Cardiac Effect of Acupuncture on the Neiguan Point

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Abstract

Background: *The acupuncture on the Neiguan point (PC6) is used in the traditional Chinese medicine to calm the mind and relieve pain. In this study, we assess whether the stimulation of this point through acupuncture influences the heart rate.*

Methods: *A resting 3-lead ECG was evaluated for 71 subjects in sinus rhythm during a 5-phase protocol (rest – sham acupuncture – rest – acupuncture on Neiguan point – rest). After a filtering procedure, the R peaks were detected and the RR intervals computed. The changes in the RR series after stimulation were assessed in both acupuncture phases (sham and on the Neiguan point) as the slope of the RR interval series post stimulation.*

Results: *Comparing the RR changes in the Neiguan point acupuncture with the ones of the sham acupuncture for all subjects, we found a higher slope for the Neiguan point acupuncture (Neiguan: 2.90 ± 11.70 vs sham: -1.02 ± 10.95, p = 0.015). This effect disappeared over time: indeed, computing the slopes of RR series further away in time from the acupuncture, a significant difference was not found between the two phases.*

Conclusion: *These results suggest that acupuncture on the Neiguan point has a transient vagal effect on the heart, that should be considered in clinical practice.*

1. Introduction

The Neiguan point (PC6) is a traditional stimulating point for acupuncture to treat cardiovascular diseases, with antiarrhythmic effects [1,2]. However, its pathophysiological underlying mechanisms have not yet been completely investigated. Neiguan (PC6) acupuncture point is the connecting point of pericardial meridian, with a specific connection with the heart and its regulatory control system.

In Traditional Chinese Medicine, acupuncture at Neiguan (PC6) is considered as having dual-directional regulation effects on the cardiovascular system and has the characteristics of specific treatment of cardiovascular disease [3]. Furthermore, the Neiguan (PC6)-based acupuncture pre-treatment can exert a cardio-protective effect in animal models of myocardial ischemia reperfusion injury (MIRI) by improving coronary vasodilation and reserve flow and by stimulating energy metabolism, inhibiting oxidative stress, inflammatory response and apoptosis [4]. Indeed, the Neiguan (PC6)-based acupuncture pre-treatment has been found to provide a new inspiration for the clinical prevention and treatment of MIRI. In a fMRI study, acupuncture at Neiguan has been reported to modulate anxiety, altering the activity of brain regions responsible for emotions [5].

In Traditional Chinese Medicine, wrist-ankle acupuncture has been also found effective in treating and managing patients with paroxysmal supraventricular tachyarrhythmias [6]. Several years ago, a few Western literature reports have been published supporting the clinical efficacy of acupuncture for the treatment of arterial hypertension [7] and for the reduction of chest pain [8].

In 1981 Akselrod et al. [9] firstly described that the analysis of spontaneous fluctuations of RR intervals could provide a direct insight into the physiology of the autonomic control pathways. From that starting point on, heart rate variability (HRV) analysis [10] has progressively become the most employed non-invasive tool to evaluate autonomic control mechanisms in several clinical conditions. As described exhaustively and in a very plain way in 1996 by the Task Force Document of the European Society of Cardiology (ESC) and the North American Society of Pacing and Electrophysiology [10], the term of HRV analysis accommodates a wide range of possible methodologies, each one with computational and physiological interpretative differences. Changes in HRV have been associated with acupuncture, even if more published work is needed to determine if HRV can be an indicator of the therapeutic effect of acupuncture [11].

The aim of the study is to assess the effect of acupuncture in the Neiguan point and whether the acupuncture in this point has a vagal effect measurable at a cardiac level. To achieve this, the RR interval variability during acupuncture in the Neiguan point was compared to the one recorded during a sham acupuncture, namely an acupuncture in a different point.

2. Methods

2.1. Dataset and Protocol

A population of 71 healthy subjects was enrolled in this study (34 males, average age, 54 ± 14 years). Among the patients, 14 (20%) were smokers, 13 (18%) suffered from dyslipidemia, 3 (4%) from diabetes and 19 (27%) from hypertension. Regarding treatments, 11 (15%) were instructed to take beta blockers, 4 (6%) flecainides, 3 (4%) cordarone, 2 (3%) propafenone, 10 (14%) ace-inhibitor, 7 (10%) sartanics, 5 (7%) calcium antagonist, 8 (11%) statins.

