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# Demonstration of Frontal Hypoperfusion in Benign Exertional Headache by Technetium-99m-HMPAO SPECT

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We present a case of benign exertional headache (BEH) in a 15-yr-old boy. The patient suffered from exclusively exercise-induced headaches with migraine-like accompanying symptoms. No pathology could be detected by routine cardiovascular or neurological examinations by CT. The postexercise $^{99m}$Tc-HMPAO brain SPECT performed during the provoked headache attack showed asymmetric bifrontal hypoperfusion. A second $^{99m}$Tc-HMPAO study during a symptom-free phase under resting conditions was normal. The detection of impaired regional cerebral blood flow (rCBF) by $^{99m}$Tc-HMPAO brain SPECT indicates a perfusion-related pathology in this type of headache. Analysis of rCBF with $^{99m}$Tc-HMPAO in larger studies could be helpful in the clarification of BEH pathogenesis.

**Key Words:** benign exertional headache; technetium-99m-HMPAO; SPECT

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Benign exertional headache (BEH) was first described in 1932 by Tinel et al. (*1*). This type of headache occurs, by definition, during different physical activities increasing the intrathoracic pressure such as coughing, breath-keeping, laughing, crying, running, etc. It is generally of short duration and can be well localized (*2,3*). The same form of headache has also been reported in relation with the tumors of the posterior fossa and the lesions of foramen magnum (*3*). The coexistence of symptoms such as nausea, vomiting and photophobia during the attacks lets one suppose a close relation between BEH and migraine (*4*). The clinical relevance of regional cerebral blood flow (rCBF) analysis by radioactive tracers is now widely accepted. Regional hypoperfusion in different types of migraine has been demonstrated by $^{133}$Xe imaging and more recently by $^{99m}$Tc-HMPAO SPECT studies (*5–8*). The well-known superiority of SPECT over planar imaging in regional analysis and the ready availability of $^{99m}$Tc-HMPAO, make the latter the most popular method. We present a case of reversible cerebral hypoperfusion demonstrated during a provoked BEH attack using $^{99m}$Tc-HMPAO brain SPECT.

## CASE REPORT

A 15-yr-old boy suffering from exclusively exercise-induced headache (after running approximately 30 m) was admitted to the neurology department of our university hospital. The headache began always suddenly during exercise in both frontal regions, was pulsating and lasted between 12 and 48 hr. It was often accompanied by photophobia, nausea and vomiting. Analgesics such as acetyl salicilic acid or paracetamol were effective to only some extent. There was no family history of migraine. Neurological examination during a symptom-free phase was normal. Routine biochemistry, telecardiography, electrocardiography, brain CT as well as electroencephalography were unremarkable. BEH was

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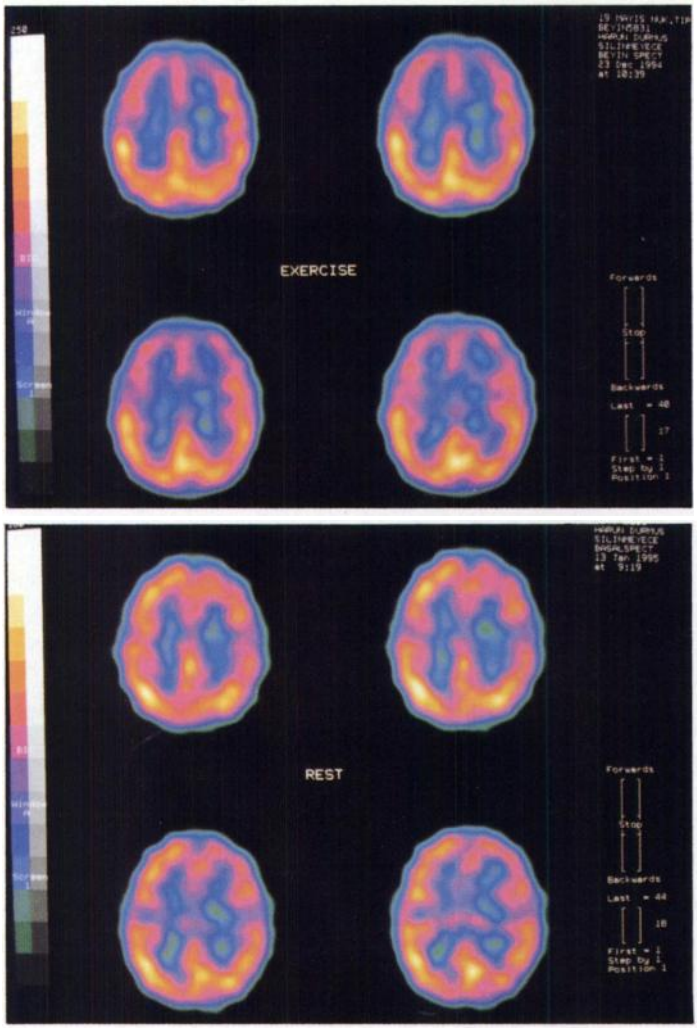


