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Effects of GV20 Acupuncture on Cerebral Blood Flow Velocity of Middle Cerebral Artery and Anterior Cerebral Artery Territories, and CO_2 Reactivity During Hypocapnia in Normal Subjects

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Abstract

Objectives: Acupuncture has been gaining popularity among practitioners of modern medicine as an alternative and complementary treatment. However, the mechanism of its therapeutic effect still remains uncertain. The present study chose the GV20 acupoint to evaluate acupoint effectiveness, hypothesizing that its stimulation induces cerebrovascular responses.

Design and setting: The effects of GV20 acupuncture treatment on middle cerebral artery (MCA) and anterior cerebral artery (ACA) blood flow velocities, and CO_2 reactivity during hypocapnia were evaluated in 10 healthy male subjects (mean age 25.6 ± 0.8 years). Measurements were done at rest and during hypocapnia, and were repeated four times each at different cerebral artery territories with an interval of 1 week. MCA and ACA blood flow velocities were measured with a transcranial Doppler flowmeter. Blood flow velocity was corrected to 40 mm Hg of end-tidal CO_2 partial pressure (P_{ETCO2}), and was expressed as CV40. CO_2 reactivity was measured as percent change in mean blood flow velocity/mm Hg P_{ETCO2}.

Results: Mean MCA and ACA blood flow velocities at rest, CV40, and CO_2 reactivity during hypocapnia increased significantly after GV20 acupuncture treatment, whereas mean arterial blood pressure and pulse rate at rest did not change significantly. The increases in MCA and ACA blood flow velocity were associated with improved CO_2 reactivity after GV20 acupuncture treatment.

Conclusions: The data suggest that GV20 acupuncture treatment increases cerebral blood flow. The results of this small-scale study provide preliminary evidence for acupuncture effectiveness.

Introduction

Use of sonography for diagnostics and monitoring is becoming more refined and relevant in neuroscience, neurology, neurosurgery, anesthesiology, and intensive care medicine. Especially, transcranial Doppler sonography (TCD) has become an important neurophysiologic monitoring method,[1] by virtue of its capabilities for rapid, noninvasive, reproducible, and dynamic examination of intracranial circulation.[2]

Recently, acupuncture has gained popularity among practitioners of modern medicine as an alternative and complementary treatment. According to the theory of Oriental medicine, each acupoint has a functional specificity; specific acupoints are carefully selected when acupuncture is used to treat disorders.[3,4] In particular, the *Bai-Hui* (GV20) acupoint is used to treat headache, dizziness, dysarthria, and stroke.[3,4] The present study chose the GV20 acupoint to evaluate acupoint effectiveness, hypothesizing that its stimulation induces cerebrovascular responses.

Studies conducted using TCD have provided evidence of the efficacy of acupuncture and herbal medicine treatments,[5–7] but comparative data concerning acupuncture and herbal medicine treatment are scant.

In the present study, changes of hyperventilation-induced carbon dioxide reactivity and corrected blood flow velocities

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at 40 mm Hg of the middle cerebral artery (MCA) and anterior cerebral artery (ACA) were assessed in 10 healthy young male volunteers. The results of this small-scale study provide preliminary evidence for acupuncture effectiveness.

Materials and Methods

Ten (10) healthy male volunteers (age, mean ± standard deviation, 25.6 ± 0.8 years, range 25–27 years) participated in this study. The study protocol was approved by the institutional review board at the hospital of Oriental medicine, KyungHee Medical Center. Informed written consent was obtained from each subject. None of the subjects had a history of psychiatric problems, hypertension, diabetes mellitus, neurologic disorders, or head trauma. The subjects were forbidden to smoke or consume alcohol and coffee during the study.

One (1) experienced acupuncturist performed all acupuncture procedures using a stainless steel acupuncture needle with a diameter of 0.30 mm and a length of 40 mm (DongBang Acupuncture, Seoul, Korea). Each needle was inserted into the skin to a depth of approximately 5 mm at the GV20 acupoint (which is on the midsagittal line at the intersection of a line connecting the right and left ear apices[4]) of each subject and left in position for 20 minutes (Fig. 1). During this time, stronger stimulation was generated by periodic physical rotations of the needle for a minute at 2 Hz, with 5 minutes between rotations.

