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Lack of prolonged cerebral blood flow change after transcranial magnetic stimulation

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Summary To study the physiological changes in the human brain induced by transcranial magnetic stimulation (TMS), we measured cerebral blood flow (CBF) before and after TMS in 3 healthy volunteers with positron emission tomography (PET). The intersecting point of the figure-of-eight coil was positioned at C3. TMS was delivered 20–32 times at maximum intensity. CBF measured at 50 sec after the termination of TMS showed no significant change in the cerebral cortex corresponding to C3 or any other area. This finding indicates that the hemodynamic change in the brain induced by TMS, if any, lasts only for a short period.

Key words: Cerebral blood flow; Positron emission tomography; Transcranial magnetic stimulation

Although transcranial magnetic stimulation (TMS) has become a very useful tool for evaluating the function of central motor pathways, the physiological changes which could be induced in the human brain by TMS have not been studied fully yet. It has already been shown that TMS has no effect on the electroencephalogram, cognitive function or serum hormone levels such as cortisol and prolactin (Krain et al. 1990; Levy et al. 1990). As far as cerebral blood flow (CBF) is concerned, only a few reports have been published (Shafran et al. 1989; Dressler et al. 1990). To further investigate the hemodynamic effects of TMS on the human brain, we measured CBF before and after TMS with positron emission tomography (PET).

Methods and materials

Three healthy male volunteers aged 20–31 (mean 33.7) were tested. Informed consent was obtained from every subject.

The precise principle and method of cerebral blood flow measurement with PET have been described elsewhere (Herscovitch et al. 1983; Raichle et al. 1983). The subjects were placed supine with the head fixed in a head-holder. Venous and arterial catheters were placed in different arms. Water labeled with oxygen-15 ($H_2{}^{15}O$, half-life 120 sec) was administered by intravenous bolus. Scanning was started immediately after tracer administration. During scanning the subjects were kept quiet with eyes closed. Arterial blood samples were obtained every 5–15 sec during scanning (90 sec) to provide the arterial input curve. Calculation of CBF was made by the inert gas exchange principle.

For TMS a figure-of-eight coil (Nihon Kohden, Tokyo, Japan), with which focal stimulation is possible, was used. The size of the coil was 185 × 100 mm and the maximum magnetic field strength generated by the device was 1.0 Tesla. The duration of the induced pulse was less than 160 msec. Its intersecting point was positioned at C3 according to the international 10–20 method with the long axis of the coil directed anteroposteriorly. TMS was delivered at a frequency of 1/5 Hz with stimulus intensities of 100% of the maximum output of the device. The motor threshold for elicitng a twitch in small hand muscles in normal subjects at rest is 60–70%. A total of 20–32 (mean 26.6) stimuli were given.

First CBF in the resting state (CBFr) was measured. Then TMS was performed with the head of the subject pulled out of the PET scanner because of the limited space and unknown effects of the induced magnetic field on the scanner. After TMS the head was placed in the previous position and measurement of CBF in the activated state (CBFa) was started. The time lag