**FIGURE 1.** (A) Transaxial slices show bifrontal hypoperfusion following stress. (B) Same slices show normal perfusion at rest without headache.

diagnosed. Technetium-99m-HMPAO brain SPECT was planned for the next day to analyze rCBF during the headache episode. The patient was requested to run in the vicinity of the hospital at the usual speed which triggered the headache. After running 25 m, the attack began. Rapid neurological examination showed no focal deficits. Ten minutes after the onset of the attack, 12 mCi $^{99m}$Tc-HMPAO were injected intravenously, with the patient in supine position with his eyes closed. Brain SPECT was performed

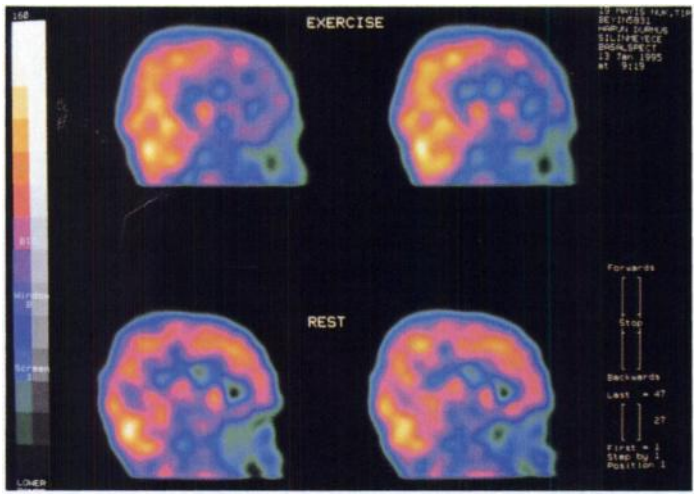


**FIGURE 2.** Right sagittal slices show the difference in cortical perfusion in exercise images compared to the rest images.

**TABLE 1**
Count Ratios of CBF Difference in Frontal Regions between Exercise and Rest Studies

| | Count ratio | | | | |
|---|---|---|---|---|---|
| | Region/Ipsilateral occipital cortex | | | | Right/Left |
| Study | RF | LF | RP | LP | Occipital |
| Exercise | 0.73 | 0.78 | 0.95 | 0.89 | 0.98 |
| Rest | 0.99 | 0.92 | 0.96 | 0.88 | 0.99 |

RF = right frontal; LF = left frontal; RP = right parietal; LP = left parietal.

with a single-head rotating gamma camera. Low-energy, high-resolution collimation was used and 64 projections into a 64 × 64 matrix with a sampling time of 15 sec were acquired.

The study was repeated 1 wk later under resting conditions and during a symptom-free phase. The acquired data were preprocessed with ramp and Butterworth filters before backprojection. After image reconstruction, regions of interest were drawn over the frontal, parietal and occipital cortices on both sides. The postexercise brain SPECT image showed asymmetrical decreased regional CBF in both frontal cortices with the dominance of the right side (Fig. 1A). Because of bilateral frontal hypoperfusion, the activities of the selected regions were compared to ipsilateral occipital activities. The resting images depicted normal CBF in both frontal regions (Fig. 1B). Figure 2 shows the CBF difference in the right sagittal slices. The region-to-ipsilateral occipital cortex ratios as well as the right-to-left ratios of the occipital cortices in the exercise and rest studies are given in Table 1. The right-to-left ratios of occipital cortices, as reference regions, showed no change between the exercise and rest studies. Reversible exercise ischemia in both frontal regions was diagnosed by $^{99m}$Tc-HMPAO brain SPECT.

## DISCUSSION

The pathogenesis of BEH is not fully understood. A possible pathophysiological mechanism similar to that of "altitude headache" has been suggested (*9*). Cerebral vasoconstriction, edema and the resulting hypoxemia could explain some of the symptoms. Increasing blood pressure after exercise may induce extracranial vasodilatation with consequent headache. Triggering factors in BEH are various and its duration is often short (*2,10*). Headache periods after physical exercise which last 16 hr or longer have also been reported (*11*).

In our patient, the duration and accompanying symptoms were compatible with a migraine attack. The demonstration of decreased rCBF by $^{99m}$Tc-HMPAO SPECT in the frontal regions during the headache phase supports a pathogenetic relationship with migraine (*8*). Speculative models, such as adhesive arachnoiditis or herniation of pachonian granulations, as pathogenetic mechanisms are not considered satisfactory (*12*). After ruling out intracranial lesions, prolonged BEH cases may be separately classified. Regional hypoperfusion during migraine attacks using $^{99m}$Tc-HMPAO SPECT has been reported (*7,8*). Moreover, a case of reversible ischemia in basilar artery migraine was reported by Seto et al. (*13*). We believe that the analysis of regional cerebral perfusion using $^{99m}$Tc-HMPAO brain SPECT in patients with BEH could help to illuminate the pathogenesis of this type of headache.

