Technetium-99m HM-PAO Brain SPECT in Epileptic Patients Before and During Unilateral Hemispheric Anesthesia (Wada Test): Report of Three Cases

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The lipophilic brain SPECT agent [^{99m}Tc]hexamethyl propylene amine oxime (HM-PAO) was used in three cases before and during unilateral anesthesia of one hemisphere for lateralization of speech dominance (Wada test). This procedure led to a decrease of regional cerebral blood flow (rCBF) in each of the hemispheres to 55 and 90%, respectively. Diminution of rCBF was significantly more pronounced in the dominant hemisphere. A second phenomenon observed during the Wada test was crossed cerebellar diaschisis. These findings support the assumption that HM-PAO allows monitoring of brain perfusion, as rapid changes of rCBF due to decreased neuronal activity cause respective alterations of cerebral and cerebellar uptake of this new brain agent.

J Nucl Med 28:1763–1767, 1987

Single photon emission computed tomography (SPECT) of the brain with iodine-123-labeled amphetamine derivatives has become a routine diagnostic procedure for the lateralization and localization of epileptic foci (*1–4*). However, since 1985 a lipophilic chelate of technetium with hexamethyl propylene amine oxime (HM-PAO), that is able to cross the blood–brain barrier, is available for brain SPECT. This agent has turned out to be the radiopharmaceutical of choice in patients with epilepsy (*5,6*) as ^{99m}Tc is inexpensive and readily available. It is well-suited for tomography because a high dose can be administered and because the energy of emission is optimal for the respective instruments. Thus, HM-PAO SPECT will play a significant role in the study of epilepsy, particularly in cases where patients are considered for surgery (temporal lobectomy). In order to obtain accurate knowledge of the lateralization of speech dominance when operating near Sylvian regions in ambidextrous and left-handed individuals, we evaluated HM-PAO SPECT using a procedure that allows one to detect the speech center described by Wada et al. (*7*).

Received Nov. 5, 1986; revision accepted June 11, 1987.

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METHODS

The test for cerebral hemispheric asymmetry of Wada (*7*) involves injection of 3 mg/kg sodium amytal into the right and 2 days later into the left internal carotid artery through a transfemoral arterial catheter. This procedure leads to anesthesia of one hemisphere, lasting ~5 min and resulting in temporary hemiparesis and in the case of the dominant hemisphere (speech dominance) in aphasia. Before injection, the patient is asked to lift his arms so that the beginning of anesthesia can be documented by the falling (plegic) contralateral arm. Speech tests are then performed over a time period of ~5 min. For all patients cerebral angiograms are obtained.

The radionuclide imaging procedure followed injection of 10 mCi of the technetium-99m- (^{99m}Tc) labeled d,l-stereoisomer of HM-PAO* into an antecutibal vein ~20 sec after the intracarotid injection of sodium amytal. As the HM-PAO is retained in the brain, the patient is transported to our SPECT unit (after removal of the transfemoral catheter) usually 2 to 3 hr postinjection of HM-PAO. For SPECT we use a rotating gamma camera system† with high resolution, low-energy collimator. During one 360° rotation 64 frames with 4k (64 × 64) matrix are acquired within 20 min. Reorientated trans-

