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THE USEFULNESS OF BRAIN SPECT WITH 123-I-IAMP AND HIPDM

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As soon as iodoamphetamine labelled with 123-I was available, brain lesions such as tumors and infarcts were clearly visible on single photon emission computerized tomography (SPECT) images with an excellent accuracy (Lafrance et al 1981, Kuhl et al 1981, Moretti et al 1982, Hill et al 1982). These initial results were very encouraging. However, it soon became evident that this costly procedure could not compete with techniques the reliability of which is excellent such as computerized tomography (CT) or scintiscans in diagnosing tumors and infarcts. The usefulness of brain SPECT was therefore questioned. In this paper we would like to evaluate the usefulness of this technique at the present time.

METHODOLOGICAL CONSIDERATIONS

SPECT systems now marketed can be classified in 2 groups, detector array systems and rotating gamma-cameras. Detector array systems have a high sensitivity but provide only a few transverse slices. Due to their large area detector, rotating gamma cameras image the entire brain which can be studied on complete sets of transverse, coronal and sagittal slices but have a low sensitivity. Details concerning individual system characteristics, which do not have their place here, will be found in several excellent reviews (Budinger 1981, Soussaline 1982). We will only insist on the necessity of careful and frequent quality control of the gantry, detector and computer, which should be carried out weekly because these device are highly sophisticated. Immobilization of the patient's head should also require full attention especially when rotating gamma cameras are used.

Indicators used in brain SPECT must penetrate normal blood brain barrier (BBB) and be labelled with gamma emitter. Two have so far been proposed, I-123-isopropyl amphetamine (IAMP) and I-123 trimethyl propane diamine (HIPDM). Their specific activity varies between 1 to 10 mCi/mg depending on the isotope producing companies.

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Labelling is done by these companies except for IAMP which can be labelled with commercial kits*. Injected amounts vary from 2 to 8 mCi depending on the type of device used.

BIODISTRIBUTION CONSIDERATIONS

After I.V. injection with IAMP, the brain activity curve increases rather slowly, reaches a maximum value of approximately 5 % of the injected dose after 30 minutes and remains in plateau for several hours (Kuhl et al 1982, Moretti et al 1982). With HIPDM the maximum brain activity value seems slightly lower (Holman et al 1982).

Kuhl et al 1982, Lassen et al 1983, Devous et al 1983, Holman et al 1983, and Drayer et al 1983, demonstrated that during the first ten minutes after injection the results obtained with IAMP and HIPDM correlate significantly with regional cerebral blood flow (rCBF), and proposed the use of these indicators in mesuring rCBF.

After thirty minutes the brain distribution of IAMP is modified,the results obtained by Lassen et al 1983, suggest a redistribution. Rapin et al and Devous et al 1983, respectively on mice with IAMP and dogs with HIPDM confirm this redistribution and the poor correlation with rCBF. The new distribution of IAMP and HIPDM may reflect the metabolic activity of the brain more accurately than the rCBF. In this paper we will only consider these late SPECT images obtained after 30 minutes.

APPLICATIONS

When the head of a patient is placed in orbitomeatal position and maintained throughout acquisition, the images obtained may be compared to those found in anatomical atlases using the same head position (Salamon 1971). It is then possible

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to propose schematic diagrams of 8 transverse, 10 frontal and 7 or 8 sagittal SPECT slices of the normal brain (Fig. 1, 2, 3). For transverse sections, the brain is sliced from the top to bottom, for frontal sections from the forehead to the occipital region, and for sagittal sections from the left to the right ear. The presentation of the latter differs from the other two because the median line of the brain may be used as an axis of symetry. Then the images placed on the left and right side of the diagram sheet are symetrical compared to the median line of the brain. The top couple of images represent the most external slices. When the slice number is odd the lower (S6) represents the middle line section ; when the slice number is even,the 2 lowest (S6 and S7), represent the two sections around the median line. Depending on an even or odd slice number one or the other sagittal diagram should be used. This schematic representation should help to lacalize a lesion. For example, the caudate nucleus is well delineate on the slicesT5 and F5, the thalamus on T6, F6, F7 and F8, and the hippocampal gyrus on T7, F6, F7 and F8. The proposed diagrams were established for a slice thickness of 12.5 mm, they will of course be different if the slice thickness was different.

