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Research paper

Hemodynamic responses to low-level transcutaneous auricular nerve stimulation in young volunteers

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ABSTRACT

Objectives: The aim of this study was to characterize cardiovascular autonomic responses during two constant current intensities below sensory threshold of transcutaneous auricular nerve stimulation (taNS). On this basis, a protocol for taNS with autonomic modulatory potential could be proposed.
Subjects and methods: We included 26 men and 24 women, mean age 26. Data were collected during three randomly allocated 20-minute right tragus stimulation sessions – a) no-stimulation (sham), b) 90 μA (arbitrary), and c) 130 μA (near the lowest sensory threshold in majority). Stimulation was 20 Hz, rectangular pulse width of 2 ms, duty cycle 2-second on/off. To assess autonomic responses, we continuously recorded ECG, non-invasive arterial blood pressure (BP) and thoracic impedance cardiography data. Ten-minute data were compared. Fast Fourier transform of RR intervals was performed on 10-minute recordings as well. Low frequency and high frequency power spectra were calculated. Friedman test or one-way ANOVA for repeated measurements and Mann-Whitney or Wilcoxon's signed-rank test, or t-test were carried out. $P < 0.05$ was considered significant.
Results: At 130 μA stimulation, cardiac output significantly decreased ($p < 0.05$), driven by significant heart rate drop in women, and stroke volume and contractility drop in men, pointing to a gender-related autonomic responses. We observed no significant changes in BP, or variability parameters. Significantly higher body size and BP were found in men, as expected.
Conclusions: It seems that tested taNS protocol has a potential for cardiac autonomic modulation in majority of young healthy men as well as women. Further studies are however needed to prove the therapeutic potential of this stimulation protocol in different patient groups.

Introduction

It is believed that transcutaneous electrical stimulation, targeting the area of auricular branch of vagus nerve (taNS), could produce therapeutic benefits similar to direct vagus nerve stimulation as well as overcome its limitations like invasiveness and costs (Yap et al., 2020; Johnson and Wilson, 2018). As most of the referenced stimulation methods differ in the parameters and protocols applied, there is currently no firm evidence on the optimal stimulation parameters that would provide the greatest therapeutic effects for a specific condition (Yap et al., 2020). A constant effort for the standardization of taNS is therefore of great importance to reach its full potential as a non-invasive, tolerable, and clinically relevant therapy (Farmer et al., 2021). With this respect, defining the autonomic responses in the range of 'low-level' electrical stimulation intensities would be one of important steps in the stimulation protocol standardization for practical purposes.

The low-level taNS seems to be a feasible option for cardiac autonomic modulation. There are firm data that intrinsic cardiac nervous system is sensitive to low-level vagus nerve stimulation (Ardell et al., 2015). The sensory fibers of auricular branch of vagus nerve are appropriate stimulation target since they mediate cardiac responses through central vagal projections (Safi et al., 2016; Tekdemir et al., 1998; Frangos et al., 2015) which deliver processed signals to the heart surface bilaterally, therefore exerting balanced cardiac autonomic effects through the network of intrinsic cardiac nervous system (Armour, 2008; Ardell et al., 2016, 2017). We speculate that therapeutic goal of

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taNS is similar to direct vagus nerve stimulation– e.g. the point where afferent-driven decreases in central parasympathetic drive are counteracted by direct activation of the cardiac parasympathetic efferent projections to the intrinsic nervous system of the heart (Ardell et al., 2017; Kember et al., 2014). At this neural fulcrum (balanced response), central and peripheral aspects of the cardiac (and vascular) nervous system become engaged, such that the reflex hierarchy maintains its capability to respond to stressors (Ardell et al., 2017).

