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Acupuncture effects on reflex responses to mental stress in humans

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Middlekauff, Holly R., Jun Liang Yu, and Kakit Hui. Acupuncture effects on reflex responses to mental stress in humans. *Am J Physiol Regulatory Integrative Comp Physiol* 280: R1462–R1468, 2001.—In animal studies, acupuncture has been shown to be sympathoinhibitory, but it is unknown if acupuncture is sympathoinhibitory in humans. Nineteen healthy volunteers underwent mental stress testing pre- and postacupuncture. Muscle sympathetic nerve activity (MSNA), blood pressure, and heart rate during mental stress were compared pre- and postacupuncture. Control acupuncture consisted of acupuncture at nonacupoints and "no-needle" acupuncture. Acupuncture had no effect on resting MSNA, blood pressure, or heart rate. After real acupuncture, the increase in mean arterial pressure (pre- vs. postacupuncture 4.5 vs. 1.7 mmHg, $P < 0.001$), but not MSNA or heart rate, was blunted during mental stress. Similarly, following nonacupoint acupuncture, the increase in mean arterial pressure was blunted during mental stress (5.4 vs. 2.9 mmHg, $P < 0.0003$). No-needle acupuncture had no effect on these variables. In conclusion, acupuncture at traditional acupoints, nonacupoints, and no-needle acupuncture does not modulate baseline MSNA or MSNA responses to mental stress in normal humans. Acupuncture significantly attenuates the increase in blood pressure during mental stress. Needling nonacupoints, but not "no-needle" acupuncture, have a similar effect on blood pressure.

sympathetic nerve activity; autonomic nervous system; blood pressure

IN TRADITIONAL CHINESE MEDICINE, acupuncture has been used for thousands of years to treat a variety of disorders, including cardiovascular disorders. Acupuncture has been used to treat angina in patients with coronary artery disease and to lower blood pressure in patients with hypertension (20, 25). According to traditional ideas, acupuncture points are located along specific meridians or channels; acupuncture at these sites facilitates and restores the flow of vital energy in the body (24). More recent work supports the concept that acupuncture activates the endogenous opioids in the central nervous system, which, in turn, inhibit central sympathetic neural outflow (4, 7).

Evidence that acupuncture increases central nervous system opioids includes early work in a mouse model of pain, in which electroacupuncture at the large intestine 4 (Li4) site produced analgesia (18). This analgesia was completely blocked by pretreatment with subcutaneous naloxone. In further experiments, microinjection of naloxone or antibodies to β-endorphins into central analgesic sites, such as the periaqueductal grey, was found to block acupuncture-induced analgesia, consistent with a central nervous system location of opioid receptors involved in acupuncture analgesia (18, 29).

Experimental evidence supports the concept that opioids in the central nervous system, in addition to modulating pain, also play a role in sympathetic neural regulation of the cardiovascular system (2, 9, 16). First, opioid receptors have been localized to central cardiovascular centers, such as the ventrolateral medulla (9). Second, the impact of interventions known to alter blood pressure is modulated by central nervous system opioid receptor agonists or antagonists (2, 16). For example, during hemorrhage, hypotension is attenuated by naloxone administered into the rostral ventrolateral medulla in anesthetized rabbits (16). Similarly, during muscle contraction, the pressor response is modulated by injection of opioid agonists into the rostral ventrolateral medulla in anesthetized rats (2). These findings are consistent with centrally released endogenous opioids playing a regulatory role in the cardiovascular system.

Experimental evidence in animal models of cardiovascular disease supports the concept that cardiovascular effects of acupuncture are mediated by inhibition of central sympathetic neural outflow, perhaps through release of endogenous opioids (4, 11, 30). In spontaneously hypertensive rats, in which hypertension is attributable to sympathetic activation, blood pressure was significantly lowered by acupuncture-like stimulation of the sciatic nerve (30). Naloxone abolished this depressor response. In a cat model of sympathetically mediated myocardial ischemia, Li and colleagues (11) reported that median nerve stimulation,

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simulating acupuncture, attenuated myocardial ischemia by attenuating sympathetic activation and reducing cardiac demand. This attenuation was blocked by intravenous naloxone and by microinjection of naloxone into the rostral ventrolateral medulla (4).

