Fighting the Opioids Crisis in Migraine with Brain Neuromodulation Digital Therapeutics

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Introduction

Relivion® is the first non-invasive multi-channel brain neuromodulation system for treating neurological and neuropsychiatric disorders. It offers precise, personalized care by delivering stimulation to six branches of the occipital and trigeminal nerves via three adaptive output channels (**Fig.1**). Electro-physiologically, it creates a cumulative effect by releasing neurotransmitters in the brainstem and modulate brain networks associated in control of pain and mood.

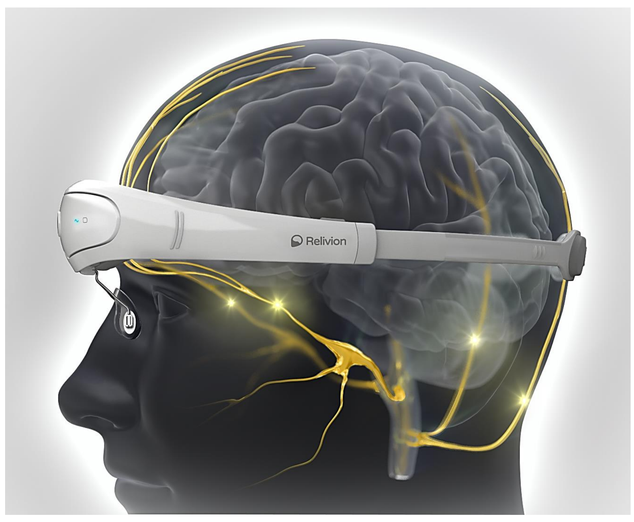

Fig. 1: The Relivion® and its target nerves

During treatment, the Relivion e-Relief™ mobile App gather treatment data from the device and upload it to a secure cloud database for analysis and treatment optimization. Using its three adaptive channels the Relivion® can deliver various combinations of treatment architectures, among which the best setup for each patient is chosen while the self-learning system continues to adapt and improve the treatment as time goes by (**Fig. 2**).

The Relivion was studies in several clinical trials to evaluate its safety and efficacy in abortive treatment of migraine.

Methods

Three clinical trials of the Relivion® were reviewed:

- **Study 1:** Combined Trigeminal & Occipital Nerve Stimulation (CTO-NS) Compared to Trigeminal Stimulation Alone for Treatment of Migraine Headache.
- **Study 2:** Efficacy and Safety of Combined Occipital and Supraorbital Transcutaneous Neurostimulation in Alleviating Migraine Headache Pain (Prospective, Randomized, Single-blind, Parallel-group, Placebo Controlled trial).
- **Study 3:** Clinical performance and safety of self-administered treatment for migraine using combined occipital and trigeminal neuromodulation (Relivion SP-301, a Prospective, Randomized, Double-blind, Parallel-group, Sham controlled trial).

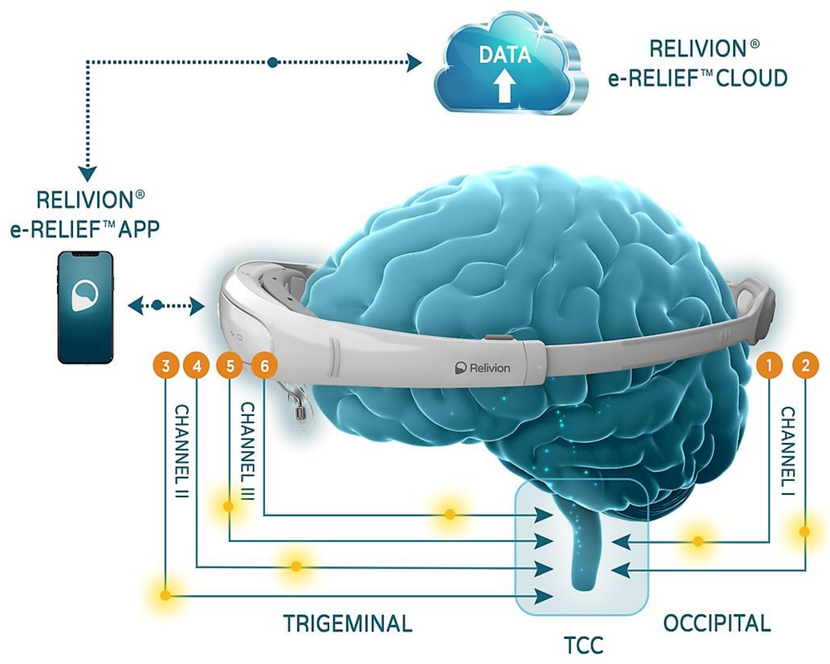

Fig. 2: The Relivion Digital Therapeutics for Brain Neuromodulation

Results

In the first study, “Combined Trigeminal & Occipital Nerve Stimulation (CTO-NS) Compared to Trigeminal Stimulation Alone for Treatment of Migraine Headache”, Ten (10) subjects suffering from episodic migraine, were treated. Treatment was initiated at no more than 120 minutes after the onset of the migraine episode. Mean VAS pain score at baseline was 5.7±2.2. Mean VAS pain score reduced to 2.7±1.8 (reduction of 56.3%) after combined occipital and trigeminal stimulation compared to only 4.1±2.2 (reduction of 31%) after trigeminal stimulation alone (**Fig. 3**).