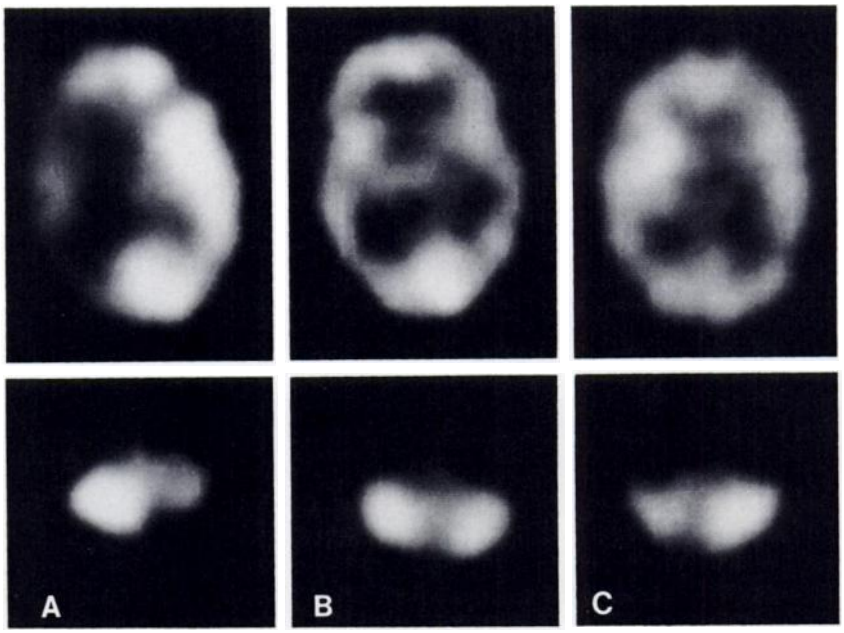

FIGURE 1
Brain SPECT with [^{99m}Tc]HM-PAO before (B) and during Wada test left (A) and right (C) in Case 1. Significantly decreased HM-PAO uptake of the left (dominant) hemisphere during hemi-anesthesia left, only slightly diminished uptake in the right hemisphere during Wada test right; crossed cerebellar diaschisis (lower portion). The patient's right side is to the reader's right.

verse slices are than reconstructed parallel to a line which passes through the lower pole of the frontal lobe and the cerebellum. This technique is useful to obtain identical slices for comparison of results gained at different days.

Each patient had a HM-PAO routine SPECT (10 min p.i.) during the 2 wk prior to the Wada test.

All three patients underwent nuclear magnetic resonance (NMR) investigation. For this purpose a superconductive NMR system‡ working at 0.15 tesla was used.

CASE REPORTS

Case 1

A 15-yr-old right-handed boy had been suffering from partial epilepsy for 5 yr. EEG showed a focus in the left temporal region; computed tomography (CT) and NMR presented with a cystic lesion in the left temporal lobe. Routine HM-PAO SPECT revealed no pathologic findings (Fig. 1B). The Wada test showed complete left-sided lateralization of speech dominance. HM-PAO SPECT during Wada test for the left hemisphere caused a significantly reduced perfusion of the left hemisphere (Fig. 1A). The Wada test of the right hemisphere (Fig. 1C) led to a corresponding, but less pronounced hypoperfusion of the respective hemisphere. Quantitative evaluation of HM-PAO SPECT before and during the Wada test yielded a blood flow reduction to 70% in the dominant (left) hemisphere and to only 90% in the right hemisphere (Figs. 2, 3). Crossed cerebellar diaschisis was present.

Case 2

A 20-yr-old right-handed female had been suffering from partial epilepsy for several years. EEG showed a right temporal focus, whereas CT was normal. NMR revealed a lesion (long T_2) in the uncus of the right hypocampus. Routine HM-PAO SPECT showed a hypoperfused area in the frontal part of the right temporal lobe. The Wada test revealed complete leftsided lateralization of the speech dominance. HM-PAO SPECT during Wada test left (Fig. 4A) showed a considerably decreased perfusion of the left hemisphere, especially of the temporal lobe. When the Wada test was performed for the right hemisphere, a corresponding yet not quite so pronounced decrease of perfusion was observed in the right hemisphere (Fig. 4C). Quantitative evaluation was performed using manually chosen ROIs (Fig. 4). This showed a reduction of blood flow in the dominant (left) hemisphere down to 55%. The respective value for the right hemisphere was only 80% (Fig.