In humans, it is unknown if acupuncture is sympathoinhibitory. We chose to address this question by testing acupuncture during an intervention known to cause increases in blood pressure and leg muscle sympathetic nerve activity (MSNA). Mental stress, produced either by the Stroop color word test or by mental arithmetic, is an established means to provoke pressor and sympathoexcitatory responses (8, 15, 21). The purpose of this study was to test the hypothesis that acupuncture decreases blood pressure responses to mental stress in healthy humans and that this effect is mediated by inhibition of MSNA.

METHODS

Humans Subjects

After written informed consent was obtained, 19 healthy volunteers participated in these protocols. The study protocols were approved by the UCLA Internal Review Board. Mean age of volunteers was 40 ± 3.5 yr. All were healthy as confirmed by medical history and physical examination and were not taking medications. Volunteers had abstained from caffeine on the day of the study. Because acupuncture may have a hypotensive effect, which may be exacerbated by fasting, subjects were studied in the nonfasted state. Eighteen of nineteen volunteers were acupuncture naïve; one had undergone acupuncture treatment for lower back pain.

MSNA

MSNA was directly recorded from the peroneal nerve using the technique of microneurography (5, 26). Multiunit postganglionic muscle sympathetic nerve recordings were made using a tungsten microelectrode. Signals were amplified by a factor of 50,000 to 100,000 and band-pass filtered (700 to 2,000 Hz). Nerve activity was rectified and integrated (time constant 0.1 s) to obtain a mean voltage display of sympathetic nerve activity that was recorded on paper. All recordings of MSNA satisfied previously established and described criteria (5, 26). Muscle sympathetic bursts were identified by visual inspection by a single investigator (H. R. Middlekauff) and expressed as burst frequency (bursts per minute) and total activity (units per minute). The interobserver and intraobserver variability in identifying bursts is $<10\%$ and $<5\%$, respectively (13).

Acupuncture

"Real" acupuncture. Acupuncture was performed as it is traditionally practiced. The skin was cleaned with alcohol. Acupuncture needles (4 cm, 0.25-mm diameter; Natural, Suzhou Guso Acupuncture and Moxibustion Appliance) were inserted into the right Li4 (Hegu), right liver 3 (Liv3; Taichong), and left spleen 6 (P6; Sanyinjiao) points and manually stimulated with a combination of rotation with lifting and thrusting motions for ~15 s to achieve the De Qi sensation of heaviness, fullness, or soreness. Needles were left in place while volunteers rested for 15 min, and then the needles were removed. These sites were chosen because they are associated with stress reduction (24).

Control Acupuncture

"Nonacupoint" acupuncture. The skin was cleaned with alcohol. Acupuncture needles were inserted bilaterally into a nonacupoint of the anterior deltoid muscle, and, similar to real acupuncture, they were manually stimulated for 15 s until a sensation of De Qi was experienced. Volunteers rested for 15 min, and then the needles were removed.

"No-needle" acupuncture. The skin was cleaned with alcohol. Volunteers were shown the acupuncture needles. An empty, plastic needle guide was then taped bilaterally against the skin overlying the upper trapezius muscle, out of the volunteers' field of view. Volunteers rested for 15 min, and then the acupuncturist simulated needle removal. No sensation of De Qi was experienced.

All acupuncture was performed by the same licensed acupuncturist (J. L. Yu). Volunteers were not told that they may undergo nonacupoint or no-needle acupuncture.

