The Diagnosis and Prognosis of Cerebral Vascular Diseases
Using Early and Late SPECT with N-Isopropyl-p-
(I-123) Amphetamine (IMP) on 35 Patients

J. L. Moretti

Département de Neurosciences, Hôpital Henri-Mondor, Créteil-94000

Initial studies with the single photon emission computerized tomography imaging (SPECT) using N-isopropyl p-iodoamphetamine-I-123 (IMP) have related brain hypoactivities during cerebral ischemia to decreased cerebral blood flow (CBF). These results were obtained with a rapid rotating gamma camera permitting tomographic imaging during the first minutes after injection of the tracer. Since it has been demonstrated that brain distribution of IMP was changing in rat as well as in man during the first hour following injection, it can be then proposed that IMP distribution could be related to the nervous tissue metabolism. Since long cerebral retention time of IMP allows SPECT examination 4 to 5 hours after IV injection it could be observed in stroke patients that regional brain activity of IMP could or could not change with time, especially in abnormal areas, showing or not showing a “redistribution activity”. Therefore, to evaluate if the change of IMP imaging with time represents an index of tissular viability, we performed a study in patients with cerebral ischemia in order to compare the early brain IMP imaging with the late one (4 hours after) and to correlate the alteration of activity with the clinical outcome.

Materials and Patients

IMP I 123 was prepared by exchange reaction using a commercial kit (CIS-ORIS). SPECT was performed with a rotating gamma camera (Gammatome 1 CGR). Blindfolded and ear-plugged patients received intravenously 5 to 7 millicuries of IMP I 123 (10 mg of IMP). Early imaging was begun 20 minutes post IV injection and sixty four views along 64 angles were accumulated during 40 minutes. Late imaging was performed 4 hours later (without injection) with the same design. Tomographic images were obtained by a filtered back projection method, a reorientation of the axial slices parallel to the cantomeatal line and compensation of attenuation by a Chang method. Seven controls (4 male, 3 female-mean age ±sd=56±11 years) were investigated as described above. In each of them, semi-quantitative analysis were performed on two consecutive transversal slices. For each slice, 3 symmetric regions of interest (ROI) were automatically defined from external outline and after manual exclusion of the parasagittal central region. Thus normal range of differential activity was calculated by using the mean of the 42 values obtained from controls ±/− 2 standard deviations. Then, differential activity was expressed as a decrease percentage of activity =DPA in comparison with the normal controlateral side. In controls, the mean DPA obtained by
automatic ROI quantification was of 1.7% +/- 4% sd (range 0–9.5% n=42). Therefore, areas presumed pathological in patients, were considered abnormal when DPA was higher than 10%. The DPA on early and late IMP was identified respectively: early index of hypoactivity (EHI) and late index of hypoactivity (LHI). In addition the redistribution amplitude (RA) of early hypoactive brain areas, defined as: \([LHI−EHI]/EHI\)×100 was studied and classified into 3 groups: complete redistribution if RA was superior to 90%; partial redistribution if 50%<RA<90%; and define lack of redistribution if RA<50%.

Twenty one Strokes, 7 permanent regressive ischemic neurological deficit (Prind) defined by a neurological deficit lasting more one day with complete or almost complete clinical recovery within the first week after cerebral ischemia and 7 transient ischemic attacks (Tia) were explored with SPECT using IMP. All patients had a clinical diagnosis of cerebral ischemia in the territory of mild cerebral artery.

Only 24 ischemic patients (14 males and 10 females) including 16 Strokes (mean age+sd=63.9 +9.5 years), 5 Prind (mean age+sd=53+13 years), 3 Tia (mean age+sd=45.3+11.6 years) were retained for the study. CT without injection (Siemens Somatom DR1 or SF) and SPECT with IMP were performed in all patients. Only one stroke patient had an almost complete recovery of his neurological deficit during the second week following his stroke. Therefore he was classified as a Prind patient for comparison between RA, clinical outcome and type of cerebral ischemia (see Fig. 1 and Table 1).

Patients were classified into 3 groups according to their clinical improvement 3 months after SPECT with IMP from a simple qualitative scale of handicap:—“poor improvement” (PI) if there was minimal or no improvement from the initial neurological symptoms i.e.: when functional handicap remained the same.

