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Bretherton, B orcid.org/0000-0003-1569-5872, Deuchars, J orcid.org/0000-0002-4445-654X and Deuchars, SA orcid.org/0000-0002-1876-3239 (Cover date: June 2019) What impact could transcutaneous vagal nerve stimulation have on an aging population? Bioelectronics in Medicine, 2 (2). pp. 59-61. ISSN 2059-1500

https://doi.org/10.2217/bem-2019-0022

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What impact could transcutaneous vagal nerve stimulation have on an aging population?

Beatrice Bretherton, Jim Deuchars, Susan A. Deuchars.

School of Biomedical Sciences, Faculty of Biological Sciences, University of Leeds, LS2 9JT, UK

Corresponding author: Beatrice Bretherton, B.E.Bretherton@leeds.ac.uk

First draft submitted: 17 September 2019; Accepted for publication: 24 September 2019; Published online: TBC

Key words: Transcutaneous vagal nerve stimulation; Aging; Autonomic nervous system

14.9 million people in the UK were over 60 years old in 2014, with estimates projected to increase to 21.9 million people by 2039 [1]. Within this total, the number of individuals aged over 85 years is estimated to grow even more – from 1.5 million people aged over 85 years in 2014 reaching 3.6 million by 2039 [1]. It is not only the UK who has an aging population: the proportion of the world's population aged over 60 years is expected to increase from 12% in 2015 to 22% by 2050 [2]. Such aging populations result from increased life expectancy, bringing individuals and their families opportunities unavailable 20-30 years ago. Similarly, the greater life expectancies anticipated in the next 30 years will provide new and different opportunities than the ones of today. For individuals to make the most of their longer lives, good health is essential, especially for maintaining independence and playing an active role in family and community life. However, a challenge to prolonging good health is associated with changes in autonomic nervous system function, characterized by shifts towards sympathetic and away from parasympathetic prevalence [3]. This resulting imbalance in autonomic function can be detrimental to heart function, gut function, emotion, mood and quality of life, playing a significant part in the development of age-related conditions, such as heart failure [4], hypertension [5] and depression [6]. To treat these conditions, pharmacological therapies are typically used, some of which have limited effectiveness, are associated with side-effects and lead to a population-wide dependence on medications. Therefore, there is an urgent need to find a way that allows people to lead healthy older lives whilst avoiding the use of pharmacological and invasive therapies. Stimulating the vagus nerve without surgery may be one way of achieving this.

The vagus nerve, originating in the brainstem, supplies many organs in the body, therefore making it a single therapeutic target with potentially widespread effects. It is a main source of the parasympathetic branch of the autonomic nervous system, which seeks to maintain homeostasis within the body but is also critically important in sensory signaling. Traditionally, stimulation of the vagus nerve (VNS), by surgically implanting a generator unit and administering electrical impulses to the left cervical vagus, has been used to treat refractory epilepsy and treatment resistant depression. However, as surgery is necessary and side-effects have been reported [7], the viability of using this form of VNS to prolong the period of healthy aging is unclear.

Fortunately, the vagus nerve has a small sensory distribution at the cutaneous ear through the auricular branch of the vagus nerve (ABVN) [8]. The ABVN can be stimulated non-invasively by applying small, pain-free electrical impulses (i.e. pulse width around 200 µs, frequency around 30 Hz and current 2-4 mA) to specific auricular dermatomes thought to be innervated by the ABVN (usually the tragus, concha or cymba concha). This transcutaneous VNS (tVNS) is relatively inexpensive: just the cost of a transcutaneous electrical nerve stimulator (TENS) machine and modified auricular electrodes to attach the TENS to the ear. More importantly, it is simple to administer, enabling individuals to administer it themselves, in their own homes; a major advantage considering the mobility and physical challenges that occur with older age.