Each subject took part in the study once a day at 3 PM on 4 separate days, at 1-week intervals. During each procedure, cerebral blood flow (CBF) of the right and left MCA, and right and left ACA were measured in order (right MCA, right ACA, left MCA, left ACA) by TCD. The use of the same measurement order avoided possible bias.

Mean MCA and ACA blood velocities, and CO_2 reactivity were measured by TCD using a Multi-Dop X4 system (Compumedics DWL, Singen, Germany) similar to previously described procedures[8–10] at rest and during 1-minute hyperventilation-induced hypocapnia. Each subject was placed in the supine position with both eyes closed. The 2-MHz pulsed Doppler probe was positioned on the temporal region (ultrasonic window), and a removable bilateral probe holder (LAM-Rack; Compumedics DWL) was used to avoid shifting of the probe and permit continuous measurements. The highest signal was sought at depths ranging from 45 to 60 mm for MCA, and 65–80 mm for ACA. The sample and gain values were adjusted to the value and recorded when the waveform of CBF was well maintained. All investigations started after the subjects were stabilized for 5 minutes (Fig. 1). The mean flow velocity was calculated continuously as the time-averaged maximum velocity over the cardiac cycle computed from the envelope of the maximum frequencies. During continuous monitoring by a Cardiocap S/5 capnometer (Datex-Ohmeda, Helsinki, Finland), the subject was instructed to breathe normally until a steady state was reached. Mean MCA and ACA blood velocities at rest were obtained in the stable normocapnic condition, and the point of the temporal window was marked for the repeated study afterward. The lowest MCA and ACA mean flow velocities near the end of the hyperventilation period were examined thereafter. All TCD spectra were recorded for later review.

Since blood flow velocity is dependent on the $Paco_2$, corrected blood flow velocity was calculated at 40 mm Hg of CO_2 tension (CV40, cm/s) as described previously[9]:

$$CV40 = V_1 \cdot e^{b(PCO_2\ 40\,mm\,Hg - P_1CO_2)}$$

where b is CO_2 reactivity and V_1 is velocity at P_1CO_2.

CO_2 reactivity refers to the percent change in mean blood velocity per millimeter of mercury change in P_{ETCO2}, as calculated by the following formula[11]:

$$CO_2\ \text{reactivity} = 100 \times [V_{rest} - V_{hypocapnia}] / V_{rest} / \Delta P_{ETCO2}$$

where V_{rest} is blood velocity at rest, obtained in the stable normocapnic condition, $V_{hypocapnia}$ is the blood flow velocity of the latter half of the 1-minute period of hyperventilation period, and ΔP_{ETCO2} is the change in P_{ETCO2} from baseline to maximal hyperventilation (Fig. 1). CO_2 reactivity was expressed as %/min.

The variables that may control CBF were controlled by various modules of the Cardiocap S/5 collector (Datex-Ohmeda). Blood pressure was obtained in a stable normocapnic condition before hyperventilation; this was done four

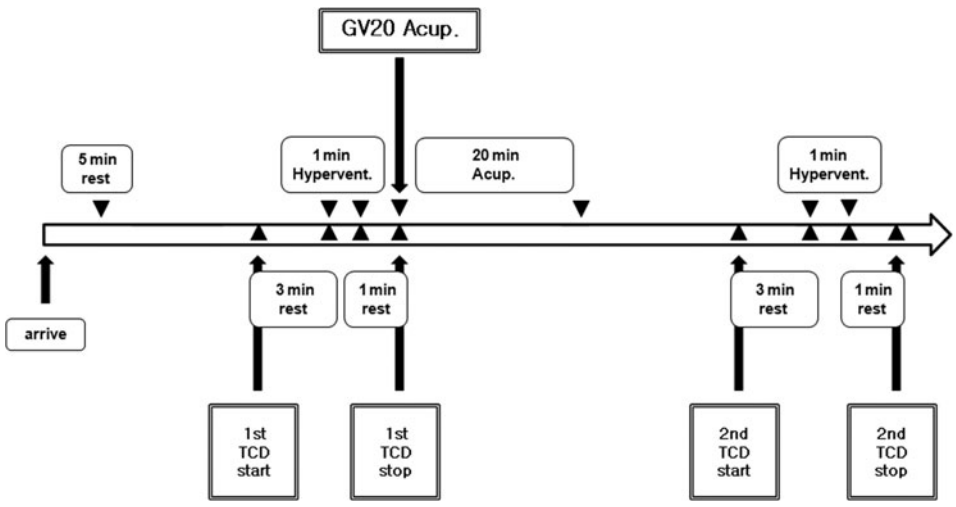

FIG. 1. Study design on the effects of GV20 acupuncture. GV20, *Bai-Hui* acupoint; Acup., acupuncture; TCD, transcranial Doppler; Hypervent., hyperventilation.