Proved useful at present, applications of brain SPECT using IAMP or HIPDM are limited to focal epilepsy and Alzheimer disease. However, results obtained in cerebrovascular patients are encouraging although not confirmed. In addition potential applications to be tested will be discussed.

1. Focal epilepsy

Results obtained by practically all groups working with IAMP or HIPDM indicate that lesional and epileptogenic areas are hypoactive during interictal period on SPECT image, as they are with positron emission tomography (PET) when fluoro-deoxy-glucose is used (Kuhl et al 1981, Kuhl et al 1982). Askienazy recently reported in a group of 32 focal epilepsy (those with brain tumor were excluded) that lesional and epileptogenic areas were detected in approximately 70 % of

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the cases with X ray CT and in all cases with IAMP SPECT. Localization of these regions (Fig. 4 and 5) correlates well with more accurate neuroradiological procedure or stereotactic techniques such as stereotactic electroencephalography. At present, in partial epilepsy, IAMP proved to be irremplaceable atraumatic method for which sensitivity and specificity must be studied.

The mechanism of the observed hypofixation is still not clarified but may not always be due to an rCBF modification.

2. Alzheimer syndrome

It was recently reported that with IAMP, multiinfarct dementia could be differentiated from Alzheimer syndrome, (Cohen et al 1983). In multiinfarct dementia, cortical defects are discrete, multiple and asymmetrical, in the second they are extensive and symmetrical. For the authors IAMP SPECT can potentially diagnose early cases of Alzheimer syndrome, a disease for which there is at present no diagnostic test.

3. In cerebrovascular patients

Infarcts are clearly visible on SPECT images as on CT scans but are generally larger. Other hypoactive areas not visible on CT scan can also be observed on SPECT images. The significance of these areas is still not completely understood. However it can be proposed - at least as a working hypothesis - that they correspond to hypofunctional areas. In this respect knowledge of their size, number and volume should be useful in establishing a functional evaluation of the cerebral parenchyma. We studied 8 patients with bilateral carotid artery occlusion who were clinically asymptomatic or paucisymptomatic. In all of these patients, hypoactive areas were found, without corresponding modification of CT scan (Fig. 6 and 7). Can the rCBF be decreased in these areas ? Can hypoactivity be improved by extracranial-intracranial by-pass shunting ? These questions are still unanswered. In transient ischemic attack (TIA) several hypoactive areas are also found and IAMP brain SPECT should be useful in determining the funtional state of whole brain (Fig. 8). In some constituted infarcts, IAMP

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brain SPECT may be necessary in appreciating the functional state of the brain on the so-called ischemic penumbra for therapeutical purposis. It should also be useful in patients with an impairment of the cognitive function associated or not with ischemic hemiplegia, in establishing the prognosis of stroke rehabilitation, and, above all, in long term amnesic syndrome of hippocampal origin.

4. Brain tumor

Brain tumor can be detected easily by competitive methods and brain SPECT is certainly not the most convenient method. However, in some tumors,obtaining an image of the whole brain in a complete set of transverse, frontal and sagittal sections may be very useful in determining the extent of a tumoral lesion on deep structures such as thalamic nuclei or basal ganglia. This is the case; for example, of tumors the evolution of which is very slow, such as low-grade astrocytoma and which are not visible on CT scan for a long period of time (fig.9).

In conclusion, the usefulness of IAMP or HIPDM brain SPECT have already been shown for focal epilepsy and Alzheimer syndrome. Several other applications are now being carefully studied including use on cerebrovascular patients which could become the most important application of the method in a near future. Such encouraging results should stimulate research on other brain parenchyma indicators labelled with a gamma-emitter. We may hope that IAMP and HIPDM are the first in a series of BBB penetrating indicators, and indicate the usefulness of this technique. However, the future of brain SPECT will certainly depend on the discovery of new BBB indicators labelled with less expensive radioisotopes which can be more easely used.

FIGURE CAPTIONS

FIG. 1 Diagram of transverse sections

FIG. 2 " " frontal "

FIG. 3 " " sagittal "

Diagram (a) should be used when the slice number is even, diagram (b) when it is odd.