Mental Stress Tests

Mental stress testing was performed for 4 min by either the Stroop color word test or mental arithmetic (21, 23). During the Stroop color word test, volunteers are shown a series of names of colors written in a different color ink from the color specified (the word "red" may be written in blue ink, for example). Volunteers are instructed to identify the color, not read the word, as quickly as possible. During verbally administered mental arithmetic, volunteers are asked to subtract one- or two-digit numbers from two- or three-digit numbers as quickly and accurately as possible. Throughout the mental stress tests, subjects were urged to work more quickly and more accurately. Because sympathetic responses to mental stress testing are strongly influenced by perception of task difficulty (1), each volunteer was asked to assess task difficulty on completion of the protocol using a standard five-point scale of 0, not stressful; 1, somewhat stressful; 2, stressful; 3, very stressful; and 4, very, very stressful.

Blood Pressure and Heart Rate

Blood pressure was monitored noninvasively from an automatic blood pressure cuff (Press-Mate 8800, Colin Medical Instrument, San Antonio, TX). Systolic, diastolic, and mean blood pressures were measured every 20 s at baseline and during mental stress. The accuracy of the Colin 8800 is within the ±5 mmHg required by the Association for Advanced Medical Instruments, and it is found to be ±2.81, ±0.04, and ±0.96 mmHg for systolic, diastolic, and mean blood pressure, respectively, compared with auscultatory methods (12). Heart rate was monitored continuously through lead II of the electrocardiogram (ECG).

Experimental Protocol (n = 12)

Volunteers rested in the supine position (Fig. 1). The ECG electrodes and blood pressure cuff were positioned, and the leg was positioned for microneurography. After an adequate nerve-recording site was identified, subjects rested for 10 min. Then blood pressure, heart rate, and MSNA were recorded at baseline and during mental stress testing. After recovery, real acupuncture or control acupuncture (nonacupoint acupuncture or no-needle acupuncture) was performed. Blood pressure, heart rate, and MSNA were recorded at baseline and during repeat mental stress testing. On occasion, volunteers underwent two types of acupuncture (real, nonacupoint or no-needle) on the same day. To prevent accommodation to mental stress testing, a different type of stress testing (Stroop color word or mental arithmetic) was

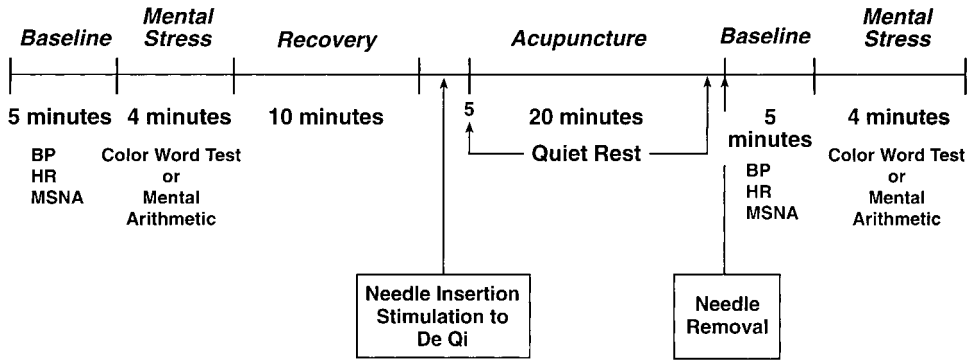

Fig. 1. Experimental protocol. After instrumentation and a 10-min rest period, baseline blood pressure (BP), heart rate (HR), and muscle sympathetic nerve activity (MSNA) were recorded for 5 min. Mental stress (color word test or mental arithmetic) was performed for 4 min. After a 10-min recovery period, acupuncture was performed (see METHODS for description of acupuncture). Needles were removed after 20 min. Repeat measurements of baseline BP, HR, and MSNA were recorded for 5 min, and then the same mental stress test was repeated.

used for the second session compared with the first. Control acupuncture was always performed before real acupuncture.

No Microneurography—Experimental Protocol (n = 7)

We considered the possibility that microneurography itself was having an acupuncture-like effect. The "real" acupuncture protocol above was performed in seven additional subjects, but the microneurography portion was omitted.