times with a 2-minute interval between measurements to determine mean blood pressure. The pulse rate was continuously monitored by an oximetry apparatus positioned on the subject's finger. Also, P_{ETCO2} was continuously monitored by a Cardiocap S/5 collector-connected nasal prong positioned on the subject's nostril, and each subject was asked to breathe only through the nose during the study. A snapshot function in the Cardiocap S/5 collector program was used to calculate the mean pulse rate and P_{ETCO2} at certain assessment times. These three controlled variables were obtained and saved in the computer, which was connected to the Cardiocap S/5 collector program with various modules.

Using the above tools, before GV20 acupuncture treatment for each subject, the blood pressure was obtained four times with a 2-minute interval. Simultaneously, during an 8-minute interval, a continuous assessment of pulse rate was made. Subsequently, CO_2 reactivity and mean blood flow velocity were obtained before and after TCD measurement. After the 20-minute GV20 acupuncture treatment, the procedure was repeated (Fig. 1).

Statistical analysis utilized Statistical Package for the Social Sciences version 12.0 for Windows (SPSS, Chicago, IL). Statistical comparisons between the values before and after GV20 acupuncture treatment were made with the Wilcoxon signed-rank test, and a p value <0.05 was considered significant. Data are expressed as mean ± standard deviation.

Results

Mean arterial blood pressure and pulse rate at rest did not change significantly after GV20 acupuncture treatment on the 10 subjects (Table 1). Corrected blood flow velocities ($P_{ETCO2} = 40$ mm Hg) of right MCA, right ACA, left MCA, and left ACA during hypocapnia increased significantly after GV20 acupuncture treatment ($p = 0.013$ for right MCA and left MCA, $p = 0.005$ for right ACA and left ACA; Table 2). Also, CO_2 reactivity of right MCA, right ACA, left MCA, and left ACA during hypocapnia increased significantly after GV20 acupuncture treatment ($p = 0.005$ for all; Table 3).

Discussion

The purpose of the present study was to determine whether GV20 acupuncture treatment would cause significant responses to CBF velocity and CO_2 reactivity of the MCA and ACA during hypocapnia in normal subjects. Since previous related studies had some shortcomings, described later in our text, it was necessary to make some corrections to draw out a more accurate result and to make a guideline relevant for future research.

The results showed that mean corrected blood flow velocities (at $P_{ETCO2} = 40$ mm Hg) of MCA and ACA, and CO_2 reactivity increased significantly after GV20 acupuncture treatment. TCD was used to directly measure CBF velocity. TCD measures blood flow velocity but not CBF. However, changes in flow velocity may be proportional to those in CBF if the vessel diameter is constant. In humans, the diameter of a large cerebral artery with an internal diameter exceeding 2.5 mm does not change significantly despite alternations in $Paco_2$.[12] The present study investigated blood flow velocities in the proximal trunk of the MCA (depth of 45–55 mm from the skull) and ACA (depth of 65–80 mm from the skull), and assumed that the diameters for the MCA and ACA (3–5 mm[13] and 2.5–3.5 mm,[14] respectively) would not change significantly after GV20 acupuncture treatment. A previous study reported a significant positive correlation between blood flow velocity in defined brain arteries and the corresponding regional CBF in resting normal subjects.[15] The reproducibility of the TCD velocimetry is acceptable for repeated measurements of MCA and ACA blood flow velocities from 1 day to the next.[16,17] Therefore, the change in MCA and ACA blood flow velocities was presently regarded as an index of CBF changes in the MCA and ACA territories. Under normal physiologic conditions, CBF is not affected by a moderate change in mean arterial blood pressure (i.e.,

Table 1. Change of Mean Blood Pressure and Pulse Rate Before and After GV20 Acupuncture

	Before acupuncture	*After acupuncture*	p-*value*[a]
BP (mm Hg)	86.3 ± 6.3	86.1 ± 5.9	0.818
PR (bpm)	65.8 ± 7.2	64.3 ± 6.5	0.097

[a]By Wilcoxon signed-rank test.
Values are mean ± standard deviation.
GV20, *Bai-Hui* acupoint; BP, mean blood pressure; PR, pulse rate; bpm, beats per minute.

