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Journal

Cortex, 29(1)

ISSN

0010-9452

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Publication Date

1993-03-01

DOI

10.1016/s0010-9452(13)80210-9

SELECTIVE INCREASE IN THE RIGHT HEMISPHERE TRANSCRANIAL DOPPLER VELOCITY DURING A SPATIAL TASK

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INTRODUCTION

Studies with positron emission tomography (PET) (Phelps, Mazziota and Huang, 1982) and Xeron[133] clearance (Risberg, Halsey, Wills et al., 1975) indicate that it is possible to detect changes in cerebral blood flow (CBF) and cerebral metabolism during cognitive activity. Transcranial Doppler ultrasonography (TCD) allows completely noninvasive measurement of the blood flow velocity of intracranial arteries (Aaslid, Markwalder and Nornes, 1982). This may be of pertinence in the evaluation of flow dynamic disturbances in disease states if TCD can reliably detect circulatory correlates of mental activity. This has prompted us to investigate flow velocity measurements, by TCD, during two tasks which have been found to result in selective activation of CBF by PET (Ginsberg, Chang, Kelley et al., 1988; Fox, Burton and Raichle, 1987).

MATERIALS AND METHODS

Subjects

In order to avoid possible effects of gender and handedness (Gur, Gur, Obrist et al., 1982) on the results, we studied 20 exclusively right handed males. The subjects ranged in age from 20 to 42, mean age = 32.2 years. All subjects were in excellent health and on no medications. All abstained from nicotine and caffeine containing products for at least six hours prior to the study.

Blood pressure and pulse were measured before and after the study. In a similarly designed study of other tasks (Kelley, Chang, Scheinman et al., 1992), we observed no significant alteration of either exhaled pCO_2 or level of anxiety. Therefore, to limit the time required for volunteers, and to avoid the discomfort of wearing a facemask, these maneuvers were not performed for this study.

Handedness was assessed with a handedness questionnaire. It was determined that all subjects visually aimed, wrote, threw and kicked on their right side.

Tests and Procedures

The two tasks assessed were the sorting of mah-jongg tiles and vibratory stimulation. The sorting of mah-jongg tiles consisted of determining whether the tile symbol was either Chinese characters, circles or lines (Figure 1).

The subject was instructed to palpate each tile placed in their hand while blindfolded.

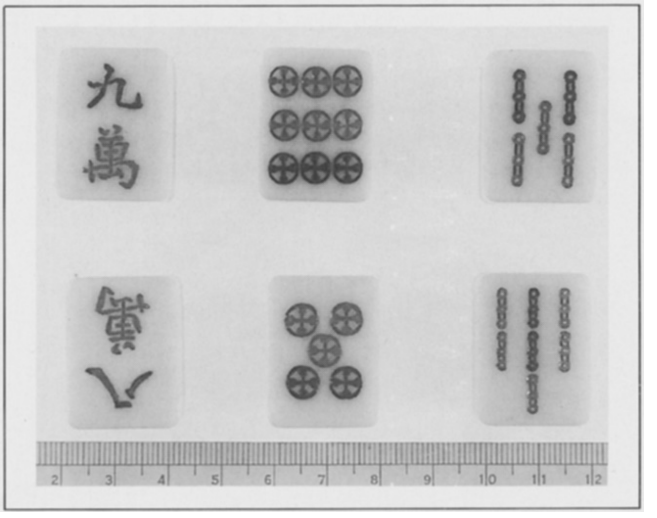

Fig. 1 – *Demonstration of the three types of mah-jongg tiles used: Chinese characters (left), circles (center) and lines (right).*

They were to make a decision, in regards to the particular symbol, within 5 to 10 seconds and to place the tile in one of three respective boxes placed in front of them. Tile sorting continued for a period of 8 minutes with TCD velocity measurements recorded every 30 seconds for each middle cerebral artery (MCA). Each activation study was preceded by an 8 minute resting study in which the subject sat in a quiet room while blindfolded. Prior to all studies, we made serial readings over several minutes in order to ensure reproducibility of the velocity measurements i.e. steady state.

The sorting of tiles was performed with both the left hand and right hand, separately, for each study. In order to avoid a possible initiation effect, 10 subjects began tile sorting with the left hand and 10 subjects began tile sorting with the right hand.

Vibratory stimulation was conducted with the use of a commercial vibrator (The Workout®, Hitachi Ltd; Tokyo, Japan). To avoid irritation, the vibrator was held in a particular hand for 10 seconds and was then turned off for 5 seconds in a serial fashion throughout the 8 minute recording period.