Statistical Analysis

Statistical analysis was performed using analysis of variance with repeated measures for two main effects: treatment (pre- and postacupuncture) and time (*minutes 1*, *2*, *3*, and *4*). If significant main effects or a statistical interaction were noted, the simple effects were analyzed using paired Student's *t*-tests. Fisher-Tukey significant difference criterion was used to control for artifacts due to multiple significance testing. Data were analyzed at baseline and during 4 min of mental stress testing. Probability values of ≤0.05 were considered statistically significant.

RESULTS

All volunteers tolerated acupuncture without difficulty or complications. No volunteer articulated any suspicions about the authenticity of the control acupuncture. Volunteers were unable to determine whether a needle had been inserted during no-needle acupuncture. Results were virtually identical when the one subject with prior acupuncture experience was removed.

Acupuncture Effects on Basal Measurements

Acupuncture (real, nonacupoint or no-needle) had no effect on resting heart rate, blood pressure, or MSNA recorded following needle removal (Table 1).

Table 1. *Resting measurements pre- and postacupuncture*

	Preacupuncture	Postacupuncture	*P* Value
HR, beats/min	67 ± 2	67 ± 2	NS
Mean arterial pressure, mmHg	82 ± 3	83 ± 2	NS
MSNA, bursts/min	26 ± 4	25 ± 5	NS
MSNA, total activity/min	1,287 ± 76	1,338 ± 87	NS

Values are means ± SE. HR, heart rate; MSNA, muscle sympathetic nerve activity; NS, not significant.

Acupuncture Effects on Responses to Mental Stress (n = 12)

The rise in mean arterial pressure during mental stress was significantly attenuated following acupuncture (overall time effect, $P < 0.001$; *minutes 2* and *3*, $P < 0.05$; Fig. 2*A*). The increase in MSNA, quantified in two different ways, and heart rate was similar before and after acupuncture (Fig. 3 and Table 2). Perceived difficulty during mental stress was similar before and after acupuncture [2.9 ± 0.1 vs. 3.2 ± 0.2, P = not significant (NS)].

Control Acupuncture Effects on Responses to Mental Stress

Nonacupoint acupuncture (n = 11). The rise in mean arterial pressure during mental stress was significantly attenuated following nonacupoint acupuncture (overall time effect, $P < 0.0003$; Fig. 2*B*). Compared with real acupuncture, the impact of nonacupoint acupuncture on mean arterial pressure was less, although this difference did not reach statistical significance ($P = 0.08$; Fig. 2*C*). The increase in MSNA, quantified in two different ways, and heart rate was similar before and after nonacupoint acupuncture (Table 2). Perceived difficulty during mental stress was similar before and after nonacupoint acupuncture (2.7 ± 0.3 vs. 2.9 ± 0.2, P = NS).

No-needle acupuncture (n = 8). The increase in mean arterial pressure, heart rate, and MSNA was similar before and after no-needle acupuncture (Fig. 2*D* and Table 2). Perceived difficulty during mental stress was similar before and after nonacupoint acupuncture (3.1 ± 0.05 vs. 2.9 ± 0.1, P = NS).

Acupuncture Effects on Responses to Mental Stress in the Absence of Microneurography (n = 7)

Microneurography was omitted to eliminate the possibility of an acupuncture-like effect of microneurography. After "real" acupuncture compared with no acupuncture, the rise in mean arterial pressure during mental stress was significantly attenuated (overall time effect, $P < 0.05$; *minutes 2* and *3*, $P < 0.05$; Fig. 4). This attenuation of the rise in blood pressure during mental stress was not different in the presence or absence of microneurography ($P = 0.13$). However, the

