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Veränderungen der Herzratenvariabilität (HRV) während Low Level Lasernadelakupunktur

Placebokontrollierte Studie an 19 herzgesunden Voluntary subjecten Changes in heart rate variability (HRV) during low level laser-needle acupuncture

A Placebo controlled trial in 19 healthy subjects

Zusammenfassung

Hintergrund: Zahlreiche experimentelle und klinische Untersuchungen an Menschen und Tieren postulieren einen neurobiologischen Wirkmechanismus der Akupunktur, bei dem Schmerzsysteme, Neurohormone und Neurotransmitter moduliert werden. Dabei spielt das autonome Nervensystem (ANS) vermutlich eine wichtige vermittelnde Rolle.

Zielsetzung: Durch Messung der Herzratenvariabilität (HRV), einem nicht-invasiven Monitoring der ANS-Aktivität, sollten in vorliegender Studie mögliche akupunktur-induzierte Veränderungen des ANS erforscht werden. Die innovative Technologie der Lasernadelakupunktur bietet erstmals eine Stimulationsmethode, die den Anforderungen einer placebokontrollierten Akupunkturstudie gerecht wird.

Methode: 19 freiwillige herzgesunde Voluntary subjecten unterzogen sich in 3 jeweils 20-minütigen Sitzungen einer Placebo-, einer 1-Punkt- (Pe 6) und einer simultanen 3-Punkt-Lasernadelstimulation (Pe 6, Le 3, Dü 3), wobei die Reihenfolge der Sitzungen randomisiert war. Die vor, während und nach der Placebo-/Lasernadelapplikation über Powerspektralanalyse (FFT) ermittelten HRV-Daten für normalisierte HF (high frequency)- und LF (low frequency)-Power (nHF, nLF) und deren Quotient nLF/nHF wurden zu fünf verschiedenen Zeitpunkten miteinander verglichen und statistisch analysiert (ANOVA, repeated measures, $p < 0,05$).

Ergebnisse: Sowohl während der 1-Punkt- (Pe 6) als auch während der 3-Punkt-Lasernadelstimulation (Pe 6, Le 3, Dü 3) zeigten sich im Vergleich zur Placebobehandlung signifikante Veränderungen der ANS-Aktivität. Am deutlichsten war die Zunahme der nHF ($p < 0,05$ [Pe 6], $p < 0,0001$ [Pe 6, Dü 3, Le 3]) als Ausdruck einer vermehrten akupunkturinduzierten vagalen Aktivität.

Schlussfolgerung: Lasernadelakupunktur bewirkt bereits als 1-Punktstimulation (Pe 6) sowie als simultane 3-Punktstimulation (Pe 6, Le 3, Dü 3) signifikante Veränderungen der HRV im Gegensatz zur Placebobehandlung. HRV-Monitoring eignet sich zur Erforschung von akupunkturinduzierten Veränderungen des ANS und könnte in Zusammenhang mit Lasernadelakupunktur als Standard für weitere wissenschaftliche Akupunkturstudien etabliert werden, deren Bedarf noch hoch ist.

Abstract

Background: Experimental and clinical studies postulate a neurobiological mechanism of acupuncture by modulating central pain systems, neurohormones and -transmitters. It seems to be quite likely that the autonomic nervous system (ANS) plays an important mediating role in this neuromodulation.

Aim: In measuring heart rate variability (HRV), as a non-invasive approach to the ANS-function, the object of this study was to monitor probable acupuncture-induced changes of autonomic balance. The innovative technology of laser-needle acupuncture offers for the first time a stimulation method which fulfils the demands on a placebo-controlled acupuncture trial not requiring controversial sham acupuncture.

