Rhythmic sensory stimulation improves fitness by conditioning the autonomic nervous system

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Background. Endurance training is known to alter the functioning of the autonomic nervous system, a major goal when pursuing fitness. Here, we test the hypothesis that the training-associated rhythmic sensations alone, hence without the usual accompanying physical exercise, accomplish this effect.

Method. We studied sixteen resting healthy male volunteers, age (mean±SD) 25.9±3.7 years. During one hour we applied, at marching pace (2 bursts per second), bipolar transcutaneous electrical sensory nerve stimulation to both feet. The stimulation intensity was controlled in such a way that discharges of sensory fibres in the tibial and fibular nerves were induced, while motor fibres were not excited. Heart rate, blood pressure, and baroreflex sensitivity were measured before and after stimulation.

Results. Baseline baroreflex sensitivity and systolic blood pressure were 8.7±4.5 ms·mmHg-1 and 117.5±6.4 mmHg, respectively. Directly after rhythmic sensory stimulation baroreflex sensitivity had increased to 10.0±4.1 ms·mmHg-1 ($p<0.05$). One day later, systolic blood pressure had lowered to 111.7±5.5 mmHg ($p<0.01$).

Conclusions. Rhythmic sensory stimulation entails autonomic adaptations that are comparable with those of exercise. This demonstration of sensory-induced autonomic adaptations without any muscular involvement may help to design alternative, low-effort fitness programmes for specific categories of sedentary, diseased or disabled persons. (*Neth Heart J* 2002;10:43-7.)

Key words: arterial baroreflex, autonomic, blood pressure, nervous system, physical fitness, transcutaneous electric nerve stimulation

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Government and health authorities widely promote fitness programmes for primary and secondary prevention.[1,2] Regular physical exercise (endurance training) is considered a prerequisite for achieving and maintaining fitness. Weeks to months of endurance training are needed to achieve structural or complex functional changes like an increase in the maximal oxygen consumption.[3] Earlier (after days to weeks) functional effects of training are a decrease in resting heart rate,[4] resting blood pressure,[5] and an increase in resting arterial baroreflex sensitivity (BRS).[5,6]

Regular exercising should preferably be part of everyone's lifestyle. Impediments are lack of compliance in the healthy, reduced exercise tolerance in the ill and the fact that exercise is impractical in the disabled. Identification of the mechanism through which exercise induces the desired autonomic adaptations may help to develop alternatives. Andersson and Lundeberg[7] noticed how remarkably the effects of rhythmic sensory stimulation and endurance training resemble each other. Both entail the production of endogenous opioids and oxytocin, substances that modulate autonomic nervous system function by the hypothalamic β-endorphinergic system. Endurance training implies rhythmic, repeated actions, and it is tempting to postulate that the attained autonomic changes are basically the result of the rhythmic sensations, instead of the exercise itself. In the study reported here, we aim to demonstrate this non-invasively in humans.

Subjects and methods

The protocol of this study was approved by the Leiden University Medical Centre Ethics Review Committee, and the procedures followed were in accordance with

the Helsinki Declaration. We studied, after they had given their informed consent, a group of 16 healthy male subjects, age (mean±SD) 25.9±3.7 years.

The protocol consisted of three sessions: the first session on day A-1, the second one on day A, and the third one on day B. Measurement sessions were between 9 am and noon. During all three sessions the subjects lay on a bed, in a supine position. Electrode pairs for bipolar stimulation of both feet were attached and tested according to the procedure indicated in figures 1-3.

After testing, the electrodes were fixated with extra tape, and the subjects rested for 30 minutes. During that period (for sessions A and B), ECG electrodes (leads I, II, and V_3) were attached. Two extra electrodes were applied to the lateral sides of the lower part of the thorax in order to monitor respiration (impedance method). The finger cuff of a continuous noninvasive arterial blood pressure measurement device (Finapres, Biomedical Instrumentation Research Unit TNO, Academic Medical Centre, Amsterdam[8]) was attached around the second phalanx of the left middle finger. The arm cuff of an automatic sphygmometer (Accutorr 3, Datascope Corp., Montvale, NJ, US) was attached around the right upper arm.