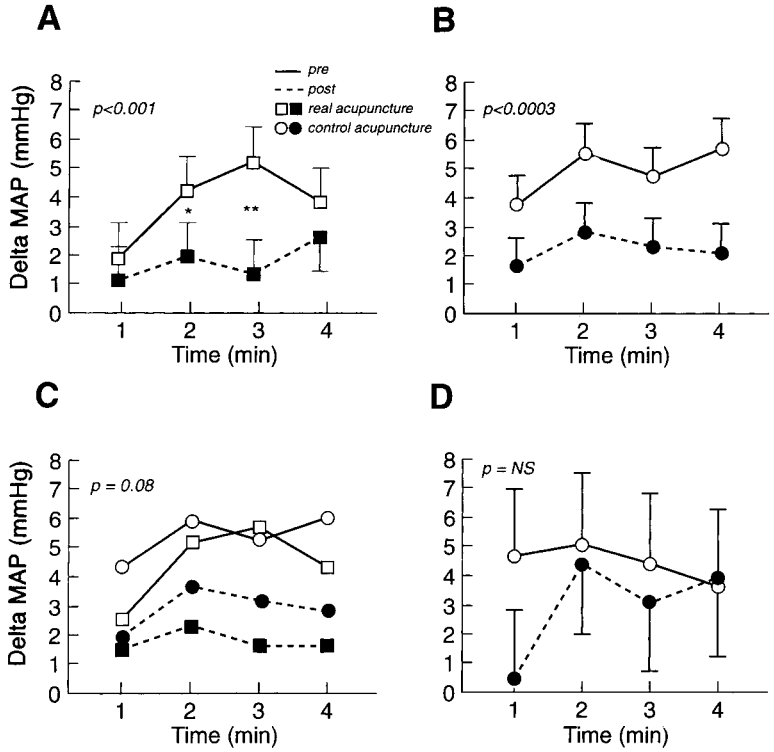

Fig. 2. Acupuncture effect on delta mean arterial pressure (MAP) during mental stress. *A*: acupuncture at known acupoints significantly attenuates the increase in MAP during mental stress (overall time effect, $P < 0.001$). Pointwise comparisons revealed greater attenuation of MAP at *minute 2* (*$P < 0.01$) and *minute 3* (**$P < 0.001$) of mental stress. *B*: acupuncture at nonacupoints significantly attenuates the increase in MAP during mental stress (overall time effect, $P < 0.0003$). *C*: compared with real acupuncture, the impact of nonacupoint acupuncture on MAP was less, although this difference did not reach statistical significance ($P = 0.08$). *D*: no-needle acupuncture does not attenuate the increase in MAP during mental stress. In all panels, preacupuncture is illustrated by solid lines and open symbols, and postacupuncture is illustrated by dashed lines and solid symbols. NS, not significant.

increase in mean arterial pressure during mental stress before acupuncture was significantly greater in the absence compared with the presence of microneurography (8.9 ± 2.0 vs. 4.5 ± 1.1 mmHg, $P = 0.04$). The rise in heart rate was similar before and after real acupuncture (overall mean 4.2 ± 0.8 vs. 5.5 ± 1.6, P = NS). Perceived difficulty during mental stress was similar before and after real acupuncture (2.8 ± 0.05 vs. 2.9 ± 0.3, P = NS).

DISCUSSION

The major new findings of this study in normal healthy volunteers are *1*) acupuncture at acupoints Li4, P6, and Liv3, at nonacupoints, and "no-needle" acupuncture does not modulate resting MSNA or MSNA responses to mental stress in normal humans; *2*) acupuncture at acupoints Li4, P6, and Liv3 significantly attenuates the blood pressure response to mental stress; *3*) acupuncture at nonacupoints also significantly decreases the blood pressure response to mental stress, although perhaps to a lesser degree, calling into question the specificity of traditional acupoints; *4*) these findings are not explained by a "placebo effect" or a time effect, because no-needle acupuncture had no effect on the blood pressure response to mental stress; *5*) these findings are not attributable to changes