Method: 19 healthy voluntary subjects underwent 3 treatments in randomized sequence, consisting of placebo-, 1-point- (PC 6) and simultaneous 3-point- (PC 6, LR 3, SI 3) laser-needle-stimulation over 20 minutes. Before, during and after placebo-/verum laser-needle acupuncture, HRV-data for normalised HF(high frequency)- and LF(low frequency)-Power (nHF, nLF) and their quotient nLF/nHF obtained by power spectrum analysis (FFT), were measured and analyzed statistically at 5 different time points (ANOVA repeated measures, $p < 0,05$).

Results: During both verum applications, the 1-point- (PC 6) as well as the simultaneous 3-point- (PC 6, LR 3, SI 3) laser-needle stimulation, significant changes of the ANS-activity were found in comparison to the placebo application. The most significant modification of HRV was an increase of nHF ($p < 0,05$ (PC 6), $p < 0,0001$ (PC 6, LR 3, SI 3)) as an expression of growing vagal activity during acupuncture.

Conclusion: Laser-needle acupuncture causes in 1-point-stimulation (PC 6) as well as in simultaneous 3-point-stimulation (PC 6, LR 3, SI 3) significant changes in HRV in comparison to placebo application. HRV-monitoring seems to be a suitable approach in exploration of acupuncture-induced changes of ANS and could possibly be established in combination with laser needle acupuncture as a standard for further scientific and clinical acupuncture investigations which are greatly needed.

Schlüsselwörter

Herzratenvariabilität, Herzfrequenzvariabilität, HRV, Laser, Lasernadel, Akupunktur, Autonomes Nervensystem, ANS

Keywords

heart rate variability, HRV, laser, laserneedle, acupuncture, autonomic nervous system

Introduction

The effectiveness of acupuncture can be proved all over the world by numerous trials testifying to the increasing clinical importance of acupuncture in the Western world; however, its mechanism of action has not been completely understood as yet. All trials describe the neurobiological effects of acupuncture; no commonly accepted perception on the procedure and the involved pathways of this neurologic modulation exists. In a review, 79 trials on acupuncture were analysed relating to the postulated physiological effect of acupuncture. In whole, only 53 studies referred to it: 62 % of them spoke about neurochemical mechanisms (transmitters, neurohormones), 11% about regulation by the autonomous nervous system (ANS), 9 % about the effects on brain function, 6 % about local effects and 4 % about segmental effects on spinal level [1]. Probably, all these mechanisms represent partial aspects of the effect of acupuncture, and it is quite conceivable that, in this context, the ANS plays an important mediating role which should be systematically investigated. For this reason, the aim of the present analysis was to examine changes of the sympathetic and parasympathetic activity during and after acupuncture by measuring heart rate variability (HRV). The HRV measurement has been an accepted non-invasive method commonly proved in cardiology over the last 25 years and applied at first in the prognostics of cardiac mortality [2]. During the last ten years, HRV measuring has also been applied in other areas of human medicine to measure the activity of the ANS in different interventions [3, 4].

According to the consensus of the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology, the main frequency components - HF (high frequency) and LF (low frequency) - of the parasympathetic and sympathetic activity, differentiable by spectral analysis [5], can be associated. For instance, it has been proved that the HF power expressing vagus activity can be blocked by antropep infusions [6]. The LF power mainly corresponds to the sympathetic nervous system, but it additionally contains intermediate frequency components (MF) which should correspond to the baroreceptor mechanism and as a consequence does not just reflect the sympathetic activity, even if neglected in common analysis.

The innovative technology of non-invasive and thus pain-free laser-needle stimulation, offered for the first time the option to comply with the requirements of a placebo-controlled acupuncture trial, because we do not only apply a standardised stimulus pain-free, but participants in a trial cannot recognise if a laser-needle was activated.

The effectiveness of the laser-needle system was confirmed through different neuro-monitoring techniques, e.g. the measurement of the cerebral blood stream speed (pulse Doppler method) and brain metabolism (fMRT) in the context of different studies [7]. Besides, the *Neiguan* point (Pe 6) which has already been often examined in a scientific context, also under the aspect of HRV measurement [8, 9, 10, 11], further spasmolytic points, i.e. yang (sympathetic nervous system) and diffusing points like the *Taichong* point (Le 3) and *Houxi* (Dü 3) were selected in order to monitor whether a reduction of the sympathetic activity to be expected according to the TCM criteria in HRV monitoring can be verified.