After 30 minutes of rest, 60 minutes of sensory stimulation was applied to the feet, at marching pace (two stimuli per second, figure 3).

On days A-1 and A, there was a one-hour sensory stimulation. On day B there was 'sham-stimulation'

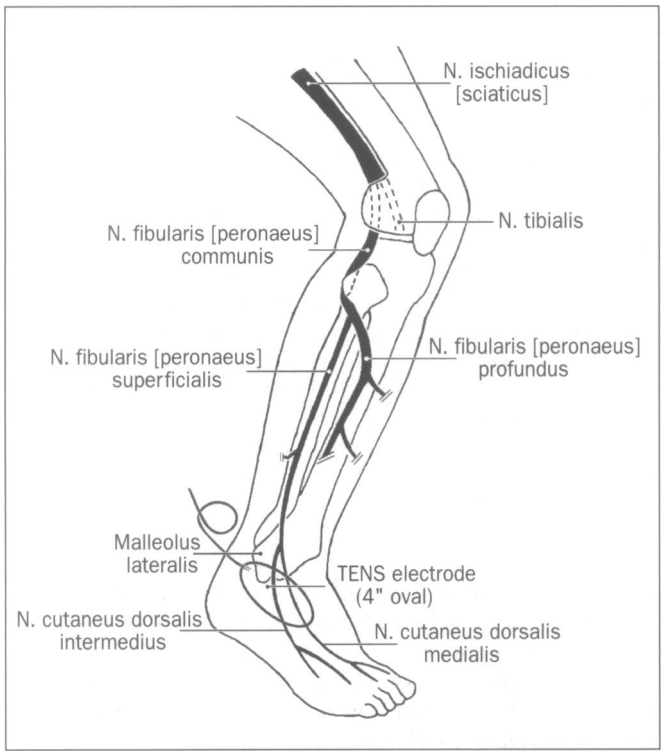

Figure 1. Lateral stimulation electrode. Anterolateral view of the right leg, ankle, and foot, with the position of the anterolateral stimulation electrode indicated (TENS=transcutaneous electrical nerve stimulation). A similar electrode is symmetrically placed on the left foot. The 10 cm foam oval electrode (AdvanTeq, Westlake Village, CA, US) for transcutaneous electrical nerve stimulation covers the two main branches of the peroneal nerve (N. fibularis superficialis). This is a mixed nerve, with afferent sensory fibres, and efferent sympathetic and motor fibres. At adequate stimulation intensities, A-α and A-β[25] sensory fibres are excited which gives rise to distinct sensations, while motor fibres are still not excited.[26] The sensory fibres that run under the electrode convey information from major areas of the dorsal part of the foot. With the stimulus that we apply (figure 3), this electrode induces sensations that can be described as the touching, stroking, or scratching of the upper part of the foot. The electrode has adhesive gel, and can be applied a number of times on a clean, dry, skin. Prior to the start of a session, we verify the correct application of the electrode: if needed several variant nearby positions around the indicated position are probed until the stimulated person experiences the sensations described above. Drawing based on, and modified from, Stuart JD, Aguayo AJ: Compression and entrapment neuropathies. In: Dyck PJ, Thomas PK, Lambert EH, Bunge R, Eds. Peripheral neuropathy, Edition 2. Philadelphia, WB Saunders, 1984: 1448.