As with tile sorting, there was an 8 minute baseline study obtained prior to each activation study. In addition, the study was initiated with the left hand or the right hand in an alternating fashion. Because of a technical problem with machine breakdown, one of the 20 subjects did not undergo vibratory stimulation.

TCD measurements were made with a commercially available continuous-wave Doppler unit (Transpect®, MedaSonics Corp, Mountain View, CA). This unit consists of two 2 MHz transducer probes fitted on a headband. Serial alternating recordings of the MCAs were made with the use of a switchbox as this unit does not allow simultaneous measurements. For this particular Doppler unit, the mean velocity (Vmean) represents the averaging of the peak systolic and peak diastolic components of the Doppler waveform envelope over one cardiac cycle. The peak systolic velocity (Vpeak) was also obtained with on-line calculation provided by the TCD unit.

Statistical Analysis

We compared the eight baseline values of a particular MCA, for both the Vmean and the Vpeak, to the eight ipsilateral activation values by paired t-test (Snedecor and Cochran, 1989). To adjust for multiple comparisons, a Bonferroni correction was used with the alpha set at .006 for statistical significance (Kleinbaum, Kupper and Muller, 1988). Hand-hemisphere interactions were further assessed by a two (hands)-by-two (hemispheres) analysis of variance (ANOVA) (Winer, 1971).

Results

The mah-jongg task resulted in a statistically significant activation of the right MCA Vmean with both left hand manipulation ($t = -4.5$, $p < .0005$) and right hand manipulation ($t = -3.4$, $p < .005$). The left MCA Vmean was increased in a statistically significant fashion with right hand manipulation ($t = -3.4$, $p < .005$) but not with left hand manipulation ($t = -1.6$, $p = .126$). The results for the Vmean, during the mah-jongg task, are summarized in Table I. For the mah-jongg task, we found a significant interaction between hand manipulation and hemisphere flow velocity by ANOVA ($F = 10.8$; d.f. = 1, 19; $p < .004$). Followup comparisons, by paired t-test, revealed that the interaction of the left hand-left hemisphere was less than the left hand-right hemisphere ($t = 4.0$, $p < .0004$), the right hand-right hemisphere ($t = 2.4$, $p = .01$) and the right hand-left hemisphere ($t = 2.4$, $p = .01$).

TABLE I

The Mean Velocity During Mah-jongg Tile Sorting

	Baseline[2]	Activation[2]	%Change[3]	t[4]	p[5]
Right middle cerebral artery[1] (N = 20)					
Left hand manipulation	54.3±8.6	58.2±9.5	+7.4%	−4.5	<.0005
Right hand manipulation	54.6±8.9	57.3±9.9	+4.9%	−3.4	<.005
Left middle cerebral artery[1] (N = 20)					
Left hand manipulation	56.1±10.3	57.1±11.9	+1.4%	−1.6	.126
Right hand manipulation	56.2±11.5	59.4±12.1	+5.9%	−3.4	<.005

[1] All velocity values in cm/sec.
[2] Mean±standard deviation.
[3] Represents averaging of all individual % change above or below baseline value during activation.
[4] By paired t-test.
[5] The p value should be compared to a significance level of .006 which is the Bonferroni-corrected error rate for eight multiple tests.

Overall, 17 of the 20 subjects had some degree of activation of the right MCA Vmean with left hand manipulation and the degree of activation, above baseline, ranged from 1.8 to 23.2%. Fifteen of 20 subjects had activation of the right MCA Vmean during right manipulation with the degree of activation ranging from 1.0 to 26.3%. Thirteen of 20 subjects had an activation of the left MCA Vmean with left hand manipulation which ranged from 1.0 to 8.4%. Fourteen of 20 subjects had activation of the left MCA Vmean during right hand manipulation and the degree of increase ranged from 2.3 to 20.7%.