Voluntary subjects and methodology

The study protocol was approved by the ethics commission of the Medical Association of Schleswig-Holstein. 19 voluntary subjects with healthy hearts and circulation (ten women, nine men; middle-aged $46,2 \pm 10,0$), who gave their written informed consent, were included. Participants suffering from heavy chronic pathologies and pregnant women were excluded.

All participants to the study underwent 3 treatments, one placebo application of a 1-point laser stimulation of Pe 6 and a 3-point laser stimulation of Pe 6, Le 3, Dü 3. The treatments were determined in randomised sequence using a casual number generator. The association with the treatments was balanced. Every treatment was carried out according to the same pattern, while the voluntary subjects did not know when an application was carried out and which application it was. After a 5-minute pause in the supine position, the first HRV measurement was carried out over 192 RR intervals in the supine position (Nerve Express System by Heart Rhythm Instruments). After that, the laser needles were applied on the skin using a special metal fastener on the acupuncture points Pe 6, Le 3 and Dü 3 (laser-needle system by Weberneedle®, starting performance on the diode 50 mW, by frequency modulations according to Reininger [12] 25 mW, infrared light area (810 nm), LaserSpot diameter 0,4 mm, performance thickness 19,9 W/cm², energy density per point 24 KJ/cm², energy quantity in total per session appr. 24 or 72 KJ/cm² [1-point or 3-point stimulation]).

During the 20-minute laser-needle application (activated = verum, inactivated = placebo) the HRV was measured in real time. In the process, new spectrograms were compiled for all the 192 RR intervals according to the heart frequency (HR), i.e. all two to four minutes. Subsequently, the spectrograms of five different points in time were respectively evaluated: 1. PRE (before the laser or placebo application), 2. BEG (first spectrogram during the laser or placebo application), 3. MID (the intermediate spectrogram during the laser or placebo application), 4. END (the last spectrogram during the laser or placebo application),

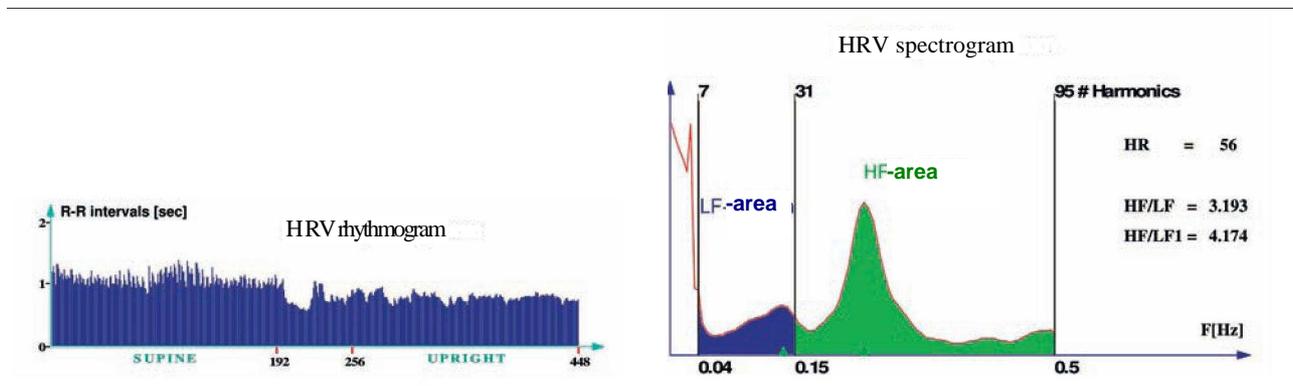


Image 1: on the left: HRV rhythmogram of a healthy voluntary subject. All the 192 R-R intervals are displayed as a blue vertical line. Different oscillations result in rhythmical fluctuations. On the right: The corresponding HRV spectrogram. The squares of the R-R intervals inside a frequency area are added up using power spectrum analysis. The resulting energy density (s in msec²) in the respective HF (green: 0.15–0.5 Hz) or LF area (red: 0.04–0.15 Hz) relating to the total power determines the normalised percentage of parasympathetic (nHF) and sympathetic (nLF) activities, indicated in normalised units (n. u.)