FIG. 4 24 year-old patient with fronto-temporal epilepsy, CT scan shows right fronto temporal porencephaly. On IAMP SPECT a large right fronto-temporal hypoactive area is visible.

FIG. 5 25 year-old young woman with left parieto-temporal epilepsy. On CT scan, the occipital horn of theleft ventricle is slightly enlarged. A large left parieto-temporo-occipital hypoactive area is visible on IAMP SPECT.

FIG. 6 50 year-old patient with asymptomatic bilateral carotid occlusion. CT scan showed moderate cortical atrophy without parenchymal lesions. On IAMP SPECT sections, four areas are hypoactive of which two are shown here, one is left prerolandic (left images), the other is located in deep right temporal region (left images). The latter appears extended to T4 and T5.
Transverse,frontal and sagittal sections are respectively shown from top to bottom on this figure.

FIG. 7 72 year-old patient with asymptomatic bilateral carotid occlusion. In fact transitory visual symptoms were noticed on left eye 3 years earlier. CT scan showed a scar from a posterior sylvian ischemic

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accident on left side. On IAMP SPECT a large hypoactive area corresponds to the CT iamge (left side images of the figure) ; other hypoactive areas are visible which can not be seen on CT scan, and especially a left temporal cortical area extended to subcortical territories including left thalamus and probably hippocampal gyrus (right side images of the figure).

FIG. 8 71 year-old woman with right TIA for 20 years (hemiparesia, focal epilepsy, aphasia and hyperthermia). The last attack occurred 30 days before examination. On CT scan, 2 scars of old infarcts (left temporo-occipital and right cerebellar) are visible. On IAMP SPECT most of the left cortex is hypoactive as are the left subcortical areas and the left cerebellum and extends to the antero-superior part of the right cerebellum. This is easily seen when comparing sagittal images of the left brain (left side of the figure) and the symmetrical sagittal images of the right brain (right side of the figure).

FIG. 9 47 year-old woman with a right fronto-temporal tumor visible on CT scan with a thalamic extension and displacement of right ventricle. An hypoactive fronto-temporal area corresponds to the CT image, but is larger, and extends to the lower part of the parietal lobe, to the right thalamus and hippocampal gyrus and seems to displace the right cerebellum and the left thalamus.

REFERENCES

1. Budinger TF (1981) Revival of clinical medicine brain imaging. J. Nucl. Med. 22 : 1094.

2. Cohen MB, Metter EJ, Graham LS, Wasterlain C, Spolter L, Lake RR, Rose G, Yamada L and Chang CC (1983) Differential diagnosis of dementia with "pure" I^{123} iodoamphetamine and a clinical camera. J. Nucl. Med. 24 : P.106.

3. Devous MD, Lewis SE, Kulkarni PV and Bonte FJ (1983) A comparison of regional cerebral blood flow measured with I-123-labelled diamine or amphetamine and radioactive tracer microspheres. J. Nucl. Med. 24 : P.6.

4. Drayer B, Albright R, Jaszczac R, King H, Coleman E, Friedman A and Greer K (1983) Quantitative rCBF in man : The SPECT-HIPDM method. J. of Cerebral Blood FLow and Metabolism. Proceed. Congress Paris, Raven Press, N.Y. P.156.

5. Hill TC, Holman BL, Lovett R, O'Leary D, Front D, Magistretti P, Zimmerman RE, Moore S, Clouse ME, Wu JL, Lin TH and Baldwin RM (1982) Initial experience with SPECT (single photon computerized tomography) of the brain using N-isopropyl-I-123 p-iodoamphetamine : concise communication. J. Nucl. Med. 23 : 191.

6. Holman BL, Lee RGL, Hill TC, Lovett RD and Lister-james J (1983) A comparison of two cerebral blood flow tracers, N-isopropyl I^{123}-p -iodoamphetamine and I^{123}HIPDM. J. Nucl. Med. 24 : P6.

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7. Kuhl DE, Wu JL, Lin TH, Selin C and Phelps M (1981) Mapping local cerebral blood flow by means of emission computed tomography of N-isopropyl-p-(^{123}I)-iodoamphetamine (IMP). J. Nucl. Med. 22 : P.16.