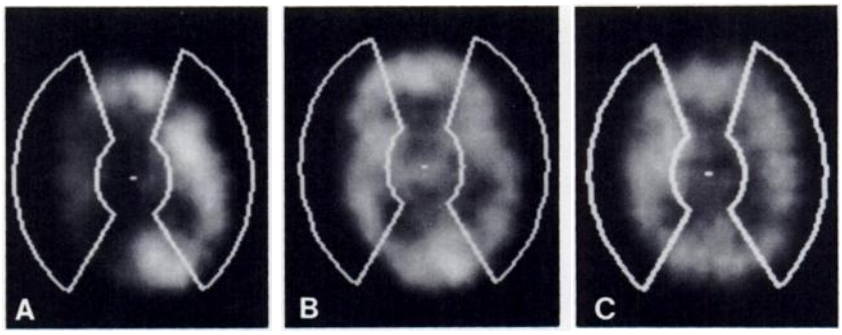

FIGURE 2
Hemispheric ROIs (unsmoothed data) for quantitative evaluation of cerebral HM-PAO uptake in Case 1.

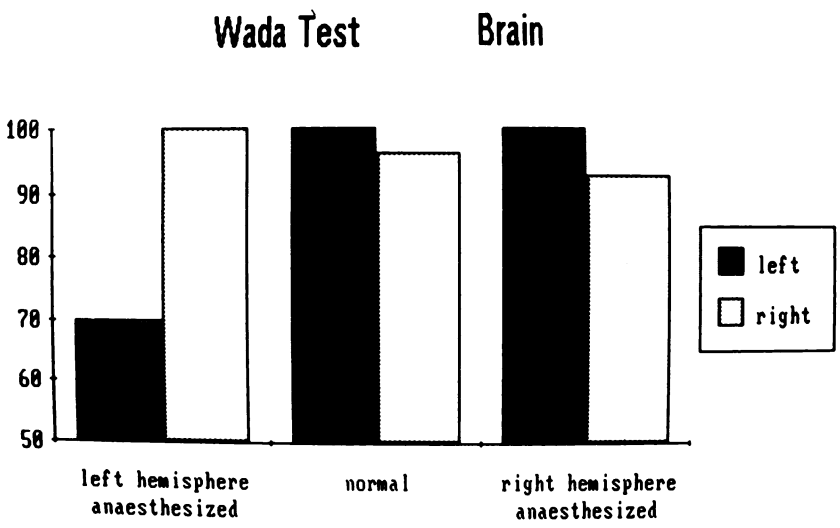

FIGURE 3
Quantitative evaluation of the decrease in cerebral HM-PAO uptake: from baseline (100%) −30% (Wada test left), −10% (Wada test right); there is a slightly decreased perfusion to the left hemisphere before Wada test which is within the standard error (±3%) probably due to mental activities.

5). During the Wada test there occurred a crossed cerebellar diaschisis with a decrease in blood flow to the contralateral cerebellar hemisphere of ~85%.

Case 3

A 39-yr-old left-handed male had been having partial epilepsy for several years. EEG revealed a focus in the right temporal region. CT was normal, and NMR presented with a lesion of the right gyrus hypocampus. Routine HM-PAO SPECT showed a hypoperfused area in the frontal part of the right temporal lobe. Speech tests during the Wada procedure showed that there was no lateralization of speech dominance. The results of the Wada test are summarized in Figure 6. Anesthesia of the left hemisphere resulted in a decrease of blood flow to the left hemisphere (Fig. 6A) down to 70% (Fig. 7). Wada test for the right hemisphere decreased the blood flow of the respective hemisphere to 60% (Fig. 6C). Again, crossed cerebellar diaschisis was observed.

DISCUSSION

Our results document that anesthesia of a single hemisphere during the Wada test results in a decreased blood flow of the affected brain regions. This decrease seems to be more pronounced when the dominant hemisphere in patients with complete lateralization of speech dominance is blocked with sodium amytal. HM-PAO SPECT is a unique procedure to monitor these temporary alterations of cerebral blood flow, as the effect of hemi-anesthesia only lasts 4–5 min. HM-PAO is rapidly accumulated in the brain, and there is no more uptake after 2 to 3 min p.i. (*8*). Amphetamines, on the other hand, show an accumulation period of at least 20–30 min, so that the normalization of brain perfusion (and amphetamine uptake) after 5 min would mask the temporary perfusion deficit.