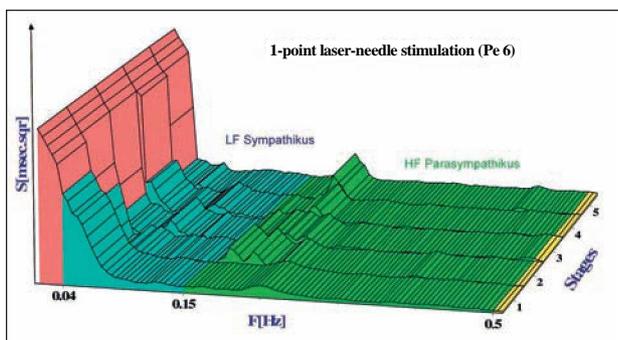


Image 2: 3D representation of consecutive HRV spectrograms during the 1-point laser-needle stimulation of point Pe6 of a voluntary subject. The energy density (s in msec²) in the HF area (green parasympathetic nervous system) slowly increases, while the power density of the LF-area (blue sympathetic nervous system) decreases.

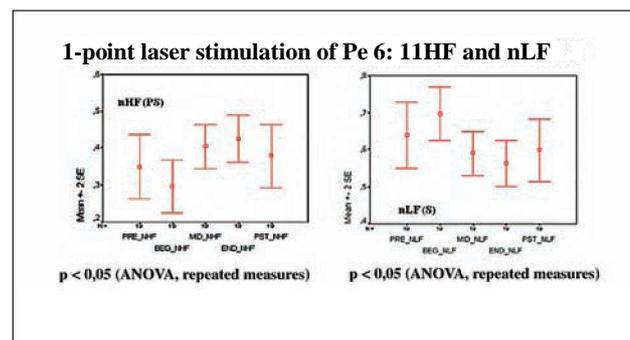


Image 3: Significant increase of nHF (PS) and decrease of nLF (S) in 19 voluntary subjects during and after the laser-needle stimulation of point Pe6 ($p < 0.05$ ANOVA) nHF: normalised HF-power, nLF: normalised LF-power, PS: parasympathetic nervous system, S: sympathetic nervous system. Average values in normalised units (n. u.)

5. POST (2 minutes after the laser or placebo application).

The HRV was quantified using a power-spectrum analysis (FFT). Here the squares of the R-R intervals are added up inside a frequency area. The values of the power density (= PDS in msec²) or the performance (variant) in the respective frequency area HF and LF were normalised on the total power (= TP) and indicated in normalised units (n. u.). Thus normalised values (nHF and nLF power) reflect the activity percentage of the sympathetic (S) and parasympathetic (PS) nervous system. The quotient nLF or nHF power was called a stress quotient (image 1).

Statistics

The average values for nHF, nLF, nLF/ nHF and HR (heart frequency) determined at five different time points in the three respective sessions were statistically evaluated using variant analysis

(ANOVA, repeated measures, test on intra-subject effects; SPSS program). The significance percentage was $p < 0.05$. the measure values were examined concerning their normal distribution using a Kolmogorov-Smirnov test.

Results

HRV values before, during and after the 1-point laser-stimulation of Pe 6

During the laser-needle stimulation of Pe 6, at the beginning of the stimulation (BEG, step 2) the average values for nHF-power (n = 19) slightly decreased and then constantly and significantly increased ($p < 0,01$) up to the conclusion of the stimulation time (END, step 4). Two minutes after the laser application the nHF-power had slightly decreased again. The average values for nLF-power (image 2 and 3) have a reciprocal behaviour.

