Vagus nerve stimulation: Invasive or noninvasive?

Autonomic imbalance with heightened sympathetic activity and withdrawal of vagal activity is critical for development and progression of chronic heart failure (1, 2). Primary characteristics of autonomic function comprise heart rate and heart rate variability. Abnormalities in both of these domains are associated with higher morbidity both in general population and in cardiovascular patients (3, 4). Both resting heart rate and a number of indices derived from heart rate variability are dominated by vagal vs. sympathetic tone, as the effects of muscarinic blockade are more significant than β-adrenergic blockade (5).

In this issue, Akdemir et al. (6) reviewed reports on the development of clinical vagus nerve stimulation (VNS) for cardiac applications. The article entitled "Vagus nerve stimulation: An evolving adjunctive treatment for cardiac disease" focuses on VNS for cardiac arrhythmias and heart failure, and discusses VNS device types and potential adverse effects. Although the review is highly relevant and sought after for discussion of invasive VNS techniques in cardiac diseases, it has to be emphasized that emerging noninvasive transcutaneous VNS (tVNS) approaches are not limited to treatments of migraine and headache.

Topical applications of tVNS are promising to exert specific and sometimes unique effects of tVNS on the cardiovascular system similar to those achieved through acupoints, which are reactive points on the surface of the body (7). For example, an increase of vagus nerve activity most likely is specifically involved in an increase of superior mesenteric artery blood flow volume induced by of manual acupuncture stimulation of ST36 (Zusanli) (8). Recent review by Murray et al. (9) entitled "The strange case of the ear and the heart: the auricular vagus nerve and its influence on cardiac control" provides fascinating discussion of the available evidence in support of modulating cardiac activity using the auricular nerve where tVNS can be delivered through electrical stimulation to the auricular branch of the vagus nerve (9).

Functional magnetic resonance imaging study demonstrates that the central projections of the auricular branch of the vagus nerve are consistent with the "classical" central vagal projections and can be accessed non-invasively via the external ear (10). Several human studies demonstrate beneficial cardiac effects following tVNS in cardiovascular patients with paroxysmal atrial fibrillation, angina pectoris, and severe heart failure (11–14). tVNS administration is associated with a significant modulation in systemic levels of tumor necrosis factor alpha, C-reactive protein (13), and heat shock proteins (14).

Interestingly, auricular stimulation may also influence the activity of the sympathetic nervous system in healthy individuals with no history of cardiovascular disease. Indeed, tVNS on the inner and outer surface of the tragus significantly improves heart rate variability (through a shift in cardiac autonomic activity toward relative parasympathetic/vagal dominance) and causes a significant decrease in muscle sympathetic nerve activity as recorded by microneurography in healthy human volunteers (15).

Considering potential specificity and better safety profile, tVNS appears to be a promising therapeutic alternative to invasive VNS. Further studies of mechanistic basis of tVNS and its clinical efficacy are required.

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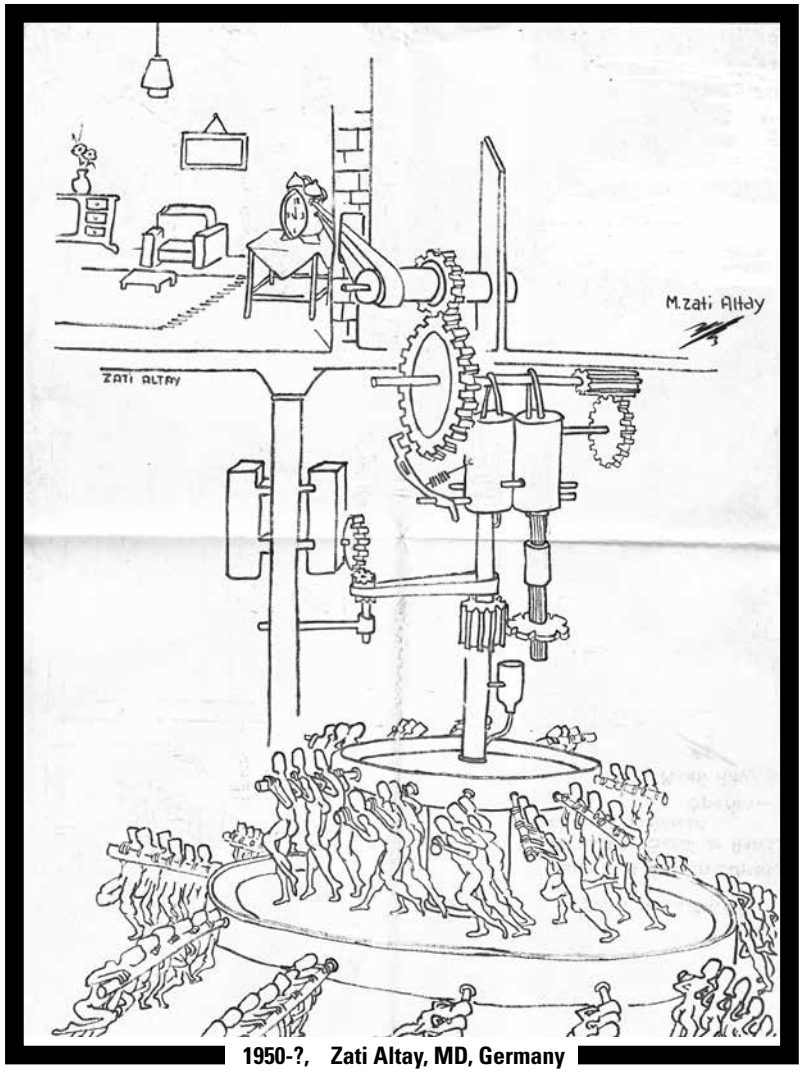

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