The Vpeak of the right MCA increased, on average, with left hand manipulation ($t = -5.1$, $p < .0006$) but this was not the case for right hand manipulation ($t = -1.8$, $p = 0.6$). The Vpeak of the left MCA did not have a statistically significant increase with either right hand ($t = -3.1$, $p < .09$) or left hand manipulation ($t = -.062$, $p = 4.3$). These results are summarized in Table II. The right MCA had an increased Vpeak in 18 of the 20 subjects during left hand manipulation with a range of 0.8 to 13.8%. There was an increase in the right MCA Vpeak, with right hand manipulation, in 14 of 20 subjects with a range of 0.4 to 12.2%. The left MCA had an increased Vpeak in 13 of 20 subjects with

TABLE II

The Peak Systolic Velocity During Mah-jongg Tile Sorting

	Baseline[2]	Activation[2]	%Change[3]	t[4]	p[5]
Right middle cerebral artery[1] (N=20)					
Left hand manipulation	95.8±18.6	100.3±19.3	+4.7%	−5.1	<.0001
Right hand manipulation	97.2±19.4	98.9±27.0	+2.0%	−1.8	.08
Left middle cerebral artery[1] (N=20)					
Left hand manipulation	97.7±18.2	98.2±18.8	+0.6%	−.62	.54
Right hand manipulation	97.7±20.2	101.3±20.5	+3.7%	−3.1	<.01

[1] All velocity values in cm/sec.
[2] Mean±standard deviation.
[3] Represents averaging of all individual % change above or below baseline value during activation.
[4] By paired t-test.
[5] The p value should be compared to a significance level of .006 which is the Bonferroni-corrected error rate for eight multiple tests.

TABLE III

The Mean Velocity During Vibratory Stimulation

	Baseline[2]	Activation[2]	%Change[3]	t[4]	p[5]
Right middle cerebral artery[1] (N=19)					
Left hand stimulation	53.6±8.3	54.5±9.3	+1.7%	−1.3	0.2
Right hand manipulation	52.7±8.5	52.6±8.3	−2.4%	−1.7	0.1
Left middle cerebral artery[1] (N=19)					
Left hand stimulation	54.2±9.7	54.3±10.2	+0.2%	−0.1	0.9
Right hand stimulation	54.6±10.6	55.2±11.3	+1.0%	−0.8	0.4

[1] All velocity values in cm/sec.
[2] Mean±standard deviation.
[3] Represents averaging of all individual % change above or below baseline value during activation.
[4] By paired t-test.

TABLE IV

The Peak Systolic Velocity During Vibratory Stimulation

	Baseline[2]	Activation[2]	%Change[3]	t[4]	p
Right middle cerebral artery[1] (N=19)					
Left hand stimulation	93.7±20.3	94.6±19.7	+1.2%	−1.0	0.3
Right hand stimulation	93.0±20.6	93.0±20.6	0.0%	0.04	1.0
Left middle cerebral artery[1] (N=19)					
Left hand stimulation	93.1±17.3	94.0±17.4	+1.1%	−0.1	0.3
Right hand stimulation	94.1±19.1	94.7±19.7	+0.6%	−0.6	0.5

[1] All velocity values in cm/sec.
[2] Mean±standard deviation.
[3] Represents averaging of all individual % change above or below baseline value during activation.
[4] By paired t-test.

left hand manipulation and the range was 0.1 to 10.4%. An increase in the left MCA Vpeak, with right hand manipulation, was seen in 15 of 20 subjects. The degree of increase ranged from 1.4 to 15.6%.

No significant activation was seen with vibratory stimulation of either the right or left hand. This was the case for both the Vmean (Table III) and the Vpeak (Table IV).

Discussion

The increase in MCA flow velocity observed is apparently reflective of a selective increase in regional CBF and cerebral metabolism which has been demonstrated by PET (Ginsberg, Yoshii, Vibulsresth et al., 1987; Ginsberg et al., 1988; Fox et al., 1987). Mental activity is associated with augmentation of regional cerebral metabolism resulting in a local increase in pCO2 with secondary dilation of the precapillary bed. This results in a focal increase in CBF at specific cortical sites which is associated with a reduction in local vascular resistance. This reduction in local vascular resistance presumably results in an increased flow velocity in the more proximal arterial segment which supplies the particular cortical territory (Reivich, 1964). Other TCD parameters, such as diastolic velocity and pulsatility index, may be of pertinence in this type of activation study but these measurements are not provided by our Doppler unit.

With the use of PET (Ginsberg et al., 1988), we have observed a 16.9% average increase in local cerebral glucose utilization and a 26.6% average increase in local CBF in normals performing the mah-jongg task. Vibratory stimulation has been reported to result in an increase in the contralateral first somatosensory cortex CBF of 16 to 25% (Fox et al., 1987).