1-point-laser-stimulation of Pe 6: Stress quotient nLF/nHF (S/PS)

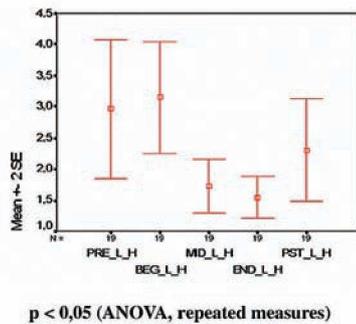


Image 4: Significant decrease of the stress quotients nLF/nHF in 19 voluntary subjects during and after the laser-needle stimulation of point Pe6 ($p < 0,05$ ANOVA) nHF: normalised HF-Power, nLF: normalised LF-Power, PS: Parasympathetic nervous system, S: Sympathetic nervous system. Average values in normalised units (n. u.)

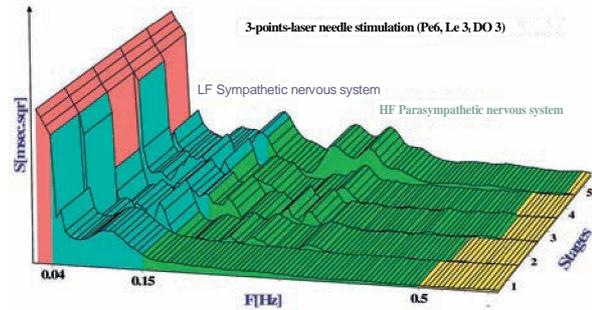


Image 5: 3D representation of consecutive HRV spectrograms during simultaneous 3-point laser-needle stimulation (Pe6, Le3, Dü3) in a female voluntary subject. The power density (s in msec²) in the HF area (green: parasympathetic nervous system) increases significantly, while it decreases in the LF area (blue sympathetic nervous system).

Simultaneous 3-point laser-needle stimulation of Pe 6, Le 3, Du 3: nHF and nLF

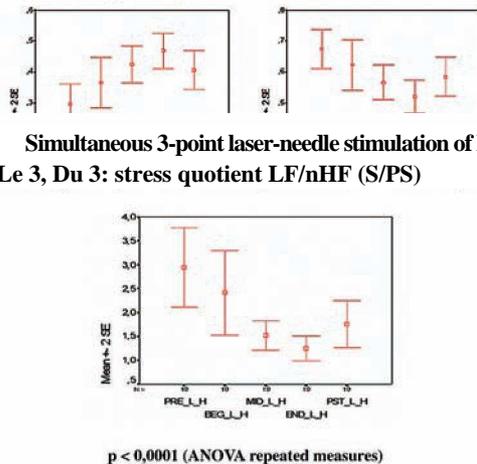


Image 6: Significant increase of nHF (PS) and decrease of nLF (S) in 19 voluntary subjects before, during and after the laser-needle-stimulation of point Pe6, Le3, Dü3 ($p < 0,0001$ ANOVA) nHF: normalised HF-power, nLF: normalised LF-power, PS: parasympathetic nervous system, S: sympathetic nervous system. Average values in normalised units (n. u.)

Image 7: Significant decrease of the stress quotient nLF/nHF in 19 voluntary subjects before, during and after the laser-needle stimulation of point Pe 6, Le 3, Dü 3 ($p < 0,0001$ ANOVA) nHF: normalised HF-power, nLF: normalised LF-power, PS: parasympathetic nervous system, S: sympathetic nervous system. Average values in normalised units (n. u.)

The average values of the stress quotient nLF/nHF increased slightly at first and then decreased significantly (image 4).