Table 2. Change of Corrected Blood Flow Velocity at $P_{ETCO2} = 40$ mm Hg (CV40, cm/sec) Before and After GV20 Acupuncture

	Before acupuncture	*After acupuncture*	p-*value*[a]
Rt MCA	51.7 ± 16.1	62.9 ± 11.6	0.013
Rt ACA	53.5 ± 16.3	61.8 ± 15.1	0.005
Lt MCA	59.1 ± 15.4	70.0 ± 15.3	0.013
Lt ACA	47.7 ± 12.7	58.0 ± 13.3	0.005

[a]By Wilcoxon signed-rank test.
Values are mean ± standard deviation.
CV40, corrected blood flow velocity at $P_{ETCO2} = 40$ mm Hg; GV20, *Bai-Hui* acupoint; Rt MCA, right middle cerebral artery; Rt ACA, right anterior cerebral artery; Lt MCA, left middle cerebral artery; Lt ACA, left anterior cerebral artery.

Table 3. Change of CO_2 Reactivity (%/min) to Hyperventilation Before and After GV20 Acupuncture

	Before acupuncture	*After acupuncture*	p-*value*[a]
Rt MCA	1.98 ± 0.41	3.08 ± 0.74	0.005
Rt ACA	1.93 ± 0.59	2.80 ± 0.83	0.005
Lt MCA	1.92 ± 0.45	2.44 ± 0.52	0.005
Lt ACA	1.73 ± 0.49	2.22 ± 0.55	0.005

[a]By Wilcoxon signed-rank test.
Values are mean ± standard deviation.
GV20, *Bai-Hui* acupoint; CO_2 reactivity, cerebrovascular reactivity to hyperventilation; Rt MCA, right middle cerebral artery; Rt ACA, right anterior cerebral artery; Lt MCA, left middle cerebral artery; Lt ACA, left anterior cerebral artery.

between 50 and 130 mm Hg).[18] Mean blood flow velocity remains unaffected by the cardiac index in the range of 2.0–4.0 L/min/m^2.[19] $Paco_2$ and arterial oxygen content can profoundly influence CBF, MCA, and ACA blood flow velocities.[20,21] P_{ETCO2} and transcutaneous (tc) Po_2 were measured instead of $Paco_2$ and Pao_2, respectively. P_{ETCO2} response curves for blood flow velocity in the MCA strongly resembled $Paco_2$ response curves for CBF.[8] In adults, $tcPo_2$ is 20–30% lower than Pao_2 because of the properties of their skin[22]; however, it correlates well within the parameters of normal cardiac output.[23] In the present study, both mean arterial blood pressure and pulse rate at rest remained within normal range, and P_{ETCO2} and $tcPo_2$ under normocapnic conditions did not change significantly after GV20 acupuncture treatment (Table 1). The oxygen content of blood depends mainly on the volume bound to hemoglobin, together with a relatively small amount of oxygen dissolved in the plasma.[24] The oxygen content did not change significantly in this study. Accordingly, it is more likely that the increases in MCA and ACA corrected blood flow velocities (at $P_{ETCO2} = 40$ mm Hg) may indicate an increase in CBF as a result of rheological improvement by GV20 acupuncture treatment without changes in oxygen content or CO_2 tension. A study reported that changes in MCA blood flow velocity correlated reliably with changes in CBF measured with intravenous ^{133}Xe when hypercapnia was induced; the authors expressed CO_2 reactivity as a percent change in mean MCA peak velocity per unit change in P_{ETCO2}.[25] Hence, the CO_2 reactivity of blood flow in the cerebral arteries can be determined from changes in flow velocity measured by TCD. Another study reported that CO_2 reactivity was proportional to resting blood flow values when mean arterial blood pressure was constant.[26] The law of initial values,[27] which states that the higher the initial level, the smaller the response to function-raising agents and the greater the response to function-depressing agents, may affect the observed improvement of CO_2 reactivity. In the present study, CO_2 reactivity increased significantly after GV20 acupuncture treatment, which seems due to the significantly increased resting CBF as the result of improvements in hemorheology. Therefore, CO_2 reactivity might be regarded as an index of CBF, with CO_2 reactivity increasing significantly after GV20 acupuncture treatment because of the acupuncture-mediated significant increase of CBF.