TCD assessment of cerebral activation has been the subject of several recent studies. Aaslid (1987) reported a flow velocity increase within the posterior cerebral artery in 10 normal subjects exposed to visual stimulation. The average observed increase in flow velocity, above baseline, was 16.4%. Intermittent light stimulation, at frequencies of 10 to 20 Hz, resulted in a detectable increase in the posterior cerebral artery flow velocity according to another study (Gomez, Gomez and Hall, 1990). Droste, Harders and Rastogi (1989) reported an increase in MCA flow velocity ranging from 1.6 to 10.6% in 70 subjects during mental activity. In a prior study of 21 subjects, who had TCD monitoring while playing a commercial video game (Kelley et al., 1992), we observed a selective increase in the flow velocity of both MCAs and the left posterior cerebral artery compared to the ipsilateral anterior cerebral artery.

The mah-jongg task was observed to result in a statistically significant increase in the contralateral MCA flow velocity, on average. This is not an unexpected finding as this task obviously involves tactile stimulation and fine motor activity which should be associated with activation of the contralateral sensorimotor cortex. Of interest, the Vmean of the right MCA was increased during both right and left hand manipulation. This was not observed with the Vpeak but it is important to note that the Vmean is the TCD velocity parameter with the greatest physiological significance as it is less dependent on central cardiovascular factors than either the pure systolic or diastolic components (Aaslid, 1986). In our previous study of TCD activation (Kelley et al., 1992), we also observed that the Vmean was more sensitive than the Vpeak.

The finding of right MCA activation with both left handed and right handed tile sorting supports the preponderant role of the right hemisphere in spatial cognition (De Renzi, 1978; Benton, 1982). Research into tactile discrimination in right handed subjects has demonstrated a right hemispheric dominance in the processing of tactile information as well as in spatial tasks in general (Bradshaw and Nettleton, 1981; Cohen and Levy, 1986; Ratcliff, 1987). The left hemisphere certainly has a role in spatial processing but to a lesser degree (Mehta and Newcombe, 1991). In addition, the perceptual processing of a novel task may demonstrate a right to left shift in hemispheric advantage as the subject adapts to the task (Kittler, Turkewitz and Goldberg, 1989). Attention, which is an important component of task performance, appears to be primarily a right hemispheric function (Mesulam, 1981). Of relevance, in this regard, is the finding that right carotid endarterectomy was associated with facilitation of bilateral attention as well as arousal responses (Greiffenstein, Brinkman, Jacobs et al., 1988).

Vibratory stimulation was not associated with a significant increase in MCA flow velocity. This suggests a specificity of the tasks with the implication that the activation observed with tile sorting was not primarily related to an anxiety effect (Rodriguez, Cogorno, Gris et al., 1989). Vibratory stimulation is not an optimal control for comparison to tile sorting, however, as tile sorting involves not only a sensory but also a motor and a spatial component. Our inability to detect a flow velocity change with vibratory stimulation may reflect the limited sensitivity of TCD compared to the PET studies which have reported an increase in CBF (Fox et al., 1987; Meyer, Ferguson, Zatorre et al., 1991). It might also be related to technical factors, such as the type of vibratory device, as we were also unable to demonstrate a response to vibratory stimulation at our PET center (Ginsberg et al., 1987) with our particular vibration device. There has been reported to be a relationship between CBF and task difficulty (Gur, Gur and Skolnick, 1988) but this would not explain the activation of the right MCA with both left and right hand tile sorting while the left MCA was only activated by right hand tile sorting.

TCD has the potential to provide noninvasive circulatory correlates of mental activity. Changes in the MCA flow velocity have been found to correlate with changes in CBF in a reliable fashion although the absolute velocity value cannot be used as an indicator of CBF (Bishop, Powell, Rutt et al., 1986). There is some question as to the validity of deriving CBF information from TCD measurements but useful approximations in steady state conditions are still possible (Kontos, 1989). Thus, TCD is capable of providing a quantitative index of cerebral activation and may have potential in the assessment of cognitive impairment secondary to vascular disease.

Abstract

Transcranial Doppler ultrasonography of the middle cerebral arteries was performed during two tasks: sorting of mah-jongg tiles and vibratory stimulation. These tasks selectively increase cerebral blood flow by positron emission tomography. The purpose of this study was to determine if analogous increases in cerebral blood flow velocity could be detected. We measured flow velocity during right hand manipulation followed by left hand manipulation, or vice versa, with resting studies in between. The average increase in the mean velocity, by paired t-test, was significant for the right middle cerebral artery with both left hand ($p<.0005$) and right hand ($p<.005$) tile sorting. For the left middle cerebral artery, there was an increase in the mean velocity with right hand ($p<.005$) but not for left hand sorting ($p=.13$). These findings support the importance of the right hemisphere in the per-

formance of this type of spatial task. No significant flow velocity increase occurred during vibratory stimulation.

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