We have recently reported results of low-level right tragus taNS on cardiovascular autonomic responses in young healthy men (Sinkovec et al., 2021). Significant decreases of left ventricular contractility, cardiac output parameters, and cardiac workload were associated with significant increase in arterial blood pressure, that was attributed to baroreceptor reflex response. However, the procedure related uncomfortable sensations during one-hour taNS could have elicited non-specific sympathetic activation, and stimulation intensity depended on the variable individual sensory thresholds. Further, we realized that the amount of electrical current delivered to the tissue is difficult to be quantified on the basis of voltage regulation because it depends on unsteady tissue impedance, properties of electrode-skin contact, type of electrodes, etc. Finally, our objective for optimal taNS, conveying a predominant parasympathetic or balanced autonomic responses, was not fulfilled.

Therefore, to refine assessment of autonomic responses, we upgraded the previously applied taNS protocol with electrical current intensity regulation, using two pre-defined current intensities, i.e. 130 μA and 90 μA, the first being just below the sensory threshold and the second well below the level of eventual perception bias. We continuously measured electrocardiogram (ECG), arterial blood pressure (BP), and impedance cardiography parameters during sham stimulation (no-stimulation) and during both above mentioned current intensities. The study was performed in a group of young women and men in a single-blind randomized manner.

Subjects and methods

In this single-blind randomized study, 50 (24 women) healthy medical students and doctors aged 26 years (range 20–39) were enrolled from July 2021 until July 2022. All signed written informed consent to participate in the study. The study was conducted at Laboratory for Autonomic Neurology, Department of Neurology, University Medical Center Ljubljana, and was approved by the State's Ethics Committee (0120–518/2021/5).

The electric current intensity level was based on a preliminary study in another group of 8 participants (4 women, 4 men, age 23–65 years) under the same conditions as in the main study. Tested current intensities were: 0, 90, 130, 170, 210, and 250 μA, applied in two minute sessions in a randomized manner. The stimulation perception was marked by participants for each session with a 10-level gradation score. In majority, the obtained results clearly distinguished between perception and non-perception level at 130 μA. Therefore, we decided to further investigate stimulation currents 130, 90 and 0 μA in order to define autonomic responses and to diminish perception bias on the final results.

The measurements were performed in non-sedated state, during single visit between 2 and 6 PM, in a quiet surrounding with air temperatures between 20 and 22 °C. A light meal was allowed two hours before the visit. Examinees were asked to avoid caffeine and nicotine for 12 h and to void their bladder before the study. They were lied down to supine relaxed position and all measuring devices were connected and calibrated. A 10-min habituation phase followed. Data were collected during three randomly allocated sessions comprised of 20-minute: a) sham stimulation ~~(no-stimulation)~~, b) stimulation with constant current 90 μA, and c) stimulation with constant current 130 μA. Sham stimulation was no-stimulation at the same location. A 5 min pause was introduced between the sessions. Stimulation perception was determined after each session with a three-level gradation questionnaire: 0 – no sensation, 1 – mild almost imperceptible sensation, and 2 – unpleasant, but non-painful 'tingling' sensation.

Stimulation was applied with transcutaneous constant electric current nerve stimulator (Mikromax ME1, Medikoel, Slovenia) using two clip mounted conductive rubber electrodes (diameter 5 mm) coated with conductive paste (Fig. 1). The first electrode was attached to the skin surface of the right ear cavum conchae area near the external auditory meatus and the second one to the outer tragus skin surface. An intermittent, duty cycle of one second "on" and one second "off", stimulation was performed to reduce the habituation effect and improve tolerability. The taNS protocol was adjusted from Stavrakis et al. (2015) in order to apply this protocol in patients with paroxismal atrial fibrillation in future. Stimulation was a train of positive rectangular pulses of 2 ms duration and frequency of 20 Hz. The current intensity was regularly checked. The ECG, non-invasive BP and thoracic impedance cardiography data were recorded continuously with the Task Force® hemodynamic Monitor (CNSystems Medizintechnik GmbH, Graz, Ver. 2.2.10.0, customer ID: 20040034) (Kubicek et al., 1966). Standard 6-lead extremity ECG was used for monitoring and recording of heart rate (HR or RR intervals). Continuous BP measurements, using the vascular unloading method from the third and fourth finger of the left hand, were automatically corrected to oscilometric brachial BP values obtained from the right arm (error ± 5 mmHg). All bio-signals were recorded in 16-bit resolution with a sampling frequency of 1000 Hz. Parameters of left ventricular (LV) contractility (acceleration index — ACI ($100/s^2$)), LV output (stroke volume – SV (mL), stroke index – SI (mL/m^2), cardiac

