

MedAutonomic's Brain NeuroModulator: A Brief Summary of the Fundamental Science and Research

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I. Introduction

The purpose of this paper is to provide an overview of the science and research that lies behind MedAutonomic's path-breaking device, the Brain NeuroModulator (BNM). Our focus is to establish that there is a body of evidence that strongly supports our approach to addressing functional diseases related to the metabolic syndrome and an imbalance in the autonomic nervous system (ANS).

A functional disease becomes a pathology of the organ if left untreated for a long period of time. For example, if GERD is not corrected then the esophagus will be damaged. If hyperglycemia is not corrected, the atherosclerosis organ damage from diabetes will become systemic. The same idea holds for diastolic hypertension and overeating in the obese.

II. Addressing the Metabolic Syndrome and Functional Diseases by Rebalancing the Autonomic Nervous System: Research and Results

In the 1990s researchers began to examine the relationship between the sympathetic tone and parasympathetic tone of the ANS and several diseases (obesity, gastro-esophageal reflux disease - GERD, type-2 diabetes and hypertension) that are

associated with what is known as the "metabolic syndrome". The initial research focused on the relationship between the ANS and obesity, with some early evidence that obese individuals were low in sympathetic tone (Nagai, et al.). However, other work demonstrated that it was the opposite, i.e. that obesity (and other functional diseases) was associated with low parasympathetic tone (Arone, et al.; Mackintosh).

It is now well accepted that the metabolic syndrome is indeed closely related to an imbalance between the sympathetic tone and the (too-low) parasympathetic tone. It follows directly that if the ANS could be brought back into balance, various diseases would be treated. In addition, it has been established that the status of the ANS and the sympathetic and parasympathetic tones can be precisely measured through heart rate variability (HRV). The research of Hirsch, et al. induced weight change in seven subjects, and established that HRV does indeed measure changes in the ANS during weight change.

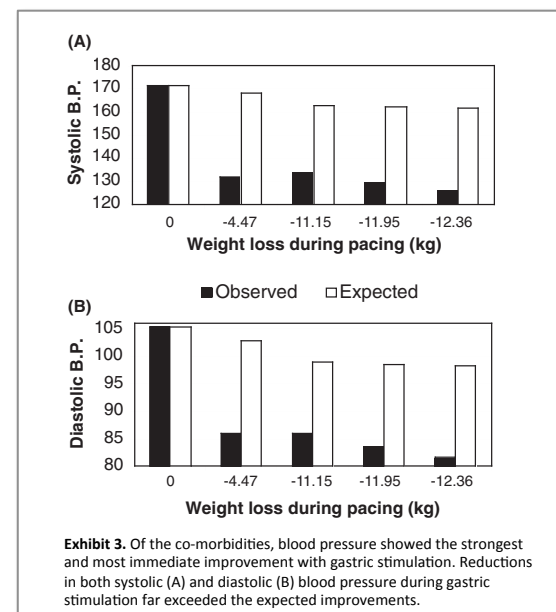
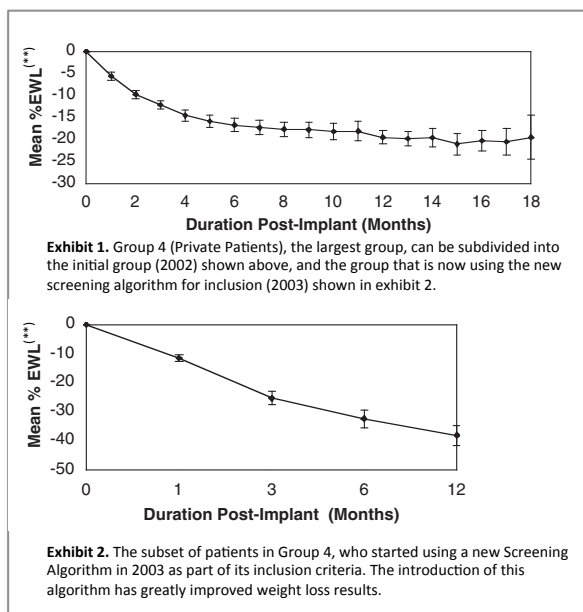
HRV power spectral analysis is a well-accepted and noninvasive method, and has provided a comprehensive quantitative and qualitative evaluation of neuroautonomic function under various clinical and research settings. The validity of spectral analysis of HRV under the

resting condition has been well documented (Nagai, et al.).