HRV data before, during and after the 3-point-laser stimulation of Pe 6, Le 3, Dü 3

During the 3-point laser-needle stimulation, the average values of the nHF-power showed a constant and significant increase, while the average values of the nLF-power constantly decreased ($p < 0,0001$). Only in the POST step, two minutes after the end of the laser stimulation (step 5), the nHF-power slightly decreased again, while the nLF-power slightly increased (image 5 and 6). The average values of the stress quotient nLF/nHF constantly and significantly decreased (image 7).

HRV data before, during and after the placebo application (check)

In contrast to the verum applications, the average values for the nHF and nLF-power and for the stress quotient nLF/nHF showed no significant differences in the placebo application (images 8 and 9). However, the low increase of the nHF-power and the reciprocally slight decrease of the nLF-power at the beginning of the placebo application (BEG, step 2) was remarkable and can probably be explained by the placebo effect.

Discussion

Heart rate variability (HRV)

HRV describes the rhythmical fluctuations (oscillations) of the time intervals between the consecutive heart actions as consequence of the autonomous modulation

of the sinu-atrial node. In this way, the HRV constantly regulates the vagal, inhibiting and sympathetic, stimulating nervous reflexes on the basis of a rhythmogram which makes them directly visible (image 1). As it quantitatively reflects the interactions between the central and the peripheral oscillators (regulation of respiration, blood pressure, thermic regulation, etc.), it is an accurate objective and non-invasive monitoring of the global ANS activity and corresponds to the TCM-conceptions of Yin (PS) and Yang (S). Thus, HRV rhythmograms are not only the expression of the adaptability of the heart, but also of the whole body to external and internal conditions. In addition the heart generates the strongest electromagnetic field of the body and could thus have a certain importance in acupuncture, quasi as a superordinate “electromagnetic centre”. Works by Zhang, a biophysicist from F. A. Popp’ team, refers to the fact that the electromagnetic body plays an important role in acupuncture [13, 14].

Acupuncture and the ANS

Many clinical and experimental experiences indicate that acupuncture determines a modulation of the ANS [15, 16]. Besides thermographic works on healthy voluntary subjects, who after the unilateral electrical and needle-stimulation of the point Di 4 showed symmetrical changes of the sympathetic activity on both sides, which could not be explained by local effect [17], experimental studies on animals, i.e. a cat model, also show that using point electro-acupuncture of the circulation meridian the reduces sympathetic activity and that reflex-induced myocardial ischemia is reversible [18]. In the same experimental model, it could be additionally shown that the bilateral electro-acupuncture of Pe 6 and Pe 5 by an opioid-receptor mechanism causes a reduction of the evoked neuronal activity in the rostral-ventral lateral medulla [19]. In addition, one of the first works applying a new imaging method like MRI supports the idea of the central participation of the ANS. After the needle-stimulation of the point Ma 36 and Di 4 activity changes are proved in the hypothalamus area and in the limbic system, which are both superordinate centres of the ANS [20].

A great difficulty in the research on mechanisms involved in acupuncture is naturally connected with the fact that single acupuncture points by their respective intrinsic characteristics probably cause different neuro-biological effects which additionally depend on the initial situation of the patient. If we contemporaneously stimulate different points, we can expect even more complex and more synergetic effects.

Study results and literature

Using laser-needle acupuncture in the context of the present study we can prove significant changes of the parasympathetic and sympathetic activity. This result generally corresponds to the few original works published until now on acupuncture and HRV, wherein pseudo-acupuncture respectively applied in the precedent studies is not undisputable.

Regarding the selection of the points, the present study can be compared very well with two studies with healthy voluntary subjects in which proved - one by magnetic stimulation of the points Pe 6 and LG 14 and the other by needle-stimulation of the points Pe 6 and Di 4 - the decrease of the normalised LF power and the increase of the normalised HF power [10, 11]. As the point Dü 3 opens the leading vessel at a cardinal point, we can suggest the effect of Dü 3 and LG 14 in the same direction. A further investigation of healthy voluntary subjects in which only the point Di 4 was stimulated by needles, and showed a significant increase of the sympathetic and parasympathetic activity [21], supports the hypothesis that not all acupuncture points cause changes of the sympathetic and parasympathetic activity in the same direction.