Fig. 1. We used two clip mounted conductive rubber electrodes attached to the inner skin surface of tragus/cavum conchae area, near the external auditory meatus, and outer tragus skin surface of the right ear. For better skin contact a conductive paste was applied and the clip was secured with adhesive tape.

output — CO (L/min),and cardiac index – CI (L/min m^2)), LV work – LVW (kg m) and LVW index – LVWI (kg m/m^2), and total peripheral resistance – TPR (dyne s/cm^5) and TPR index – TPRI (dyne s m^2/cm^5), were analysed off-line (Fortin et al., 1998, 2006). The time-domain analysis was performed for: HR (beats/min), RR intervals (ms), systolic BP (sBP), diastolic BP (dBP), and mean BP (mBP), all in mmHg.

The power frequency-domain spectra of heart rate dynamics were analysed by the fast Fourier transform of instantaneous RR intervals as HR variability power (ms^2). Power spectral analysis was calculated for: low frequency spectrum (LF-RRI: 0,04–0,15 Hz), and high frequency spectrum (HF-RRI: 0,15–0,4 Hz) (Malik and Camm, 1993). All parameters were analysed for two 10-minute periods of each 20-minute sham and two stimulation sessions.

For the integral responses with predominant sympathetic over parasympathetic modulation were considered increases of: ACI, SV (SI), LVW (LVWI), TPR (TPRI), HR, and BP. Responses with predominant parasympathetic over sympathetic modulation were considered decreases of: SV (SI), LVW (LVWI), TPR (TPRI), HR and BP, and an increase of HF-RRI. The marker of sympatho-vagal balance was considered quotient LF/HF-RRI. The decrease of this quotient would reflect the parasympathetic predominance (Malik and Camm, 1993).

All datasets were gathered, stored and analysed on PC HP Compaq using CNSystems software (Ver. 2.2.10.0). The Anderson-Darling and Kolmogorov-Smirnov normality tests were performed before statistical analysis. For descriptive statistics Excel software (version 16.0.10382.20010) was used. The first 10-minute and the second 10-minute average values of each session (mean, standard deviation of mean – for normally distributed data; median, 25–75% rank – for non-normally distributed data) were evaluated and presented. A minimum of 32 subjects was necessary to ensure that the power of the test was 80% to detect the 0.3 L difference between the known and estimated mean of cardiac output. For normally distributed data, two-tailed t-test for unpaired and paired samples and one-way ANOVA for repeated measurements were used. The Mann-Whitney test, Wilcoxon's matched-pairs signed-rank test and Friedman test were carried out for non-normally distributed data using GraphPad Prism statistical software (version 9.4.1.681). Value $p < 0.05$ was considered significant.

Results

The obtained results are listed in Table 1 and significant data for all measurements are also presented in Figs. 2 and 3. Data are average values of all cardiac beats from two 10-minute periods for each session (sham, 90 μA, and 130 μA, respectively). Finally, 44 measurements were available for women and 46 for men. Normally distributed data were for HR, BP, and SV (mean and SD) and non-normally distributed data were for ACI, CO and variability parameters (median and 25–75% percentile

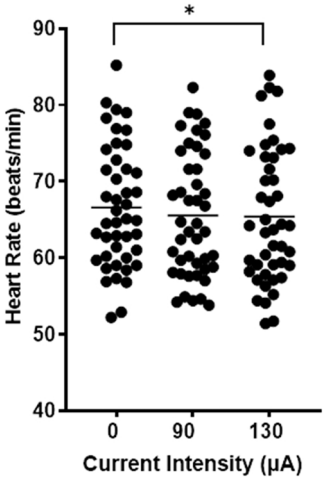

Fig. 2. We demonstrated small but statistically significant drop of heart rate at 130 μA right tragus stimulation in women only ($p = 0.047$).