Research exploring how tVNS impacts the physiological health of individuals is beginning to show that it could have positive effects for aging populations. A single 15-minute session of tVNS, albeit in young healthy volunteers, significantly reduced sympathetic nerve activity [9] and improved measures of vagal tone [10]. Interestingly, the most pronounced improvements in autonomic balance occurred in individuals who had higher sympathetic prevalence at baseline [9], suggesting that tVNS may be of particular benefit for older individuals who show this autonomic imbalance. Interestingly, a single 15-minute session of tVNS in healthy volunteers aged ≥55 years was also associated with improvements in autonomic function [11]. These improvements appeared to be distinct from autonomic changes associated with sham stimulation (machine turned off without participant knowledge): tVNS was associated with greater increases in baroreceptor reflex sensitivity [11] and lower sympathetic prevalence compared to sham [9]. In addition, when administered for 15 minutes every day for two weeks, tVNS improved measures of autonomic function, with response to tVNS becoming more pronounced after the two-week period [11].

As well as benefitting healthy older individuals, tVNS holds potential for patients with age-related conditions. For instance, ABVN stimulation for 15 minutes every day for two weeks in individuals with coronary artery disease improved exercise tolerance and reliance on vasodilator medication [12]. There is also evidence that tVNS has anti-inflammatory effects; an important quality given that pro-inflammatory mechanisms strengthen with aging. For instance, in individuals with paroxysmal atrial fibrillation, tVNS significantly reduced plasma levels of TNFα, a pro-inflammatory cytokine, along with atrial fibrillation [13]. In addition, inflammatory responses in the left ventricle of a rat model of heart failure were significantly reduced after 4 weeks of tVNS [14]. Therefore, age-related conditions characterized by chronic inflammation may be important targets for future tVNS trials. Potential conditions include heart failure with reduced ejection fraction, diabetes, hypertension, irritable bowel syndromes and chronic pain conditions. Furthermore, due to increasing interest in and limited effective treatments for heart failure with preserved ejection fraction (HFpEF), tVNS could be a potential treatment modality. Of course, careful consideration should be made of control groups and control arms. This is because the perceptible quality of tVNS and controversy in the literature about which nerves actually innervate the auricular dermatome make it difficult to determine a valid control and to implement double-blinding.

As well as having positive effects on physiological health, there is increasing support for the role tVNS could play in enhancing psychological well-being. Two weeks of daily tVNS in healthy older individuals significantly improved aspects of mood, including depression, tension and vigor [11]. The effects on depression may be far-reaching: tVNS applied for two weeks [15] and one month [16] in patients with depression significantly reduced depression scores. These findings are noteworthy given the prevalence of depression, and other mood disorders (e.g. anxiety), in the older age-groups. Deteriorations in cognitive ability are also a common feature in the aging process. Fortunately, tVNS has been shown to enhance associative memory in older individuals [17], the recognition of emotions [18] and divergent thinking [19]. Together these findings provide increasing support for using tVNS to combat some of the age-related changes in psychological and cognitive impairments. Indeed, it would be prudent to explore the impact of tVNS in Alzheimer's Disease, particularly for individuals who are experiencing the initial stages of memory loss.

As individuals age, they are often caught in the throes of deteriorating sleep quality. Since sleep plays such an important role in health, mood and cognitive function, it could be a key target for tVNS. Our recent evidence suggests that aspects of sleep can be improved with tVNS: for individuals who had low sleep quality and difficulties falling asleep and waking up, two weeks of daily tVNS was associated with improvements [11].

In conclusion, research clearly shows that tVNS has considerable potential to positively impact aging populations. Use of tVNS could delay the progression of age-related conditions for older individuals who want to maintain their good health, thereby prolonging the period of healthy aging. Additionally, for those who have underlying age-related health conditions (e.g. diabetes, hypertension, depression, anxiety, insomnia etc.), tVNS could aid with symptom management, thereby reducing the severity of their symptoms, and reliance on medications and healthcare utilization. In turn, this could enable older populations to live a healthier longer life that maximizes their independence, enabling them to engage with opportunities that are presented to them. Positive effects on wider society and the healthcare system could also be realized. With further research, the diversity of age-related conditions tVNS can help and the role it can play in healthy aging will be realized.

Financial & competing interests disclosure

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

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