From our data it seems obvious that depressed neuronal function during anesthesia causes decreased regional brain perfusion. This diminution of rCBF is related to the lateralization of speech dominance, as the most pronounced changes of perfusion were observed during anesthesia of the dominant hemisphere in two right-handed subjects. In contrast, in the left-handed patient who was not lateralized (as evidenced by speech tests), brain perfusion during the Wada test was only slightly different in both hemispheres. This is in accordance with the findings that 20 to 30% of left handed subjects are not lateralized. Our results allow the assumption that in cases with equivocal speech tests HM-

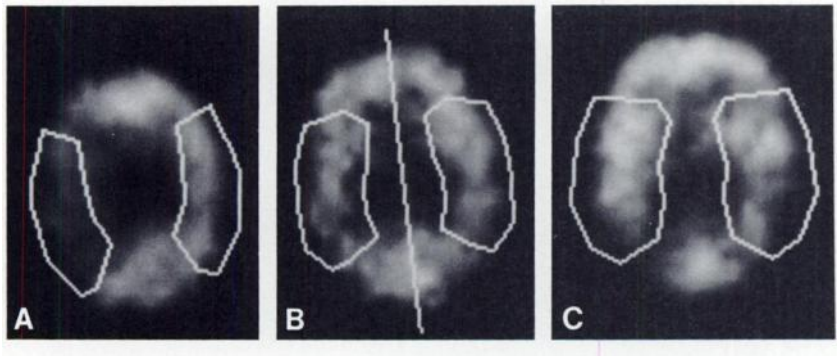

FIGURE 4
Brain SPECT with [^{99m}Tc]HM-PAO before (B) and during Wada test left (A) and right (C) in Case 2 (ROIs for quantitative evaluation of cerebral HM-PAO uptake). Significantly decreased HM-PAO uptake of the left (dominant) hemisphere during Wada test left (A), less pronounced diminished uptake during Wada test right; slightly reduced perfusion to the right hemisphere before Wada test due to epileptic (hypoperfused) focus right.

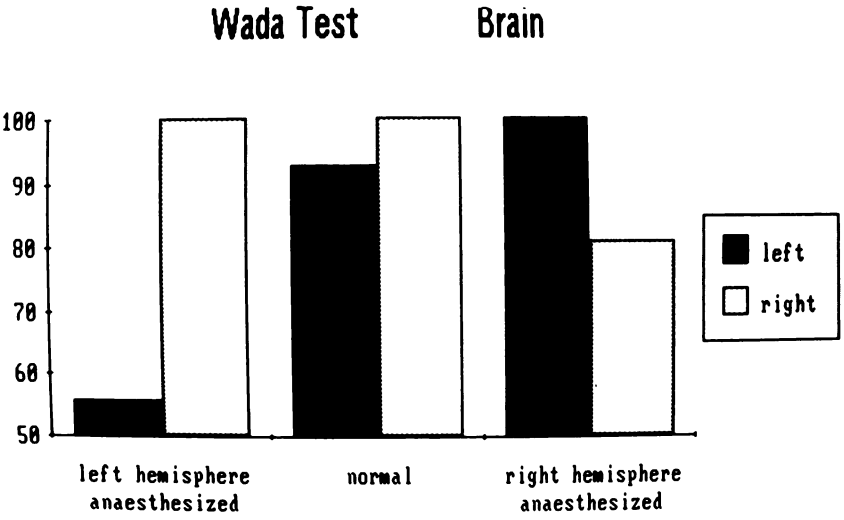

FIGURE 5
Quantitative evaluation of cerebral HM-PAO uptake: −45% (Wada test left), −20% (Wada test right).