Table 1
Aggregate data for transcutaneous auricular nerve stimulation in young women and men during random sequence of no-stimulation (0 μA, sham), 90 μA stimulation, and 130 μA stimulation.

Current intensity		0 μA	90 μA	130 μA	p value
***Heart Rate (beats/min)**	**F** (n = 24)	67 (7.9)	66 (8.1)	65 (8.8)	**0.047 (0–130 μA)**
	M (n = 26)	64 (7.6)	65 (8.2)	64 (8.1)	NS
	All	65 (7.8)	65 (8.1)	65 (8.4)	NS
***Arterial Blood Pressure (mmHg)**					
Systolic	F (n = 24)	108 (9.5)	109 (9.3)	108 (11)	NS
Diastolic	M (n = 26)	119 (12)	118 (11)	118 (13)	NS
Mean	All	113 (12)	113 (11)	113 (13)	NS
	F (n = 24)	69 (7.8)	69 (8.5)	70 (9.8)	NS
	M (n = 25)	73 (7.8)	73 (7.4)	74 (9.1)	NS
	All	71 (8.9)	71 (8.1)	72 (9.5)	NS
	F (n = 24)	85 (9.8)	86 (8.7)	86 (10)	NS
	M (n = 25)	91 (8.7)	90 (8.6)	91 (10)	NS
	All	88 (9.0)	88 (8.9)	88 (10)	NS
***Stroke Volume (mL)**	F (n = 24)	97 (22)	97 (21)	97 (22)	NS
	M (n = 26)	103 (20)	102 (20)	101 (20)	**0.039 (0–90–130)**
	All	100 (21)	99 (21)	99 (21)	NS
* ***Acceleration Index (100/s^2)**	F (n = 24)	112 (83–122)	108 (82–120)	107 (79–124)	NS
Median (25–75%)	**M** (n = 25)	77 (64-90)	74 (64–100)	75 (61–94)	**0.041 (0–90–130)**
	All	87 (70–117)	92 (71–116)	88 (68–113)	NS
* ***Cardiac Output (L/min)**	F (n = 24)	6.3 (5.4–7.7)	6.1 (5.5–7.0)	5.9 (5.3–7.2))	NS
Median (25–75%)	M (n = 26)	6.3 (5.6–7.5)	6.4 (5.4–7.4)	6.0 (5.4–7.1)	NS
	All	6.3 (5.5–7.6)	6.1 (5.5–7.3)	6.0 (5.4–7.2)	**0.011 (0–130 μA)**
* ***HF-RRI**	F (n = 24)	642 (232–1508)	838 (192–1930)	728 (183–1946)	NS
Median (25–75%)	M (n = 26)	648 (360–1012)	723 (406–940)	656 (366–1313)	NS
	All	645 (344–1319)	732 (322–1559)	635 (278–1559)	NS

Data are 10-minute mean values* (standard deviation of mean) for normally distributed data and 10-minute median values* * (25–75% percentile range) for non-normally distributed data. Only significant p values are displayed in bold.
F – female; M – male; LV – left ventricle; HF – high frequency power spectrum; RRI – interval between R waves; NS – non-significant
*Calculated by one-way ANOVA for repeated measurements or paired t-test for normally distributed data
* *Calculated by Friedman or Wilcoxon's matched-pairs signed-rank test for non-normally distributed data

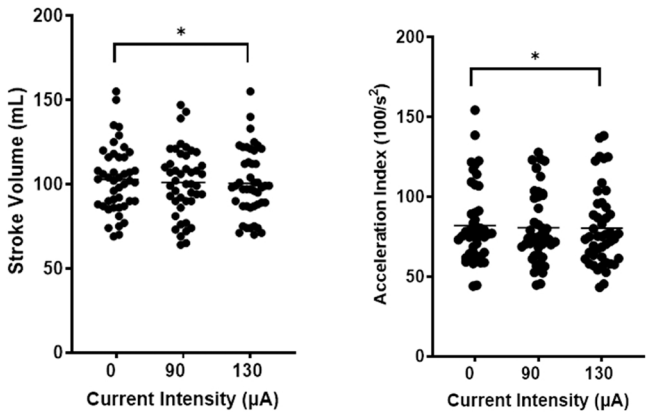

Fig. 3. We demonstrated small but statistically significant drop of stroke volume ($p = 0.039$) and acceleration index ($p = 0.041$) at 130 μA right tragus stimulation in men only.