Placebo application: nHF and nLF

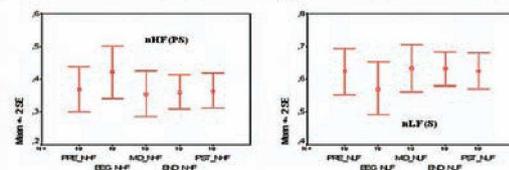


Image 8: Slight but insignificant increase of nHF (PS) and decrease of nLF (S) at the beginning of the placebo application (BEG). nHF: normalised HF power, nLF: normalised LF-power, PS: parasympathetic nervous system, S: sympathetic nervous system. Average values in normalised units (n.u.)

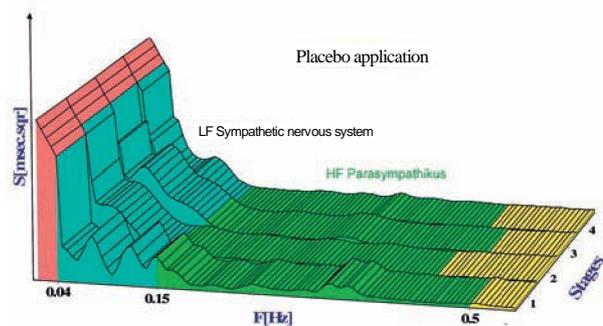


Image 9: 3D representation of consecutive HRV spectrograms during a placebo application on a voluntary subject. The energy density (s in msec²) in the HF area (green, parasympathetic nervous system) shows no essential changes, but it usually decreases.

A study on patients affected by depressions and phobias it also revealed that a significant increase of the HF and a decrease of the LF-power in comparison with the placebo application was obtained by needle-acupuncture of the points He 7, Pe 6, Du 20, Bl 62 and Ex 6 [22].

Up to now, only one study has been published which could not prove HRV changes after the stimulation of point Pe 6 [9]. Interestingly, this study also used laser acupuncture. However, there are unclear points as concerns the laser application. In the methodical part of the work, the authors state they used red and infrared light simultaneously, while according to the manufacturer's information, the laser-needle system used is only equipped with red-light laser diodes. No dosimetric indications were done on the component of the non-monochromatic infra-red light reputedly applied in addition and having a wave length of 880–950 nm. Given its low penetration depth, the red-light laser alone should not be sufficient to reach a point for which in the acupuncture manual the indicated stitching depth is of 1–2 cm [23, 24].

Beyond it, the divergent results of the present and the above study could also be connected to the fact that in the present study the applied laser light was not continuous but frequency-modulated, and this by means of meridian-specific resonance frequencies according to Reininger [12] which could possibly have strengthened the stimulus.

Limitations of the study

The statement of the study results is limited by the relatively low number of examined voluntary subjects. A double blind study would have gone beyond the scope of the technical and logistic framework of medical practice.

Conclusion

Already as 1-point stimulation (Pe 6) and simultaneous 3-point stimulation (Pe 6, Dü 3, Le 3), laser-needle acupuncture causes significant changes of the HRV, by increasing parasympathetic (nHF-power) and by decreasing sympathetic activity (nLF-power) compared with the placebo treatment. HRV monitoring is suitable for the purpose of quantifying acupuncture-induced changes of the ANS and could be established as a standard for further acupuncture studies in connection with a laser-needle system.

The examination of further meridian points in view of their effects on the ANS would be of interest and so would be the

question concerning the changes by micro system-acupuncture and synergetic effects of different acupuncture systems (meridian and micro system). In conclusion, the HRV measurement is also suitable for the therapy control as changes happen not only during and immediately after the acupuncture, but also in the longitudinal section observation of patients long-term changes are proven [25].

Authors

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Declaration on conflicts of interests

No commercial interests were pursued by the present study.

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