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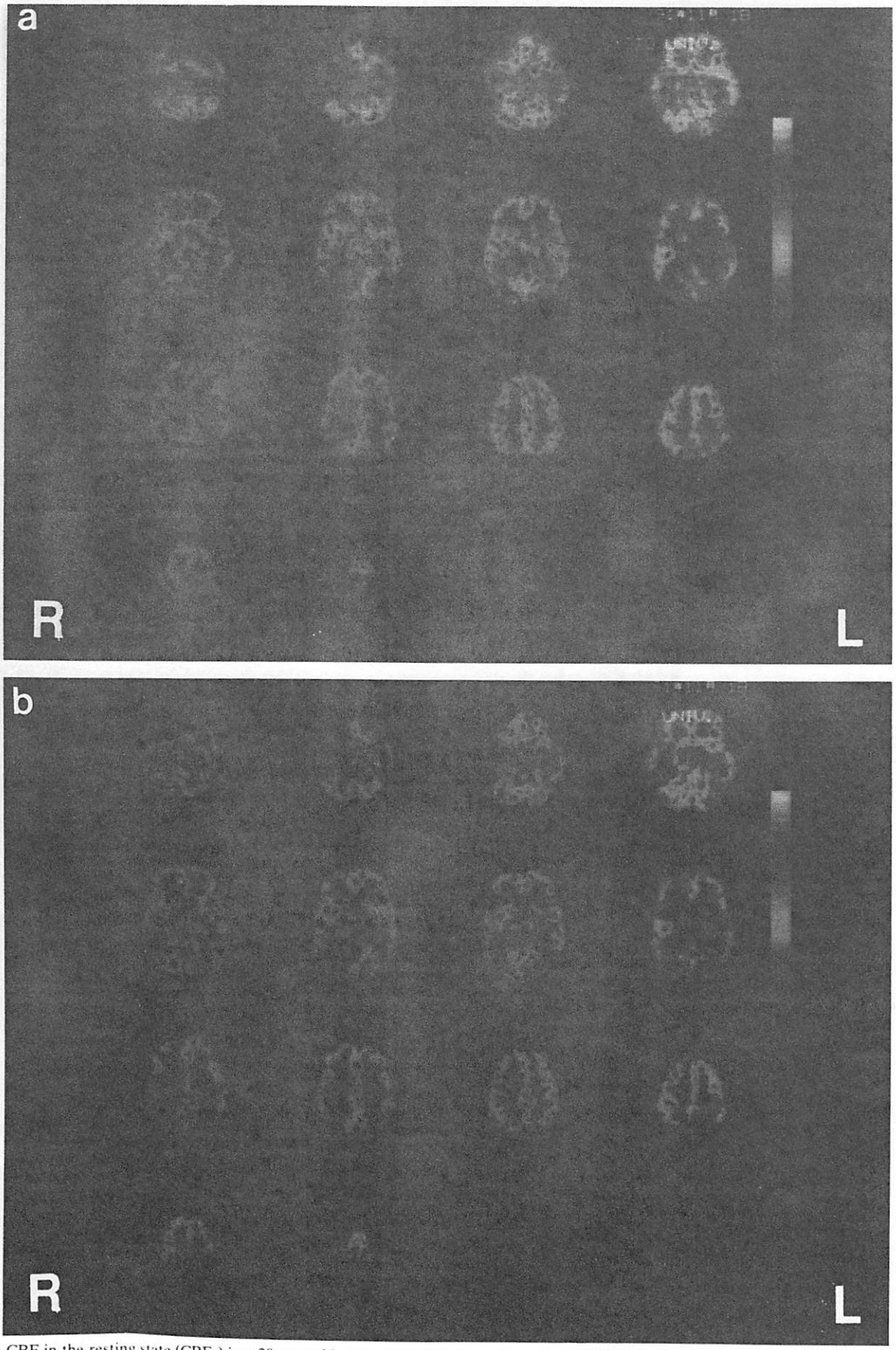
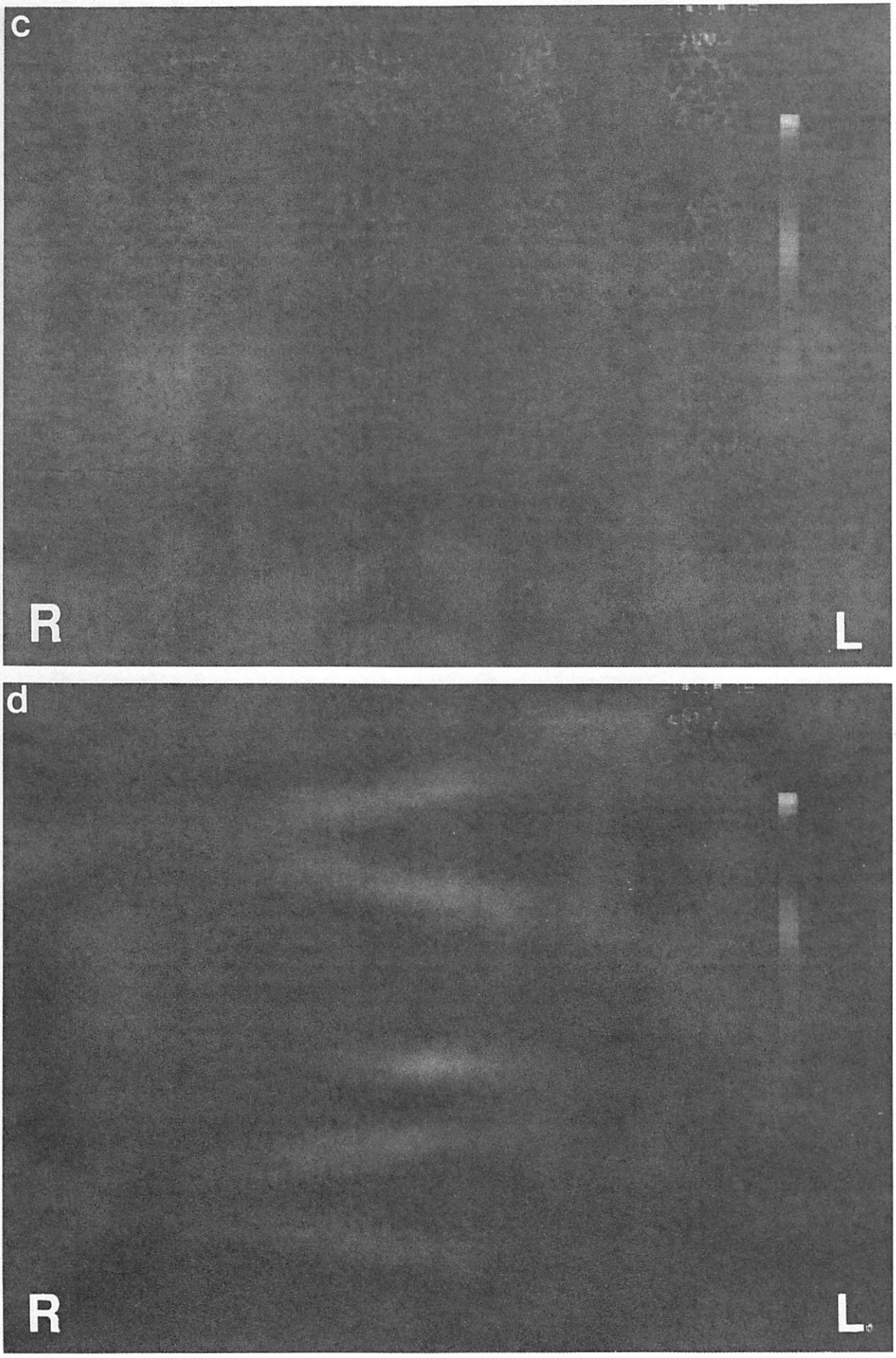