range). For pooled data, a statistically significant CO decline at 130 μA was demonstrated, compared to no-stimulation ($p = 0.011$); with non-significant decline at 90 μA (Table 1). This was related to significant HR drop in women ($p = 0.047$) (Fig. 2) and SV ($p = 0.039$), and ACI ($p = 0.041$) in men (Fig. 3). No significant stimulation effects were seen with respect to BP, LVW, TPR and spectral variability parameters.

There were significant differences in body size between men and women (height: 183 cm vs. 169, weight: 79 kg vs. 62, body surface area: 2.0 m^2 vs. 1.7, respectively; $p < 0.001$), as well as significant gender-related differences in some hemodynamic parameters. Blood pressure was significantly higher in men than in women at baseline and during stimulation ($p < 0.05$) (Table 1). The scaled values, like CI, ACI and SI, were significantly higher in women than men and were attributed to large differences in body size. Therefore, we avoided gender-related evaluation of scaled data. Similarly, TPRI was significantly higher in men ($p < 0.01$) due to significantly higher mean BP in men.

Regarding the stimulation perception, 26 out of 50 (52%), and 32 out of 49 (one missing value, 64%) reported mild sensations with 90 μA stimulation, and 130 μA stimulation, respectively. Tingling sensation was reported by one man during 90 μA stimulation, and 5 men and one woman during 130 μA stimulation. Notably, five examinees out of 50 (10%) reported mild sensation also with no-stimulation, probably due to electrode clip compression.

Discussion

The main finding of this study is demonstrated decline of cardiac output with right tragus taNS, reaching statistical significance at 130 μA stimulation, compared with no-stimulation ($p = 0.011$). The decline was driven by a significant drop of heart rate in women and ventricular contractility (ACI) and stroke volume in men ($p < 0.05$, Table 1, Figs. 2 and 3). Variability parameter HF-RRI increased during 90 μA but did not reach statistical significance (Table 1). These findings suggest a predominance of parasympathetic cardiac modulation over sympathetic and therefore potentially beneficial neuromodulatory outcome. Importantly, no other variability or hemodynamic responses attributed to sympathetic predominance were detected and the protocol was well tolerated by majority of participants. Therefore, it seems that the low-level taNS protocol tested in this study has a potential for clinical application.

It seems that the stimulation intensity of taNS is in correlation with evoked autonomic responses. With low-level stimulation, parasympathetic predominance may have been expected due to parasympathetic activation or sympathetic withdrawal. The decreases of heart rate, stroke volume and ventricular contractility as demonstrated in this study (Figs. 2 and 3) are in favour of this speculation. With more intense stimulation protocol (e.g. continuous stimulation for 60 min, up to 150 μA), a significant increase of blood pressure had been encountered and attributed to reflex sympathetic activation (or parasympathetic withdawl) (Sinkovec et al., 2021). Nevertheless, the low-level stimulation protocol tested in this study might be in the therapeutic range for optimal autonomic nerve stimulation suggeted by Ardell et al. (2017), Kember et al. (2014). Further studies in specific patient groups are needed to prove this indicating hypothesis.