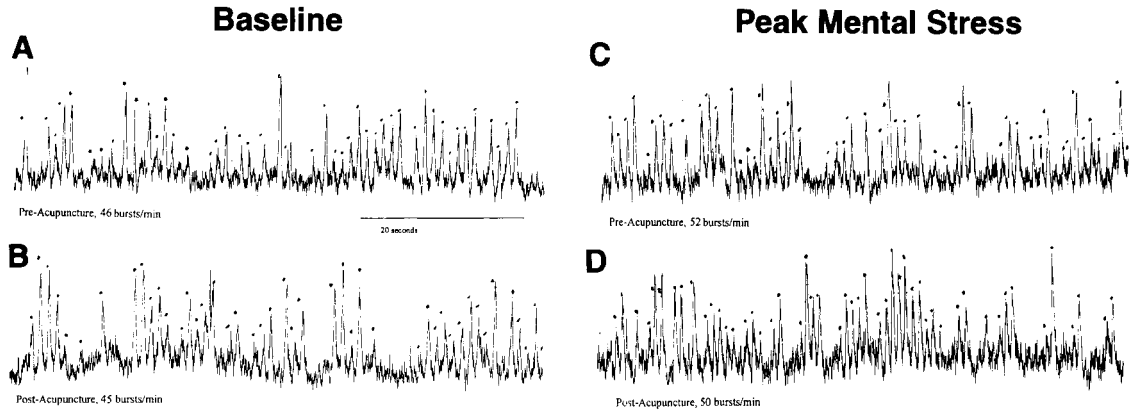

Fig. 3. Sympathetic neurograms. Sixty seconds of MSNA recorded in a normal volunteer (J. S., age 66 yr) at baseline pre- and postreal acupuncture (*A* and *B*) and at peak mental stress pre- and postreal acupuncture (*C* and *D*). Preacupuncture compared with postacupuncture, baseline MSNA is not different (46 vs. 45 bursts/min). Similarly, preacupuncture compared with postacupuncture, peak mental stress MSNA is not different (52 vs. 50 bursts/min). A dot identifies each burst of MSNA.

Table 2. *Hemodynamic and neural responses to mental stress pre- and postacupuncture*

Pre-/Postreal Acupuncture	*Minute 1*	*Minute 2*	*Minute 3*	*Minute 4*	*P* Value
Delta HR, beats/min					
Pre	6.8 ± 0.6	7.4 ± 0.8	7.2 ± 0.6	6.5 ± 0.5	NS
Post	5.8 ± 0.1	6.8 ± 0.5	6.4 ± 0.4	6.4 ± 0.5	
Delta MSNA, bursts/min					
Pre	1.7 ± 0.5	3.3 ± 0.8	5.4 ± 0.8	6.4 ± 0.7	NS
Post	0.7 ± 0.5	4.0 ± 0.7	3.6 ± 1.0	3.4 ± 0.7	
Delta MSNA, total activity/min					
Pre	136 ± 33	299 ± 58	392 ± 61	527 ± 63	NS
Post	34 ± 30	259 ± 48	361 ± 63	302 ± 53	
		Pre-/postnonacupoint acupuncture			
Delta HR, beats/min					
Pre	4.9 ± 0.4	7.4 ± 0.5	6.8 ± 0.5	7.1 ± 0.6	NS
Post	3.8 ± 0.5	7.0 ± 0.5	6.2 ± 0.5	5.4 ± 0.5	
Delta MSNA, bursts/min					
Pre	1.0 ± 0.6	2.7 ± 0.5	1.4 ± 0.6	3.8 ± 0.8	NS
Post	1.4 ± 1.0	4.5 ± 0.5	6.6 ± 0.8	5.2 ± 0.9	
Delta MSNA, total activity/min					
Pre	225 ± 21	336 ± 35	224 ± 42	333 ± 38	NS
Post	153 ± 33	418 ± 53	587 ± 67	652 ± 92	
		Pre-/post-no-needle acupuncture			
Delta HR, beats/min					
Pre	7.4 ± 0.7	7.8 ± 0.7	7.7 ± 0.7	6.6 ± 0.6	NS
Post	6.4 ± 0.5	6.6 ± 0.5	7.1 ± 0.6	7.7 ± 0.5	
Delta MSNA, bursts/min					
Pre	−0.13 ± .4	5.2 ± 2.0	5.2 ± 1.8	1.2 ± 2.0	NS
Post	−1.8 ± 0.2	2.8 ± 1.3	2.8 ± 1.2	6.1 ± 0.6	
Delta MSNA, total activity/min					
Pre	−18 ± 7	395 ± 131	565 ± 98	294 ± 175	NS
Post	57 ± 19	331 ± 73	174 ± 56	456 ± 84	

Values are means ± SE.

in MSNA, because the muscle sympathetic nerve response to mental stress was unchanged following acupuncture; and *6*) microneurography had an "acupuncture-like" effect, because the increase in mean arterial pressure during mental stress before acupuncture was significantly greater in the absence compared with the presence of microneurography.