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# Hyperperfusion and Hypermetabolism in Brain Radiation Necrosis with Epileptic Activity

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We report a case of high uptake of $^{11}$C-methionine (MET), $^{18}$F-FDG (FDG) and $^{201}$Tl-Cl (Tl) in brain radiation necrosis. Twenty-one years previously, the patient had undergone surgery and radiation therapy consisting of 60-Gy for ependymoma in the anterior horn of the right lateral ventricle. The clinical features consisting of frequent seizures of the left face and arm suddenly appeared 2 wk before admission. MRI depicted a Tl- and T2-prolonged lesion in the right frontal lobe. Abnormally high uptake in this area demonstrated by MET-PET, FDG-PET, Tl-SPECT or HMPAO-SPECT suggested the presence of a recurrent tumor. A craniotomy was then performed and an intraoperative electrocorticogram showed continuous epileptic spikes in the lesion. The epileptic foci were resected and the histological features of the lesion were consistent with radiation necrosis. After surgery, the seizures disappeared and the postoperative examinations with MET-PET, FDG-PET, Tl-SPECT and HMPAO-SPECT no longer showed abnormally high uptake. Hypermetabolism and hyperperfusion related to epileptic fits are therefore thought to result in high uptake of MET, FDG and Tl in radiation necrosis.

**Key Words:** radiation necrosis; thallium-201-chloride; carbon-11-methionine; fluorine-18-FDG; SPECT; PET

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Brain radiation necrosis is one of the late complications of radiotherapy for tumors of the central nervous system. The recurrence of clinical symptoms suggesting a recurrence of the tumor may also represent radiation necrosis of the brain. Distinguishing between radiation necrosis and tumor recurrence may be difficult with either CT (*1*) or MRI (*2*) because the information provided by these modalities are based on structural changes and is not specific to any histological lesion type. PET has been used to evaluate the metabolic activity of tumors by using $^{11}$C-L-methionine (MET) and [$^{18}$F]fluorodeoxyglucose (FDG). Both MET-PET and FDG-PET have been reported to be useful in detecting primary brain tumors (*3,4*) as well as differentiating recurrent tumors from radiation necrosis after radiotherapy (*5,6*). SPECT with $^{201}$Tl chloride (Tl) also has been reported to be useful in differentiating recurrent tumors from brain radiation necrosis after treatment (*7,8*). We, however, recently encountered a case of radiation necrosis in which the patient demonstrated high uptake of MET, FDG and Tl.

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## CASE REPORT

A 37-yr-old woman was admitted to our hospital with frequent seizures of the left face and arm for 2 wk. Twenty-one years earlier, the patient had undergone surgical resection of the ependymoma in the anterior horn of the right lateral ventricle through a frontal transcortical approach. Postoperative radiation therapy was performed with 30 Gy/15 Fraction (F) of whole-brain irradiation (14 × 16 cm) with additional local regional irradiation (6 × 9 cm) of 30 Gy/15 F by using $^{60}$Co gamma rays, both irradiations were weighed on the right side by 2:1, followed by whole-spine irradiation with 30 Gy/15 F to prevent spinal dissemination. The patient was free of any clinical symptoms for 21 yr after the above therapy and suddenly developed seizures of the left face and arm 2 wk before admission. Her seizures began with an abnormal sensation in her left arm, followed by rapid grimace like contractions of the lower half of the left face and jerking pronating-supinating movements of the forearm. Postictally, mild weakness in these areas occurred for about 1 hr. Despite treatment with 400 mg of sodium valproate and 200 mg of zonisamide, she developed frequent seizures several times a day during her hospitalization.

MRI (Tl-weighted spin-echo images were obtained with sequences of 500/18/1 (TR/TE/excitations). T2-weighted fast spin-echo images were obtained with 2500/110/1) demonstrated a Tl- and T2-prolonged lesion in the right frontal lobe just posterior to the surgical defect of the previous corticotomy (Fig. 1A). The Tl-weighted MR image after the administration of Gd-DTPA (0.1 mmol/kg) demonstrated patchy enhancements on the lesion (Fig. 1B).

MET-PET images (acquired 15 postadministration of 370 MBq MET) demonstrated widespread, high uptake in the right frontal lobe (Fig. 2A). The most intense uptake was observed in the area just posterior to the surgical defect, which was 3.2 times that of the contralateral frontal cortex. FDG-PET images (acquired 20 min after administration of 185 MBq FDG) also demonstrated high uptake in the area (Fig 2B), which was 1.2 times that of the contralateral frontal cortex. The cerebral blood flow increased in the right frontal lobe and was 1.7 times that of the contralateral frontal cortex (Fig. 2C). The Tl-SPECT images (obtained 15 min after administration of 148 MBq Tl) also demonstrated an abnor-