Borges et al. (2019) investigated the effects of different taNS stimulation intensities as well as different stimulation methods delivered, with a pulse width of 0.2–0.3 ms, at 25 Hz, and an on–off cycle of 30 s. They found an increase in cardiac vagal activity from resting to at least one of the stimulation phases. Inversely to our speculation, this increase was general and thus not dependent on the different stimulation intensities or methods used to determine them, including the comparison between active and sham stimulations. However, the stimulated area was the cymba conchae of the left ear and the sham protocol was stimulation on the earlobe. Recently, Gauthey et al. explored, in a group of young healthy men, the right cymba conchae stimulation responses on peripheral sympathetic outflow, using microneurograpy (MSNA) (Gauthey et al., 2020). The stimulation was based on sensory treshold and was delivered for 10 min with a pulse width of 0.2 ms. They compared cymba stimulation-20 Hz to active control (earlobe stimulation-5 Hz) in crossover trial with randomly allocated stimulation sequences. Significant reduction of MSNA burst frequencies from baseline were documented during active as well as sham earlobe stimulations. They concluded that cervical somatosensory pathways may also be involved during taNS. This observation was confirmed in the rat model (Mahadi et al., 2019). The cardiovascular autonomic effects of taNS via the tragus involved also spinal cervical sensory afferent pathways. It seems that vagally mediated stimuli would compete with incoming pain stimuli, or may trigger non-specific reflexes that activate pain inhibition (e.g. pain related trigeminal nerve – central sympathovagal inhibitory response). Therefore, the sham protocol of no-stimulation as we used in this study, would be more appropriate. In addition, the number of different afferent A axons of auricular branch of vagus nerve as well as other neural networks, connections, hijacking axons from cranial nerves and cervical sympathetic ganglions, the inhomogeneous distribution of perivascular sympathetic nerves, and intrinsic/extrinsic auricular muscles in the auricular zone varied greatly between individuals, explaining why some individuals demonstrate divergent taNS responses (Cakmak, 2019). These data clearly illustrate the challenges in current research on taNS and difficulties in the protocol standardization. We therefore changed the terminology from "auricular vagus nerve stimulation" to "auricular nerve stimulation".

Although non-significant, the gender-related differences in some hemodynamic responses at 130 μA stimulation are demonstrated. It seems that women responded primarily through the sinus node autonomic modulation (e.g. heart rate) and men through the ventricular contraction. Gender related differences in cardiovascular autonomic modulation have already been described. Joyner et al. reported that women have lower resting sympathetic activity than young men (Joyner et al., 2015). Women also, differently than men, responded to orthostatic stress (Fu et al., 2004). And finally, men regulate blood pressure through different physiological processes than women – with young women generally showing enhanced parasympathetic (vagal) input to cardiac regulation, compared to the predominance of sympathetic vascular regulation observed in men (Hart et al., 2011; Reulecke et al., 2016).

We have demonstrated also some baseline gender related differences. Arterial blood pressure was significantly higher in men ($p < 0.05$). In addition, stroke volume was somewhat higher in men than women ($p = NS$). It has long been recognized that young women have in general, lower resting arterial blood pressure, stroke volume, and cardiac output (Joyner et al., 2015). These differences may partially be explained by differences in autonomic regulation (Joyner et al., 2015;

Fu et al., 2004; Hart et al., 2011; Reulecke et al., 2016). Second, estrogen mediated central sympathetic inhibition and peripheral beta-2 mediated vasodilatation in young women cannot be neglected (Joyner et al., 2015). It should be pointed out that both sexes show marked inter-individual variability of cardiovascular parameters with significant overlap seen. According to some gender related differences, women and men ought to be investigated separately (Reulecke et al., 2016).

With increasing stimulation intensity, up-to two-thirds of our examinees reported some kind of local perception, becoming in 10% unpleasant at 130 μA stimulation. Therefore, individualized small adjustments of current intensity would have been necessary for clinical application.

Another opportunity for protocol optimization is respiratory synchronization of taNS, since respiration influences nucleus tractus solitarii (NTS) activity. Exhalation-gated and non-respiratory-gated taNS exerted cardioinhibitory effects in healthy subjects, whereas inhalation-gated taNS did not affect heart rate (Paleczny et al., 2019). This finding has been confirmed by 7 T fMRI study (Sclocco et al., 2019). The auricular taNS (cymba conchae) delivered during exhalation enhanced response of ipsilateral area of NTS, compared to inhalation-gated or ear-lobe exhalation stimulation (control), and induced cardiovagal modulation.