Fig. 1. a: CBF in the resting state (CBFr) in a 20-year-old male. b: CBF in the activated state (CBFa) in the same subject. Vertical scales indicate absolute CBF values in a and b (full scale 100 ml/100 g/min). c: CBF increase obtained by subtracting CBFr from CBFa. d: CBF decrease obtained by subtracting CBFa from CBFr. The vertical scale indicates the ratio of the CBF increase in c or decrease in d to CBFr (full scale 20%).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from the termination of TMS to the start of scanning was about 50 sec in all subjects. Two series of measurements of CBFr and CBFa were performed. At least 15 min were taken between every measurement.

Results

During TMS contraction of the right small hand muscles was observed. Fig. 1a shows the CBFr of a 20-year-old male (two data were averaged). Fig. 1b shows the CBFa of the same subject. Fig. 1c indicates the CBF increase after TMS obtained by subtracting CBFr from CBFa (CBFa – CBFr). The vertical scale denotes the ratio of CBF increase to CBFr. At the cortex corresponding to C3 (hand area of precentral gyrus), where the induced current was localized, the CBF change did not differ from that in other areas. Thus there was no significant CBF increase at that point. Similarly, a CBF decrease was obtained by subtracting CBFa from CBFr (CBFr – CBFa). There was also no significant decrease in CBF (Fig. 1d). The other 2 subjects also showed no significant CBF changes in the region corresponding to C3, which was demonstrated in the same way.

Discussion

There are few reports concerning the effect of TMS on CBF. Shafran et al. (1989) reported an increase of CBF in the bilateral motor cortex after unilateral TMS in man. Dressler et al. (1990) studied the effect of magnetic and electric brain stimulation on CBF with single photon emission-computed tomography (SPECT) in a human subject. They found a slight increase of CBF with both stimulations.

However, we could find no change in CBF with TMS. The discrepancy could be explained by the difference of the methods for measuring CBF. In the study of Dressler et al., a tracer (^{99m}Tc-labeled hexamethylpropyleneamine amino oxime) which displays blood flow dependent brain uptake and long-term retention with little redistribution was used. When the tracer was injected during TMS, the obtained values demonstrated CBF in the midst of TMS irrespective of the time lag between TMS and scanning.

When the water labeled with oxygen-15 ($H_2{}^{15}O$) is used for a tracer in PET, it is possible to measure CBF rapidly and repeatedly because of its short half-life (120 sec) (Herscovitch et al. 1983; Raichle et al. 1983). Due to the time lag of about 50 sec in our method, it was impossible to detect CBF change which lasted less than 50 sec. We probably failed to detect such short-lasting CBF change. Lack of CBF change in the cortical auditory area, which is expected to show a CBF increase due to the loud click produced by the magnetic coil, supports this possibility.

In spite of the limitation of the method of measuring CBF, it was demonstrated that CBF change, if any, was transient and did not last more than 50 sec. In conclusion, TMS was not accompanied by a lasting change in CBF, which is an indicator of brain metabolism. This finding provides a useful piece of information with regard to the safety of TMS.

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