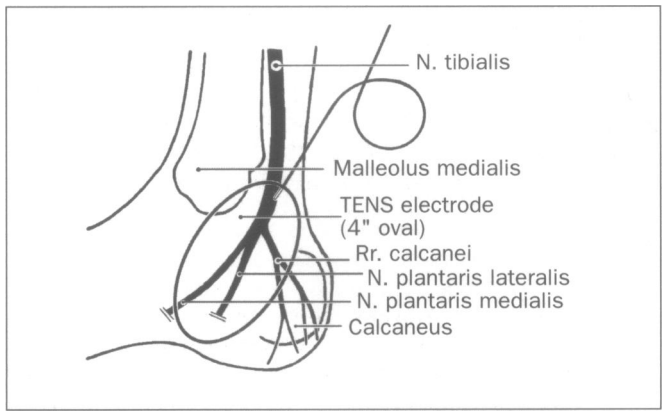

Figure 2. Medial stimulation electrode. Medial view of the right ankle and foot, with the position of the medial electrode indicated (TENS=transcutaneous electrical nerve stimulation). A similar 10 cm foam oval electrode is symmetrically placed on the left foot. The electrode is positioned above branches of the tibial nerve (N. tibialis) that innervate the heel and the plantar part of the foot. Like the peroneal nerve (figure 1), the tibial nerve is a mixed nerve. At adequate stimulation intensities, the sensory fibres are excited, while motor fibres are not or barely.[26] With the stimulus that we apply (figure 3), this electrode induces sensations that can be described as the touching, stroking, or scratching of the heel and the sole of the foot. Prior to the start of a session, several variant nearby positions around the indicated position are probed until the stimulated person experiences the above-described sensations. Electrical stimulation is two-lead bipolar (using the medial and anterolateral electrode on the same foot as a pair). In this way, current remains confined to a limited part of the feet. Drawing based on, and modified from, Stuart JD, Aguayo AJ: Compression and entrapment neuropathies. In: Dyck PJ, Thomas PK, Lambert EH, Bunge R, Eds. Peripheral neuropathy, Edition 2. Philadelphia, WB Saunders, 1984: 1448.

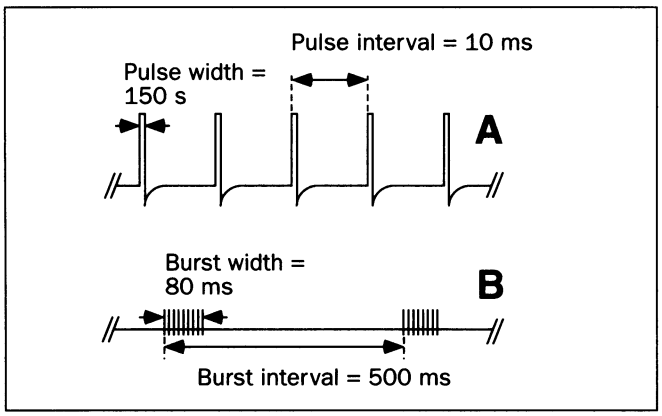

Figure 3. Electrical stimulation parameters. The two-lead, bipolar stimulation unit was an in-house modified version of Kit 866 (Magenta Electronics LTD, Burton-on-Trent, Staffs., UK). Modifications were made to make pulse rate, pulse width and burst width adjustable, and a balance between leads was added to facilitate symmetrical left-right stimulation. Pulse rate was set at 100 Hz (panel A), pulse width at 150 υs (panel A). Pulses in panel A have been drawn wider than in reality, to show the pulse shape. The trailing negative part of a pulse neutralises the preceding narrow positive part; total current is zero. The rhythmic sensation is attained by gating the pulse train during 80 ms, twice per second (panel B). Each gated burst consists of nine pulses in succession. The subject controls pulse amplitude. Prior to the start of a session the stimulation amplitude is slowly increased until the sensations become unpleasant, or muscle movements are induced. Then, the amplitude is reduced to a comfortable level. During the one-hour long stimulation period the amplitude is increased from time to time to compensate for adaptation effects.

only. This was achieved by including 10-megohm resistances in the electrode circuits, after the initial testing procedure (see legend of figure 1). This made electrostimulation too weak to provoke any sensation (the subjects was told that they received potentially effective subthreshold electrical stimulation).

Session B was held between one and three months after session A. Assuming that after such a long period, effect of sensory stimulation can no longer be observed, we may call session B the control session. Session A is called the stimulation session. Initial session A heart rate, blood pressure, and BRS values, before sensory stimulation was applied, reflect the long-term, 24-hour effect of the stimulation on the previous day. Re-measurement of these values after application of one hour TENS reveals the acute effect of this stimulus.