There are some limitations of the present study. No clear consensus exists on the auricular sites that are most densely innervated with auricular brunch of vagus nerve. At present, concha and inner tragus are suggested as suitable locations for taNS (Butt et al., 2020). The laterality of taNS may not have been that important in comparison with direct vagus nerve stimulation, since taNS exerts more balanced cardiac autonomic effects as mentioned previously (Armour, 2008; Ardell et al., 2016, 2017). Even bilateral taNS has been shown to be safe as demonstrated by He et al. (2013). Another limitation may be the inclusion of sham protocol at the same visit as the interventions, since stimulation response may still have been present during next session as the carry-over effect and therefore blurring the differences. A 5-minute pause introduced between the sessions and no laborious threshold adjustments performed at the beginning may have diminished this bias to some extent. More appropriate would be that sham and interventions are performed randomly on different days. The third limitation may be small sample size when divided for gender comparisons. However, the homogeneity of the sample and the paired statistical testing approach assured a reasonable power for the concept verifying results. In addition, gender comparisons were not the primary objective of this study. Furthermore, non-invasive determination of cardiac output and contractility parameters with impedance cardiography does require cautious interpretation. The estimation of electrical participating thoracic volume depends importantly on the subject's body size and composition, shape of the thorax, and position of the heart. The transthoracic impedance cardiography is therefore best applied to evaluate changes within a subject during acute interventions, as we considered in this study, rather than comparing absolute values. It should be pointed out that TPR is a calculated variable (from mean BP and CO), and it is the absolute value of CO which contributes directly to BP and not the scaled value for the body surface area (Joyner et al., 2015). In addition, the difference in body size between men and women was in our study substantial. Therefore, we avoided scaling of the most measured parameters as we mentioned previously. Another limitation of our and other studies is selection of healthy young examinees. The extent of taNS responses that might be observed in some patient groups, sedentary or older populations which characteristically have different parasympathetic modulatory capacity seems likely to be different. Recently, taNS responses in elderly have been reported by Bretherton et al. (2019). They investigated a group of healthy volunteers aged over 54 years. The taNS was performed 15 min daily for two weeks (sensory threshold, tragus stimulation, pulse width of 0.2 ms, at 30 Hz). The results were promising. After treatment, measures of autonomic function, and some aspects of quality of life, mood and sleep improved. Improvements were more pronounced in participants with greater baseline sympathetic prevalence. Another interesting study from Tran et al. (2019) was reported (Tran et al., 2019). They evaluated acute effects of taNS (20 Hz, low-level, right tragus) on LV function and autonomic tone in a small heterogenous group of patients with diastolic dysfunction and preserved LV ejection fraction. LV global longitudinal strain significantly improved and low and high frequency heart rate variability parameters altered in the direction of parasympathetic predominance. This result may have been in conflict with our result of stroke volume and ACI reduction in male examinees. Some parameters of stimulation were however different (one-hour stimulation against 20-minute, 0.2 ms pulse width against 2 ms) as well as the responses to taNS may have been different in patients compared to healthy examinees. In addition, LV strain parameters are particularly suited for the assessment of regional contractile function, being an early systolic event that is more closely related to contractility than the ejection fraction which we measured by thoracic impedance volumetry (Dandel et al., 2009). An interesting case report has been published recently in a patient with congestive heart failure with preserved ejection fraction (Nagai et al., 2022). The left ear tragus taNS was performed that resulted in an acute ipsilateral renal decongestion due to dramatic improvements in renal venous flow and consequently on right ventricular function, possibly due to supression of sympathetic renal activity and reduction of right ventricular filling pressure. Since we did not find any sympathetic response in our examinees, it is possible that parasympathetic predominance was due to sympathetic withdrawal. Nevertheless, these data are intriguing and suggest the direction of future research.

Conclusion

In conclusion, it seems that the applied low-level transcutaneous constant current stimulation, targeting the auricular vagus nerve area at the right cavum conchae-tragus location, has a potential for beneficial cardiac autonomic modulation. It seems that slight individual current intensity adjustments would be necessary for clinical application. Further studies are however needed to prove the therapeutic potential of this stimulation protocol in different patient groups.

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