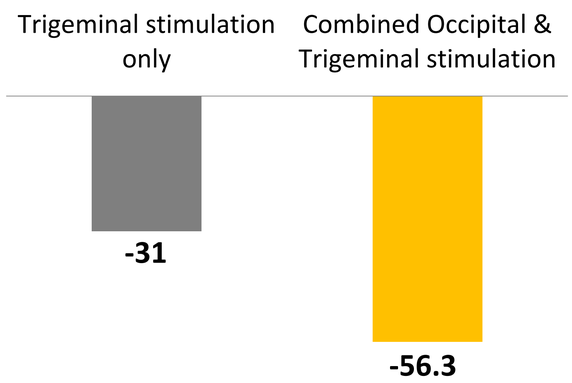

Fig. 3: Mean % pain reduction post trigeminal and post combined occipital & trigeminal stimulation

In another study (“Efficacy and Safety of Combined Occipital and Supraorbital Transcutaneous Neurostimulation in Alleviating Migraine Headache Pain: A Prospective, Randomized, Single-blind, Parallel-group, Placebo Controlled Clinical Study”), 30 patients treated with an active (N=15) or sham device (N=15). The treatment group showed significantly reduced mean pain VAS score compared to an increased pain VAS score in the sham group at end of treatment (-79.2% vs.+14.9%, respectively; P=0.0001) and at two hours post treatment (-75.8% vs. +12.8%, respectively; P=0.0001). Two hours post treatment 53% of the patients in the treatment group were pain free compared to non in the sham group (P=0.0031). No serious adverse events were reported. Responders rate (subjects with reduction of pain ≥50%) at 2 hours were 80% in the treatment group compared to 16.7% in the sham (P=0.001) (**Fig. 4**).

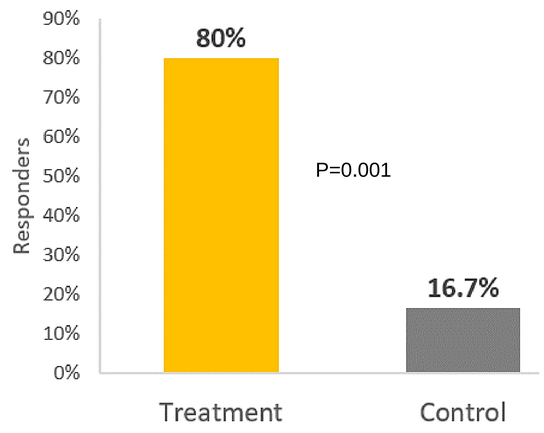

Fig. 4: Responders rate at 2 hours

The third clinical trial (SP-301,a prospective, randomized, double-blind, parallel-group, sham controlled) evaluated the clinical performance and safety of the Relivion® in abortive treatment of episodic and chronic migraine. 55 subjects were randomized. 1 hour post treatment, the treatment group showed an average 53.1% reduction in pain VAS score compared with only 10.3% in the sham group (P=0.0002). Responders rate was significantly higher in the treatment group compared to sham at 1, 2 and 24 hours post treatment (P<0.05). In the treatment group, 43% of the subjects with severe or moderate baseline pain level were pain-free two hours post treatment compared to only 10.5% in the sham group (P=0.027). At 2-hours, 76.2% of the subjects in the treatment group reached Headache Relief compared to 31.6% in the sham group (P= 0.01)**. (Fig. 5).** No serious adverse event were reported.

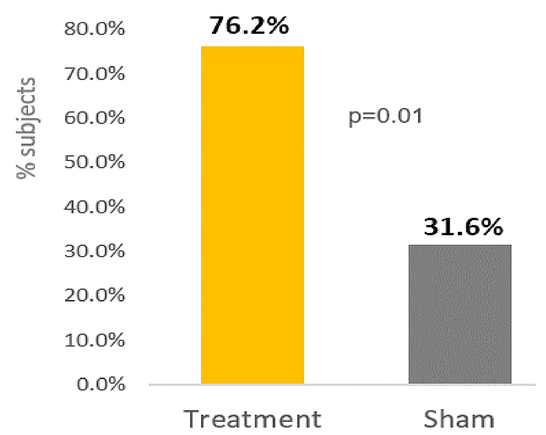

Fig. 5: Headache Relief at 2 hours

Discussion & Conclusions

The results of the reviewed clinical trials demonstrate that self-administered abortive treatment of migraine by the Relivion® was safe and highly effective.
We hypothesize that the synergistic neuromodulatory effect elicited by concurrent activation of the occipital and trigeminal neural pathways contributes to the superior therapeutic results shown in these studies.

References:

1. Combined Trigeminal & Occipital Nerve Stimulation (CTO-NS) Compared to Trigeminal Stimulation Alone for Treatment of Migraine Headache; Alon, Gad. Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation, Volume 12 , Issue 2 , e63 - e65 (Proceedings #6),2018
2. A prospective, randomized, single blind, parallel-group, placebo controlled clinical study to evaluate the short-term effectiveness of combined occipital and supraorbital transcutaneous nerve stimulation (OS-TNS) in treating migraine; Hering-Hanit R. Cephalalgia, vol. 37, 1 suppl: pp. 52-171, 2017