Preceding and following the one-hour stimulation episode, three arm cuff blood pressure measurements were recorded and averaged, and the subjects performed 15/minute metronome respiration for a total of four minutes at a freely chosen breathing depth. The ECG and the finger blood pressure obtained during metronome respiration were used for later baroreflex sensitivity calculation.[9] On day A-1 the subjects came to our hospital to become familiarised with the investigational procedure and to become conditioned for the next day by the same one-hour electrostimulation that they would then be receiving. Maximal oxygen consumption was measured by bicycle ergometry after the day A session was concluded. No conditioning or extra measurements were done in relation to day B.

Results

The results of the control and the stimulation session have been summarised in table 1. There were no significant differences between the initial and final measurements in the control session. The immediate effect of one hour of rhythmic sensory stimulation was, apart from a limited blood pressure increase (systolic 3.6 mmHg), a 15% increase in baroreflex sensitivity from 8.7 to 10.0 ms·mmHg-1. We assessed the delayed, 24-hour effect of one hour of rhythmic sensory stimulation by comparing the initial values of the

Table 1. Results of the measurements in 16 subjects.

	Control		Stimulation	
	Before	After	Before [1)]	After [2)]
Heart rate (bpm)	66.7±8.4	67.6±9.3	68.0±7.6	66.6±7.9
Systolic blood pressure (mmHg)	117.5±6.4	117.7±6.1	111.7±5.5**	115.3±7.4**
Diastolic blood pressure (mmHg)	65.9±7.5	66.6±6.7	62.8±6.5	65.4±5.3*
Mean blood pressure (mmHg)	85.3±7.0	86.2±6.4	82.1±4.7*	84.5±5.5**
Baroreflex sensitivity (ms·mmHg-1)	8.9±3.6	9.3±3.7	8.7±4.5	10.0±4.1*

Results (mean plus or minus standard deviation) of the measurements in 16 subjects, done in the stimulation session and in the control session. Symbols and abbreviations: 1. asterisks in the 'Stimulation, Before' column denote significant differences with the 'Control, Before' values; 2. asterisks in the 'Stimulation, After' column denote significant differences with the 'Stimulation, Before' values; bpm=beats per minute; mmHg=millimeter mercury; ms·mmHg-1=milliseconds per millimetre mercury; *=significantly different (paired t-test, $p<0.05$); **=significantly different (paired t-test, $p<0.01$). Main findings were that immediately after one-hour electrical sensory stimulation blood pressure was slightly increased, while baroreflex sensitivity rose by about 15% (comparison of the 'Stimulation, Before' and the 'Stimulation, After' values). The long-term effect is a substantial blood pressure lowering (comparison of the 'Control, Before' and the 'Stimulation, Before' values).

control and the stimulation sessions. Blood pressure lowered strikingly: the systolic blood pressure fell by 5.8 mmHg.

Discussion

Ambulatory blood pressure measurements have made clear that blood pressure is demonstrably lower until 24 hours after acute exercise.[10] We demonstrated that 24 hours after application of the rhythmic sensory stimulation protocol blood pressure was also lower. This suggests that the potency of the sensory stimulation stimulus is comparable with that of an exercise session. Indeed, we studied healthy young men, most of them engaged in recreational sports activities, with corresponding maximal oxygen consumption values of 41.1 ± 8.9 ml $O_2 \cdot min\text{-}1 \cdot kg\text{-}1$. As opposed to inactive healthy or diseased[10] persons, this group had no lack of rhythmic sensory input, and, consequently, no substantial long-term effects would be expected. The finding of a lowered blood pressure in healthy young persons 24 hours after rhythmic sensory stimulation underscores the efficacy of the stimulation protocol. A distinct response in healthy subjects indicates that rhythmic sensory stimulation has substantial potential for purposes like primary prevention.

Afferents from somatosensory receptors located on the body surface, in joints and in muscles, converge in the lower brainstem. Sensory stimulation at different parts of the body might, therefore, yield similar effects.[11] There are two studies in humans regarding the effect of rhythmic sensory stimulation on blood pressure with unilateral stimulation of one hand. In these two investigations (in cardiac patients during catheterisation,[12] and in untreated hypertensives[13]) stimulation intensity was increased until local rhythmic movements of the fingers occurred. In contrast, we performed pure sensory nerve stimulation, thus avoiding any muscular involvement.