When Dr. Cigaina began to develop the gastric pacer to treat obesity, his focus was on stimulating the stomach with an electric shock to induce satiety. He collected a significant amount of data from performing about 250 implants in animals and 900 implants in humans. As the graphs below indicate, the gastric pacer worked well (Cigaina). The weight loss resulting from Dr. Cigaina's gastric pacer was confirmed by Shikora, et al.

In his 2004 paper, Dr. Cigaina concluded: "We suspect that gastric stimulation influences the autonomic nervous system."

This thought prompted him to re-examine the trove of data he possessed from patients that had his gastric pacer. Dr. Cigaina's suspicion was correct, and he determined that the gastric pacer worked not because it was stimulating the stomach, but rather because it was producing a signal to the brain that rebalanced the ANS. Many of the diseases related to the metabolic syndrome were treated when the ANS was rebalanced. This result (see exhibits 1-3) is consistent with the work of Wang, et al., who found that gastric stimulation activates the hippocampus and other regions that are part of the brain circuitry related to eating behavior.



(**) Excess Weight Loss: defined by the 1983 Metropolitan Life Insurance Height/Weight tables, using medium frame as midpoint.

Importantly, there were no medical side effects from the gastric pacer but a major drawback was that it required surgery. In addition, there were two negative technical issues: the lead connecting to the stomach could become detached, and the battery would have to be replaced a number of times (each requiring another surgery). Also, as pointed out by Famm, et al., existing stimulation devices send out a very broad set of signals without understanding all the effects and do not target a specific problem.

III. The Brain NeuroModulator

Dr. Cigaina realized that stimulating the stomach was not the key to addressing the metabolic syndrome. ***Rather, the metabolic syndrome could be addressed by directly sending a signal to the brain to increase the parasympathetic tone in order to rebalance the ANS.*** From the approximately 900 gastric pacer implants he performed on humans, he was able to collect a significant amount of data on the relationships among sympathetic tone, parasympathetic tone and HRV. Through detailed research, Dr. Cigaina was able to identify the precise signal that was being sent to the brain to increase the parasympathetic tone and rebalance the ANS.

After Transneuronix was sold to Medtronic, Dr. Cigaina began to work on a completely new, cutting-edge device, the Brain NeuroModulator. The BNM sends the precise signal identified by Dr. Cigaina to the region of the brain associated with ANS activity: the hippocampus and basal ganglia. The research of Wang, et al.

established “the importance of the hippocampus in modulating eating behaviors linked to emotional eating and lack of control.” The BNM pinpoints the appropriate area of the brain and sends a very specific signal in order to increase the parasympathetic tone.

The BNM is implanted in the wall of the stomach with a digestive endoscope in a simple outpatient procedure. It is important to re-emphasize that the BNM is not interacting with the stomach, but is sending a direct, precise signal to the brain. The BNM is placed in the wall of the stomach, as this has proved to be an efficient location for sending a signal to rebalance the ANS.

The BNM definitively ends the age of “nervous stimulation” and introduces the new era of ***precise signaling*** to the brain. The BNM acts as an artificial neuron, producing an action potential of the parietal gastric neuronal network cells. The digestive signals delivered to the brain adjust the ANS by increasing the ***original*** parasympathetic tone. Using the stomach as the gateway, the BNM becomes part of the nervous system in a simple and nonaggressive manner.

Famm, et al. have identified “electroceuticals” as an area that will revolutionize medicine, and they begin their article with the following: “Imagine a day when electrical impulses are a mainstay of medical treatment.” Later, they state: “We believe that it is now possible to create medicines that control action potentials in individual neurons and in functional groups of them.” This is

precisely the focus of the BNM on a holistic level, as our bioelectric medicine directly rebalances the ANS.

IV. Summary and Conclusions

Applying therapy to a functional disease must continue forever. A medical approach with drugs has to consider the negative side effects. Only a neurological balancing of the body's system can eliminate the need for continued therapy and the side effects from drugs. MedAutonomic's technology has a solid grounding in the science and research related to the ANS. Based on the 20-year experience of Dr. Cigaina, MedAutonomic is developing the BNM to address various functional diseases related to the metabolic syndrome. Neuromodulation is a new way to treat these diseases, and we are on the cutting edge of bioelectric medicine.

V. References

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