8. Kuhl DE, Barrio JR, Huang S, Selin C, Ackerman RF, Lear JL, Wu JL, Lin TH and Phelps ME (1982) Quantifying local cerebral blood flow by N-isopropyl-p-(^{123}I)-iodoamphetamine (IMP) tomography. J. Nucl. Med. 23 : 196.

9. Lafrance ND, Wagner HN Jr, Whitehouse P, Corley E and Duelfer T (1981) Decreased accumulation of isopropyl-iodoamphetamine (I-123) in brain tumors. J. Nucl. Med. 22 : 1081.

10. Lassen NB, Henriksen L, Holm S, Barry DI, Vorstrup S, Rapin J, Le Poncin-Lafitte M, Moretti JL, Askienazy S and Raynaud C (1983) Cerebral blood-flow tomography : xenon-133 compared with isopropyl-amphetamine-iodine-123 : concise communication. J. Nucl. Med. 24 : 17.

11. Moretti JL, Askienazy S, Raynaud C, Mathieu E, Sanabria E, Cianci G, Bardy A and Le Poncin-Lafitte M (1982) Brain single photon emission tomography with isopropyl-amphetamine I-123 : preliminary results. Proceedings of third World Congress of nuclear medicine and biology, Ed. C. Raynaud, Pergamon Press, Paris Vol I : 135.

12. Moretti JL, Askienazy S, Cesaro P, Chauvel P, Sanabria E, Raynaud C, Bardy A and Rapin J (1983) I^{123}N-isopropyl amphetamine (I-123 AMP) SPECT in epilepsy and cerebral ischemia. J. Nucl. Med. 24 : P.108.

./.

13. Rapin J and Le Poncin-Laffite M. Unpublished observations.

14. Salamon G (1971) Atlas of the arteries of the human brain. Sandoz editions.

15. Soussaline F (1982) The single photon tomograph. In : Kuhl DE (ed) Principles of Radionuclide emission imaging, Pergamon Press, Paris, p. 153-185.