Challenges to performing rigorous investigations of acupuncture include finding objective end points, because the end point of pain is inherently subjective and prone to bias, and designing adequate control experiments (14, 27). In this study, acupuncture effects on measurable and quantifiable physiological end points, such as blood pressure and MSNA, largely addressed the first challenge. The issue of adequate control experiments remained. Some investigators have advocated performing needling at putatively ineffective acupoints on the same meridian, on another meridian or at nonacupoints, so that "sham" acupuncture would be indistinguishable from real acupuncture (14). However, this form of sham acupuncture has been found to have specific analgesic effects in 40–50% of subjects (compared to 60–75% of subjects undergoing real acupuncture) and therefore may not be a satisfactory placebo (27). Controls that avoid penetration of the needle through the skin include a "no-needle" approach during which the plastic needle guide is taped against the subject's skin (14) or a "placebo needle," in which a blunt needle touches the skin and then collapses within the needle handle (22). These approaches are credible and avoid actual skin penetration, which may produce physiological effects (14, 22, 27). Because there is no consensus regarding the optimal control procedure for acupuncture, we used both general approaches, needling at nonacupoints and no-needle acupuncture. Indeed, sham acupuncture performed at nonacupoints had a real, quantifiable effect on the blood pressure response to mental stress, which was similar, but perhaps slightly smaller, than the effect of real acupuncture. Why might this be so?

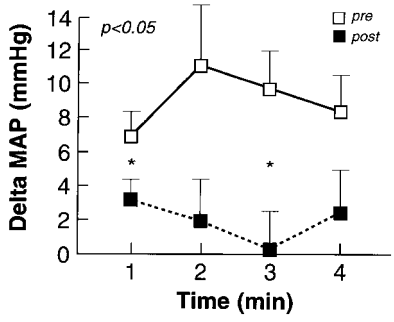

Fig. 4. Acupuncture effect on delta MAP during mental stress in the absence of microneurography. Acupuncture at traditional acupoints significantly attenuates the increase in MAP during mental stress (overall time effect, $P < 0.05$). Pointwise comparisons revealed greater attenuation of MAP at *minutes 1* and *3* (*$P < 0.05$) of mental stress. Symbols are defined in Fig. 2.

One explanation for the effect of nonacupoint acupuncture on the blood pressure response to mental stress lies in the physiological changes that occur during needling and needle manipulation. As discussed in the introduction, the analgesic and perhaps cardiovascular effects of acupuncture may be mediated through release of endogenous opioids in the central nervous system. Several lines of evidence support the concept that the stimulus to this release of endogenous opioids is activation of peripheral sensory neurons during acupuncture located in skeletal muscle (3, 11, 30). First of all, Thoren and colleagues (30) stimulated the sciatic nerve in unanesthetized spontaneously hypertensive rats. Blood pressure and heart rate fell significantly after 30 min of sciatic nerve stimulation and remained depressed for 12 h. Second, in a cat model of ischemia, Li and colleagues (11) stimulated median nerve fibers. Median nerve stimulation decreased reflex-mediated cardiac ischemia. Finally, local anesthesia of the skin underlying the acupuncture needle does not blunt acupuncture analgesia, but anesthesia of the underlying muscle bed does (3).