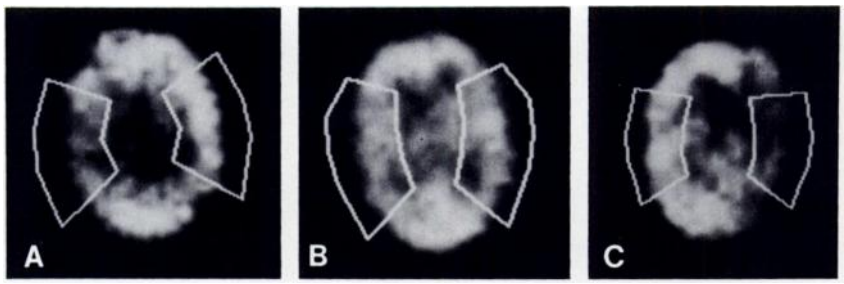

FIGURE 6
Brain SPECT with [^{99m}Tc]HM-PAO before (B) and during Wada test left (A) and right (C) in Case 3 (left-handed subject) (ROIs for quantitative evaluation of cerebral HM-PAO uptake). Significantly decreased cerebral HM-PAO uptake right and left during respective Wada test, yet less pronounced in the left hemisphere.

PAO brain SPECT may render possible the correct lateralization of speech dominance. However, it should be considered that the cognitive dominance might not be the only reason for the lateralization of HM-PAO uptake. This may also be due to hitherto unknown factors which correlate to morphologic hemispheric differences (*9*).

A second phenomenon that we observed during Wada tests was crossed cerebellar diaschisis (*10,11*): anesthesia of one hemisphere caused a decrease in blood flow to the contralateral cerebellar hemisphere of ~15%. We assume that this phenomenon is due to decreased neuronal spino-cerebellar input from the spinal cord in temporary hemiplegia. This assumption is supported by a paper from Kennedy et al. (*12*) who have reported *increased* glucose metabolism in the ipsilateral cerebellar hemisphere accompanying *motor activity* of the extremities.

From the results of HM-PAO brain SPECT during the Wada test it may be concluded that this tracer

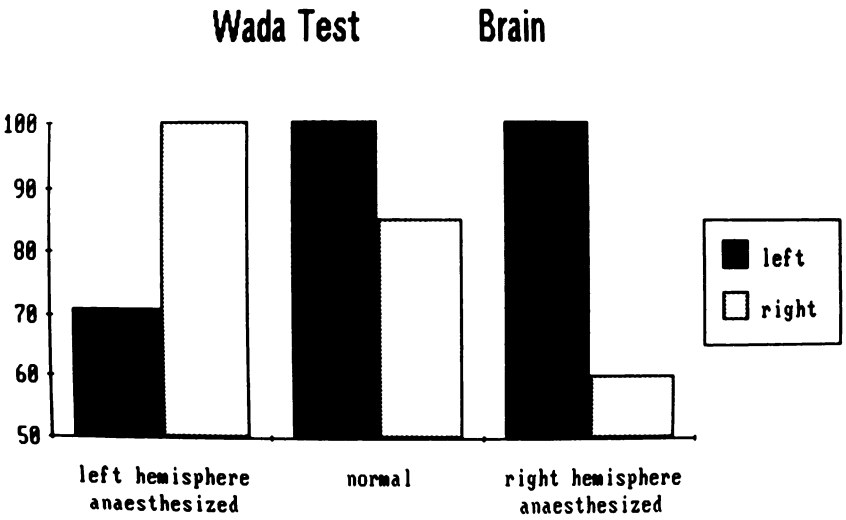

FIGURE 7
Quantitative evaluation of cerebral HM-PAO uptake: −30% (Wada test left), −40% (Wada test right); reduced perfusion to the right hemisphere before Wada test due to epileptic (hypoperfused) focus right.

allows the monitoring of brain perfusion, as rapid changes of rCBF due to decreased neuronal activities lead to respective alterations of HM-PAO uptake, such as hypoperfusion of an anesthetized hemisphere and crossed cerebellar diaschisis.

NOTES

* Amersham International, Buckinghamshire, UK.

† Gammatome T9000, CGR.

‡ (Picker NMR 2000) Picker International, Highland Heights, OH.

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