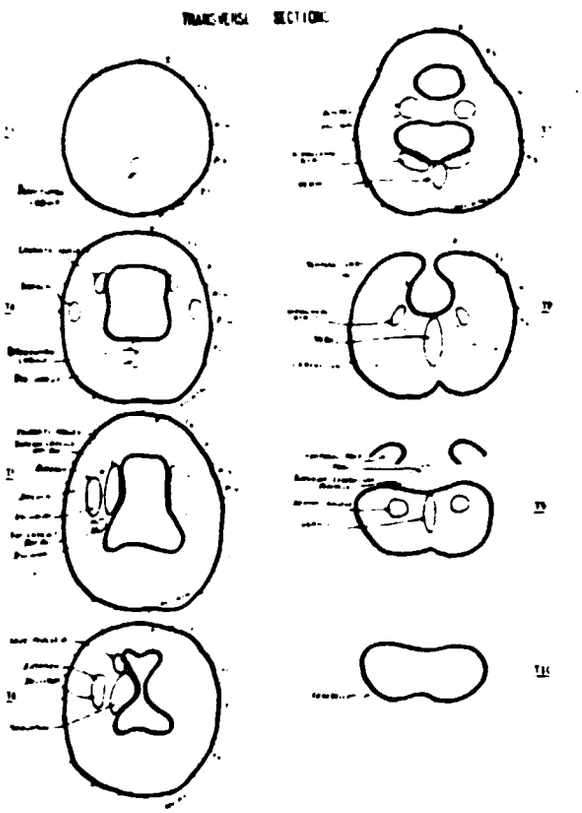

Fig 1

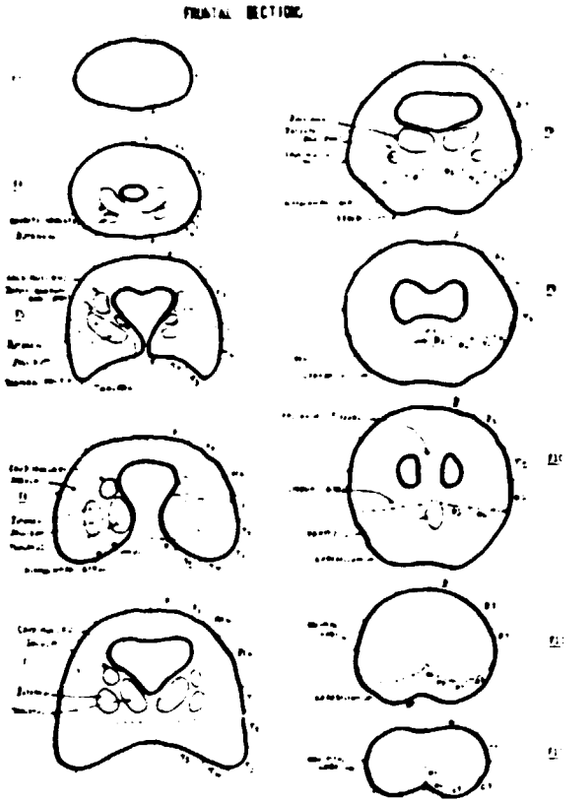

Fig 2

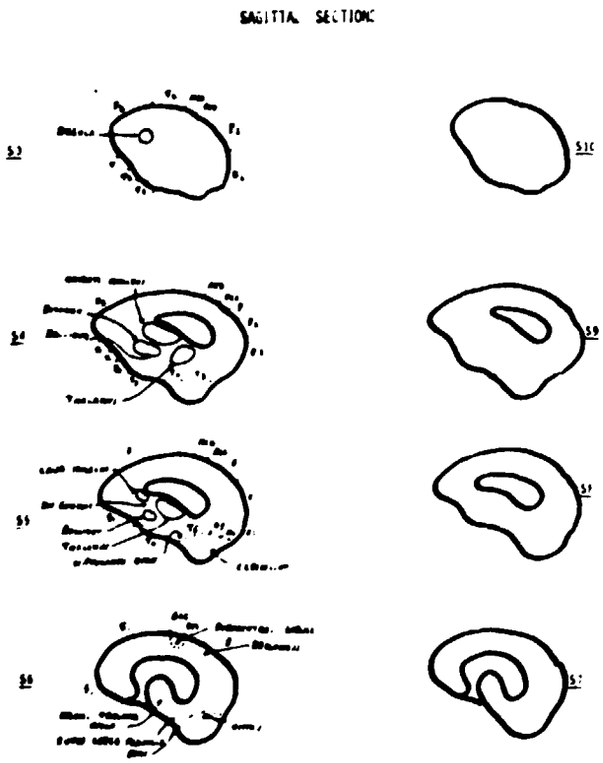

Fig 3a

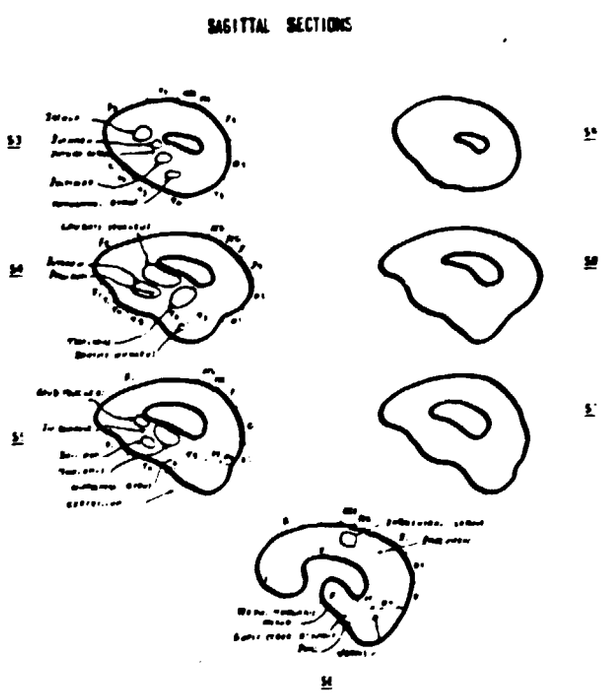

Fig 3b

Fig 4

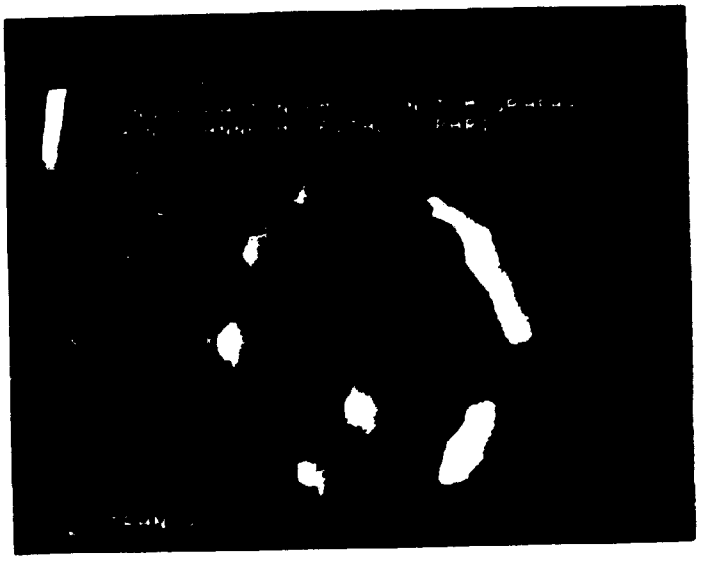

Fig 5

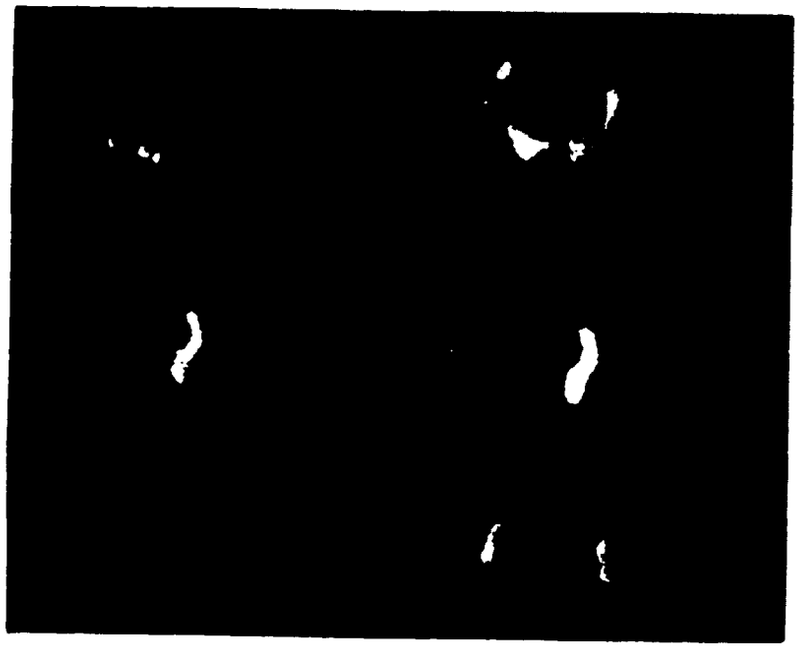

Fig 6

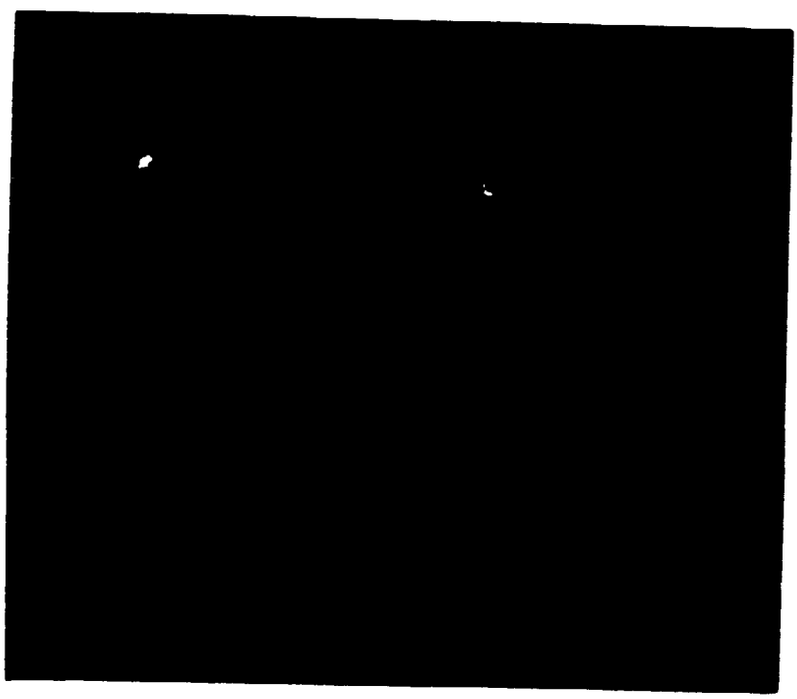

Fig 7

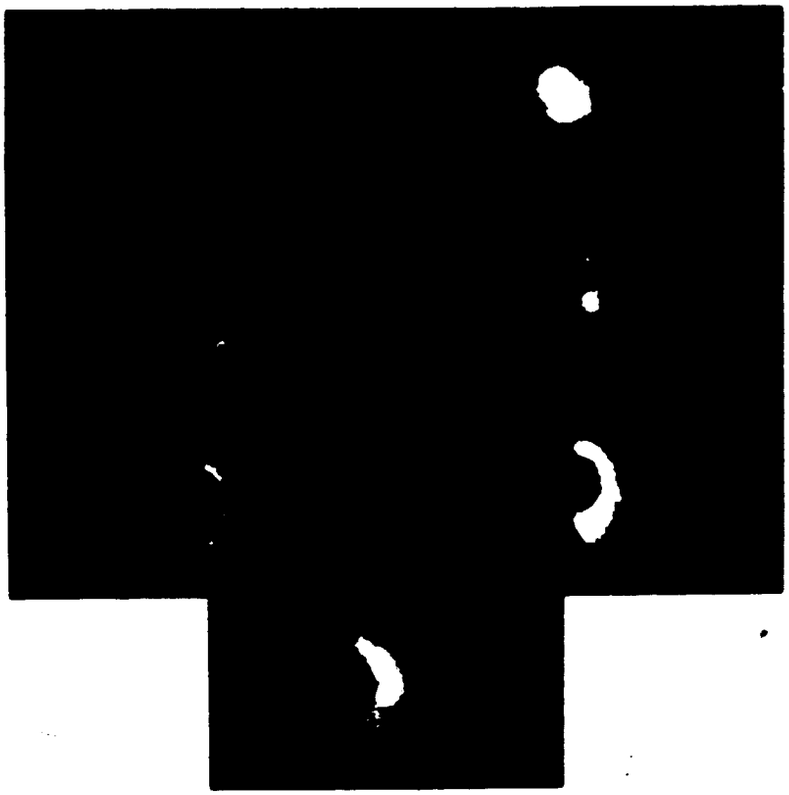

Fig 8

Fig 9

RESUME

The usefulness of brain SPECT 123-I-IAMP and HIPDM

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L'isopropyl amphétamine I^{123}(IAMP) et le trimethyl propane diamine I^{123} (HIPDM) sont les 2 premiers indicateurs réellement cérébraux marqués par un émetteur gamma qui sont disponibles. Leur taux de fixation cérébral de 5 % de la dose injectée, atteint environ 30 minutes après l'injection, permet la réalisation d'images tomographiques du cerveau sain. Les lésions cérébrales apparaissent sous la forme d'hypofixation qu'elles soient tumorales ou ischémiques. A l'heure actuelle la tomographie cérébrale à l'aide de l'IAMP ou du HIPDM est indiquée dans les épilepsies localisées où elle permet de localiser le foyer épileptogène ou (et) le foyer lésionel et donne les démences où elle permet de différencier à un stade précoce le syndrome d'Alzheimer et la démence d'oxygène vasculaire. Son utilité dans la pathologie vasculaire cérébrale est à l'éude et pourrait représenter une des indications majeures de ces deux substances.

Soumis à : Cerebral Blood Flow and Metabolism