To explain the analgesic effect of needling nonacupoints, it has been suggested that this intervention would also be expected to stimulate sensory afferent neurons. It has been hypothesized that real acupoints located peripherally or over trigger points may result in even more effective stimulation of sensory afferent neurons, and therefore be preferable sites, but by no means be the only sites capable of this type of stimulation (24). In our study, nonacupoint acupuncture would have been predicted to stimulate sensory afferent neurons, explaining the decrease in blood pressure response during mental stress following nonacupoint stimulation. Our study calls into question the specificity of traditional acupuncture sites. No-needle acupuncture would not have been expected to activate sensory neurons, providing a possible explanation for the absence of attenuation of blood pressure during mental stress in the absence of needling and needle stimulation.

Interestingly, microneurography may have an "acupuncture-like" effect. After acupuncture, in the presence compared with the absence of microneurography, the increase in mean blood pressure during mental stress was similar, but before acupuncture it was not. That is, the increase in blood pressure during mental stress before acupuncture was significantly smaller in the presence compared with the absence of microneurography. Peroneal microneurography appears to blunt the increase in blood pressure during mental stress. During peroneal microneurography, afferent nerve fibers are stimulated at 1 Hz during microelectrode placement, which is very similar to the 2–4 Hz used in electroacupuncture. This is consistent with the hypothesis that acupuncture is mediated by activation of afferent nerve fibers. The role of afferent nerve fibers in mediating acupuncture depressor effects is under active investigation in our laboratory.

Although acupuncture significantly attenuated the blood pressure response during mental stress, this effect was not mediated by an attenuation of the muscle sympathetic nerve response to mental stress. To our knowledge, only one other study has addressed the question of whether acupuncture inhibits MSNA in normal humans. Knardahl and colleagues (10) found an increase in resting MSNA following acupuncture. The method of acupuncture performed in their study differed from ours in that they used manual needle stimulation followed by electroacupuncture for 30 min at acupoints Li4 and Li11. Furthermore, they did not perform an intervention to increase MSNA but only studied MSNA levels at rest. To explain our findings of attenuated blood pressure response during mental stress in the absence of an attenuated muscle sympathetic neural response, we propose two hypotheses: *1*) acupuncture attenuates sympathetic nerve activation to nonmuscular vascular beds, such as the splanchnic or renal vascular beds; and/or *2*) acupuncture augments vasodilatation during mental stress, countering sympathetic vasoconstrictor influences. These hypotheses are currently being tested in our laboratory. It is unlikely that the attenuated blood pressure response during mental stress is due to acupuncture modulation of cardiac parasympathetic and sympathetic activity (17, 28), because the increase in heart rate during mental stress was not attenuated following acupuncture.

Limitations

We recognize several limitations of this study. Real acupuncture was only performed one time during this study, whereas in practice, it is common to perform a series of acupuncture interventions over several weeks for maximum effect. Nonetheless, despite this limited acupuncture intervention, a significant decrease in blood pressure during mental stress was seen. An even more dramatic attenuation of blood pressure response to mental stress may be predicted during a prolonged course of acupuncture. The design of our study required volunteers to undergo repeat bouts of mental stress testing, before and after acupuncture, which may result in accommodation and a blunted response, including a blunted blood pressure response, during mental stress. We do not believe this is the explanation for our findings, because volunteers' self-reported level of perceived task difficulty was not different between the two bouts of mental stress in our study and MSNA and heart rate responses were not blunted. Furthermore, no decline in blood pressure response was observed during our no-needle acupuncture control experiment.

In summary, real acupuncture and needling nonacupoints decrease the blood pressure response to mental stress, whereas placebo no-needle acupuncture does not. This depressor effect of acupuncture is not mediated by acupuncture modulation of muscle sympathetic nerve activation, which increases similarly before and after acupuncture.

Perspectives

Although acupuncture did not decrease resting MSNA or muscle sympathetic nerve activation during mental stress in these normal volunteers, the impact of acupuncture in pathological states characterized by sympathetic excitation, such as heart failure, is unknown. In spontaneously hypertensive rats, a rat model of sympathetic excitation, the impact of acupuncture on blood pressure was markedly greater than on normotensive rats (2). Studies in humans with sympathoexcitation, such as patients with heart failure, will be necessary to characterize fully the role of acupuncture as a modulator of sympathetic tone.

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