Several aspects in previous studies need to be addressed. One (1) study, which used the same intervention and TCD introduced in our study, reported that mean, systolic, and diastolic velocities increased significantly, whereas pulsatility index decreased significantly at different depths of both MCAs in normal subjects.[6] However, the results of this study need to be confirmed because it lacked information about CO_2 reactivity and corrected blood flow velocity (at $P_{ETCO2} = 40$ mm Hg) mentioned in previous studies[5,11,28–30] and the present studies. Furthermore, previous studies with medication intervention assumed that all territories of cerebral arteries were influenced,[5,7,31] whereas in studies with acupuncture using single-photon emission computed tomography,[32,33] only specific brain regions were affected by particular acupoints. Given the differing information, it was presently necessary to measure the mean blood flow velocities and CO_2 reactivity on territories as much as possible. Hence, the present study measured not only both sides of MCA but also ACA, unlike the previous study,[6] whose conclusions were based only on measurements of the temporal region of MCAs. As a result, corrected blood flow velocities (at $P_{ETCO2} = 40$ mm Hg) and CO_2 reactivity of all groups increased significantly, which meant that GV20 acupuncture treatment may influence both sides of MCA and ACA territories due to GV20 acupoint's specific function and mechanism.[3]

Several interesting studies have investigated significant CBF changes after acupuncture on different acupoints. An et al.[34] reported that there were specific increases in both regional CBF and glucose metabolism following electroacupuncture in both frontal regions. This common brain response in localized regions was induced from stimulation of specific acupoints (LI4 and LI11). Backer et al.[35] showed that different modes of manual acupuncture stimulation at LI4 differentially modulate CBF velocity, arterial blood pressure, and heart rate in human subjects. Also according to Litscher et al.,[36] acupuncture at PC6, CV6, ST36, and SP6 significantly changed mean CBF velocity. These results are interesting in that they provide crucial evidence of acupuncture effectiveness on CBF. Compared with the present study, however, the acupuncture scheme, needle manipulation, methods of measurement, and selection of acupoints introduced in these studies were different; thus, data have to be compared with caution.

One limitation of this study was the absence of evaluation on the posterior cerebral arteries. The reason for this was due to large individual variation of the TCD incidence angle, blood flow velocity, and difficult continuous monitoring resulting from the location and structural nature of the artery.[2] Therefore, this study can only discuss the influence of the GV20 acupuncture on both sides of MCA and ACA. Further studies including an evaluation on the posterior cerebral artery will be needed to confirm the present findings. Another limitation of this study was the sample size, statistical power, and the number of related references. Not only studies with a larger sample size and attendant greater statistical power, but also more similar studies on hemodynamics of cerebral and carotid artery after acupoints stimulation as reported by Zhao et al.[37] are necessary to confirm the present findings. Also, a crucial nonacupoint control group should have been arranged, but due to an ongoing debate about the effectiveness and ethics of sham-acupuncture, we decided not to make our results controversial by adding a nonacupoint control group. Zaslawski et al.[38] reported that the experimental design of sham acupuncture may be applicable to many other acupuncture trials. However, Moffet[39] showed that most studies comparing acupuncture to sham acupuncture found no statistically significant differences in outcomes, and most of them found that sham acupuncture is efficacious, especially when superficial needling was applied at nonpoints. Moreover, as reported by Hammerschlag and Zwickey,[40] in the absence of well-documented mechanisms for most CAM therapies, with acupuncture, as representative cases, an appropriate sham control cannot be designed rationally. These findings highlight the difficulty of conducting controlled trials of acupuncture in the absence of theories about what, exactly, one is controlling for. Therefore, until the mechanisms of acupuncture are fully discovered, a sham acupuncture control group must be arranged in extreme precaution. More

attention should be shifted to the question of clinical relevance, with research focused on comparing acupuncture to standard (biomedical) care, as reported by Hammerschlag[41] and Hammerschlag and Morris.[42]

Conclusions

In conclusion, rheological improvement by GV20 acupuncture treatment results in increases in MCA and ACA blood flow velocities, which are associated with improvements in CO_2 reactivity during hypocapnia in healthy subjects. These results may be of importance in various types of brain ischemia and stroke because rheological factors may likewise be of great importance as the determinants of CBF velocity in ischemic brain, where vasodilation is maximal and autoregulation is impaired.

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Disclosure Statement

No competing financial interests exist.

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