To our knowledge there are no animal or human studies about the effect of rhythmic sensory stimulation on baroreflex sensitivity. The functional importance of the arterial baroreflex[6] is to be found in the dampening of cardiovascular reactivity. Many stressors tend to elevate blood pressure and heart rate. Due to the increased blood pressure pulsations, the stretch receptors ('baroreceptors') in the aorta and in the sinuses of the carotid arteries intensify their beat-to-beat neural firing pattern. This information travels through the vagus and glossopharyngeal nerves to the vasopressor centre in the lower part of the brain, the medulla oblongata, where a reflex response is generated in the form of inhibition of the sympathetic autonomic activity plus enhancement of parasympathetic autonomic activity. This, in turn, reduces the initial rise in blood pressure and heart rate.

Baroreflex sensitivity (the efficacy of the arterial baroreflex) is expressed as the reflex-induced prolongation of the interval between heartbeats per unit increase of systolic blood pressure induced by the primary challenge (e.g., muscular effort, mental stress, cold). It has been demonstrated that the baroreflex remains active during exercise,[14] and that a single training session already increases baroreflex sensitivity.[15] In contrast, baroreflex sensitivity decreases when a training programme is interrupted,[16] or after a long period of bed rest.[15,17] Patients confined to wheelchairs have a lower baroreflex sensitivity than matched control subjects.[18] It has been demonstrated that higher baroreflex sensitivity values are associated with improved survival after acute myocardial infarction.[19]

The clinical relevance of the arterial baroreflex sensitivity is obvious from its physiology. An important effect of the arterial baroreflex is the negative feedback loop from blood pressure to blood pressure, effectuated by sympathetic control of vascular resistance. If arterial blood pressure rises, the sympathetic outflow decreases. This results in a lessening of α-adrenergic vasoconstriction. This decrease in peripheral resistance counteracts the rise in blood pressure. Mutatis mutandis, a fall in arterial blood pressure, is counteracted by an increase of peripheral resistance. Hence, the arterial baroreflex buffers blood pressure.

Also, by parasympathetic and sympathetic control of the heart, the heart rate and the electrophysiological and mechanic properties of the cardiac muscle are influenced or modulated by the arterial baroreflex.[20] An arterial blood pressure rise causes a decrease in sympathetic outflow and an increase in parasympathetic outflow. These reciprocal changes in the sympathetic and parasympathetic outflow decrease heart rate and cardiac contractility. Together with the mentioned effect on peripheral resistance, this helps to limit the blood pressure change. However, changes in atrial and ventricular electrophysiology may also contribute to arrhythmogenesis or protect against arrhythmias, depending on the substrate under consideration.[21] Also, the arterial baroreflex, by limiting the rate-pressure product, limits changes in myocardial oxygen consumption, which may be relevant in ischaemic hearts.

Our finding of an acute increase in baroreflex sensitivity after rhythmic sensory stimulation opens a new perspective to intervene with this protective functional property of the autonomic nervous system. Our bipolar electrical stimulation protocol on the feet is practical and safe, and the acute blood pressure and heart rate changes due to one hour of rhythmic sensory stimulation remain limited to values also seen with light mental or isometric stress.[22] Portable electrostimulation devices and reusable adhesive electrodes, usually applied for analgesia and for muscular toning, are commercially available and inexpensive.

In conclusion, the novel finding of a short-term baroreflex sensitivity increase and a long-term blood pressure lowering after rhythmic sensory stimulation in humans strongly supports the concept that rhythmic sensory stimulation is a major conditioning stimulus for

the autonomic nervous system. This principle may help in the design of new training programmes for healthy sedentary persons or patients forced to a sedentary lifestyle (for example due to old age,[23,24] handicaps, or to congestive heart failure). In such programmes the accomplishment of rhythmic sensations (by means of electrostimulation or otherwise) should prevail over the aim of exercising at a target heart rate or energy expenditure. The potential beneficial impact of rhythmic sensory stimulation on blood pressure and on cardiovascular reactivity warrants further study. ■

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