The study protocol comprised of 5 phases: resting (6 min) – sham acupuncture (12 min) – resting (6 min) – acupuncture in the Neiguan point (12 min) – resting (6 min). Stainless-steel acupuncture needles (25 mm x 0.25 mm) were inserted at PC6 to a depth of 2-3 mm without rotation. The needles were left in place for 12 minutes before being removed. The sham experiments were conducted similarly but in a different body location, with the insertion of an acupuncture needle into the skin in a sham position. An acupuncturist with over 20 years of experience carried out all the experiments. Acupuncture treatment did not cause bleeding, hematoma, or infections. No pain or major clinical reactions were reported with needle insertion. This minimally invasive procedure appears to be safe and well tolerated in all subjects.

Three orthogonal leads (X, Y, Z), a periodic reference arterial pressure (AP) measurement and a continuous beat-to-beat non-invasive recordings of AP were obtained with a Task Force Monitor (CNSystem; Austria) recording system. Surface ECG and blood pressure signals were recorded for about 12 min during sham and Neiguan stimulation. The sampling frequency was 1 kHz for the ECG signal and 100 Hz for continuous AP recording. Raw data were exported as ASCII text files for off-line analysis. The study protocol was conducted according to 1964 Declaration of Helsinki and informed consent was obtained from each participant.

2.2. ECG preprocessing

All recorded ECGs were imported on Matlab R2022a (The MathWorks, Natick, MA). If abnormal off-scale spikes were identified in the signal due to artefacts or temporary detachment of the electrodes, the outlier values were replaced by interpolation of closest ECG points. Then, the ECG was filtered with a high-pass filter (Butterworth, 4th-order, fc = 0.5 Hz) to reduce baseline wander, with a low-pass filter (FIR, Hamming window, f_c = 80 Hz) to reduce high-frequency/muscle interferences and with a Power Line Removal filter (50 Hz). On the filtered signal, QRS detection was performed by an algorithm similar to the Pan Tomkins' [12] applied on lead Y. To identify abnormal beats, several procedures were implemented: firstly, the beats that were separated from the precedent beats for less than 0.5 times the median RR interval were discarded as T waves; secondly, a window around each R peak candidate was considered, starting 80 ms before the peak and ending 500 ms after. Each window was cross-correlated with all the others and the 20 beats with the highest cross-correlation mean value were averaged to obtain a template. The beats with a maximum correlation with the template lower then 0.8 were considered as abnormal and discarded from further analysis [13]. Finally, a visual inspection was performed to identify possible false detections.

From the R peaks thus obtained, the RR series was computed as the differences between consecutive R peaks.

2.3. ECG analysis

To assess the vagal effect of the Neiguan point acupuncture versus sham insertion, the cardiac response to acupuncture was analyzed, evaluating the changes in the RR intervals immediately following the procedure. We considered as starting point the last RR of the resting phase preceding the acupuncture and we computed the slope of the RR series in the period immediately following the procedure. The slope was computed as the angular coefficient of the line between two RR points:

$$k = \frac{y_2 - y_1}{x_2 - x_1}$$

where y_1 and y_2 are the RR values, x_1 is always considered equal to 1, being the first point of the line and x_2 was the position of the second RR in comparison to the first. Indeed, we considered different RR intervals as second points of the slope (x_i, y_i), being i=3,4,5, to assess the effect over time: the third, fourth and fifth RR in the acupuncture phase were used. Moreover, the number of subjects with a positive slope (an increase in the RR intervals, thus a vagal effect) was counted.

2.4. Statistical Analysis

A paired t-test was used to compare the changes in RR intervals after the Neiguan procedure in comparison to the sham acupuncture. Moreover, the number of subjects with a positive slope in the two phases was compared through a two-proportion z-test. A p-value <0.05 was considered statistically significant. All analyses were performed using Matlab R2022a (The MathWorks, Natick, MA).

3. Results

3.1. Slope Comparison

Out of 71 participants, 5 had more than 50% of the beats

that were abnormal or noisy, thus these participants were discarded from analysis.

In Fig. 1, the RR series of all subjects standardized on the last point of the resting phases are showed in blue with the average RR series superimposed in red. The black lines mark the end of the resting phase before the sham acupuncture (Fig. 1a) and the Neiguan acupuncture (Fig. 1b). The last RR interval of the resting phase is considered as reference point (point zero) and offset to zero in all the series. Considering the average behavior, it is noticeable how the stimulation of the Neiguan point determines an increase in the average RR series that disappears over time. Instead, for the sham acupuncture, this effect is not noticeable.

In Table 1 the values of the slopes are reported, considering as second point different RR intervals, namely the third, fourth and fifth interval after the acupuncture. Moreover, for each condition, the number of subjects for which the slope was positive is reported. We found a significantly higher slope in the Neiguan stimulation than in the sham when the third (2. 90 ± 11.70 vs -1.02 ± 10.95, $p = 0.015$) and fourth (2.81 ± 10.92 vs -1.17 ± 10.95, $p = 0.049$) RR intervals were considered.

