temporal migraine headache” concluding that both are appropriate and helpful. Such foolery.¹⁸

The proponents of migraine surgery have an easily understood claim. The scientific principle that a claim is untrue unless proven differently runs counter to our natural tendency to accept as true that which we can conceptualize quickly. It is Spinoza’s conjecture that belief comes quickly and naturally, skepticism is slow and unnatural, and most people have a low tolerance for ambiguity.^{19,20} Treatment beliefs are formed for

a variety of personal, subjective, economic, cultural, emotional, and psychological reasons in the context of our practice environments and professional organizations.²¹ We then defend our treatment beliefs with intellectual arguments and rational explanations, as exemplified by all the nonscience (alternative) medicine literature. Hence, belief in therapy is far from a dispassionate distillation of available evidence, and smart people are better able to rationalize the beliefs that they hold for nonsmart reasons. Failure to appreciate this leads to bafflement at how physicians can have markedly different passionate beliefs for the same treatment. Once belief is declared, it is easier and less painful to dig in.

Peculiarities of American medicine allow growth of migraine surgery centers. There is a large free medical market with fee for service, ability to advertise, surgeons and medical facilities eager to differentiate themselves, and the tendency of physicians in a free market to hold patient desires and opinion on outcomes more highly than expert consensus and even evidence-based medicine. Couple these factors with the large body of desperate treatment-refractory patients unaccustomed to the complexities of migraine, who see face validity in an operation on their head, and perhaps there is no surprise. Surgery always carries some risk, however small, so when all else fails migraine surgery should not be recommended.

The American Headache Society does not recommend surgical deactivation of migraine trigger points outside of a clinical trial.²² I would add that a legitimate future clinical trial would have to be one designed to answer whether this intervention works. Even with that, clinical equipoise is on shaky ground for this modern day trepanation.

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