No significance was found for the fifth RR interval ($p = 0.212$). Regarding the percentage of subjects with a positive slope (vagal effect), we found a higher number of positive slopes for the Neiguan point acupuncture in comparison to the sham acupuncture for all three RR intervals considered, but the differences were not significant.

4. Discussion

The main findings of our analysis are: 1) the acupuncture on the Neiguan point has a vagal effect measurable on the ECG; 2) this is a short-time effect mainly due to the role of the autonomic nervous system in the genesis of vasovagal or neurologically mediated responses, having a fast activation and a subsequent rapid return to the basal conditions determined by a sudden vasovagal balance impairment.

In our study, we measured the Neiguan Point acupuncture effect on the heart rate as the slope of the line joining the last RR interval before stimulation to the RRs (third, fourth and fifth) after stimulation. We found a significant higher slope for the Neiguan point in comparison to the sham acupuncture when considering the third and fourth RR, but not the fifth. Moreover, the percentage of subjects with a positive slope was not significantly higher in the Neiguan stimulation in comparison to the sham. This fact can be explained by various reasons: firstly, by the presence of a percentage of subjects that are resistant to this stimulation; secondly, the difference between the two phases is not due to a change in the sign of the slope, but to the amplitude of the effect, as noticeable from Fig. 1.

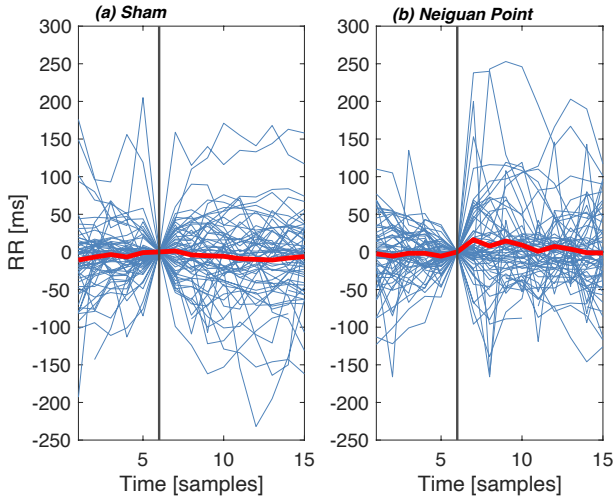

Figure 1: RR series. RR series (blue) of all the subjects are showed for the sham acupuncture (on the left) and the Neiguan point (on the right). The acupuncture time is marked by the black line and the corresponding RR (the last of the resting phase) is put to zero. The red line represents the average RR series. It is noticeable how the increase in the average RR series of the right panel is higher than the one on the left panel. Furthermore, this increase in the RR series disappears over time.

Table 1. Slope analysis: values are given as average (std) or number (%).

		Sham	Neiguan	p
Rest vs 3rd RR	Slope	-1.02 (10.95)	2.90 (11.70)	0.015*
	Slope>0	28 (46%)	32 (55%)	0.312
Rest vs 4rd RR	Slope	-1.17 (10.95)	2.81 (10.92)	0.049*
	Slope>0	28 (46%)	32 (55%)	0.312
Rest vs 5rd RR	Slope	-1.17 (10.95)	2.81 (10.92)	0.212
	Slope>0	22 37%)	28 (47%)	0.233

It is known that acupuncture influences HRV [11]. Nishijo et al. and Uchida et al. reported a transient reduction of HR during acupuncture at the Ximen (P4) and Shousanli (LI 10) points, respectively [14,15]. In the study of Huang et al., an increase in vagal modulation by acupuncture at Neiguan point was found through comparison of metrics of heart rate variability [16]. They compared three groups (no acupuncture, sham acupuncture, acupuncture at Neiguan point) and found no differences in the control group, increased normalized high-frequency power in the Neiguan acupuncture group and higher mean RR interval in both groups with

acupuncture (sham and Neiguan). Differently to their study, we compared the RR slope due to acupuncture in both sham and acupuncture at the Neiguan point in the same subject, thus removing the subjective bias of the acupuncture itself. Moreover, we also noticed that the vagal effect on the heart rate has a short duration, not visible using a frequency analysis.

In conclusion, the acupuncture on the Neiguan point has a vagal effect on the cardiovascular system through an action on the autonomic nervous system, measurable on the ECG [16]. This effect could be exploited in clinical practice to relax the subject; at the same time, it should be considered during acupuncture procedures on subjects with cardiovascular problems because an imbalance of autonomic control mechanisms, due to either an increase in vagal or sympathetic neural activity directed to the heart, may favor the initiation and maintenance of atrial and ventricular arrhythmias [17].

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