![Fig. 1](image-url)  
**Fig. 1** Mean decrease percentage of activity (DPA) in early and late SPECT with IMP according to the degree of improvement observed 3 months later in Tia, Prind and Stroke patients. *included the Stroke patient with good improvement. Vertical bars represents standard deviation.
Table 1 Classification of Tia, Prind and Stroke patients related to amplitude of RA and clinical outcome

<table>
<thead>
<tr>
<th>REDISTRIBUTION</th>
<th>IMPROVEMENT AT 3 MONTHS</th>
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<tr>
<td></td>
<td>GOOD</td>
</tr>
<tr>
<td>Complete</td>
<td></td>
</tr>
<tr>
<td>RA &gt; 90%</td>
<td>Tia 2</td>
</tr>
<tr>
<td>Partial</td>
<td>Tia 1</td>
</tr>
<tr>
<td>50 &lt; RA &lt; 90%</td>
<td></td>
</tr>
<tr>
<td>Lack RA &lt; 50%</td>
<td>Stroke 1</td>
</tr>
<tr>
<td>TOTAL PATIENTS</td>
<td>n=24</td>
</tr>
</tbody>
</table>

* including the Stroke patient with good clinical recovery.

—"medium improvement" (MI) if partial improvement was observed i.e. if a persistent neurological deficit was observed with a reduction of the functional handicap.
—"good improvement" (GI) when major improvement had occurred resulting in an absence of handicap.

Repartition of sex, age, day of CT and SPECT related to day of cerebral ischemia were compared between the 3 groups of patients (GI, MI and PI) by the Chi 2 test for sex and the Mann and Whitney test for the other clinical parameters.

Results

All patients had SPECT with IMP a visual hypoactive brain area location congruent with the neurological symptoms. Relations between RA, clinical outcome and type of cerebral ischemia are shown in Table 1.

Figure 1 shows the DPA mean in early and late SPECT according to the type of ischemia and the degree of improvement observed 3 months later. In stroke patients the early DPA mean was lower in patients with PI than those with MI as it was lower than in Prind or Tia patients. The RA mean was of 44.5% in the PI group, of 83.7% in the MI group and of 96% in the GI group. Table 1 shows that a complete redistribution was not observed with PI or a lack of redistribution with a GI. Partial redistribution was found in 2 strokes with MI and 4 strokes with PI and in 3 patients with GI. Therefore partial redistribution do not suggest GI in Stroke patients (0/9 in this study).

No difference was found for EHI between the PI and MI groups nor between the MI and GI groups (MW test = 13 and 16 respectively). EHI only differed between patients with PI and GI (MW test = 4 p < 0.01). On the contrary, LHI was different between patients with PI and patients with MI (MW test = 6 p < 0.01) as well as between patients with PI and patients with GI (MW test = 2 p < 0.01) whereas no difference was observed between patients with MI and GI (MW test = 26). Statistical analysis of RA led to the same results using MW test (MW = 9 p < 0.05 for PI vs. MI,
MW = 3 p < 0.01 for PI vs. GI) or ANOVA (Fisher = 7.83 p < 0.01) as for LHI. Therefore, in Stroke patients, LHI or RA was significantly different between patients with PI and patients with MI (all Strokes except one) whereas EHI did not differ in these patients (MW test = 13). Finally, EHI and LHI were related by a significant correlation: r = -0.887 Y = 0.842X + 16.45 p < 0.01.

Discussion

We have previously reported persistent IMP hypoactivity in reversible cerebral ischemia even after several weeks. In this study the lowest EHI were observed in patients with Prind or Tia whereas the highest ones were found only in Stroke patients. Indeed, except in one case, patients with GI had an EHI lower than –30% (mean = 20%) whereas 11 patients out of 15 of the PI and MI group had an EHI that did not reach this “threshold”. However EHI differs significantly only between patients with PI and GI and therefore could not represent a good index for an early evaluation of the prognosis of Stroke patients since it did not differ significantly between PI and MI patients.

The mean LHI was higher in Tia and Prind patients than in the Stroke patients as well as in the patients with GI compared to those with MI and to those with PI. Since a significant difference for LHI and RA was observed between patients with PI and MI and that RA was related to the type of cerebral ischemia and clinical recovery. Thus, in Stroke patients RA may represent a prognostic index of clinical improvement within the first months following cerebral ischemia.

Little is know about brain binding and metabolism of the molecule that would be of particular interest for brain imaging interpretation in humans. Metabolism implies an initial desalkylation. Redistribution of activity on late IMP could reflect a balance between cellular uptake from blood: wash-in (related to cerebral blood flow and lung reservoir) and going out of IMP after metabolism from brain tissue: wash-out. During cerebral ischemia brain cells metabolism was reduced. Then IMP redistribution in ischemic area could reflect slowed kinetic of the tracer without specific changes in the mechanisms of uptake and metabolism of IMP. Impairment of the normal wash-in wash-out balance of IMP led to a variable redistribution phenomenon that represents brain functional tissular capacity. Complete or partial redistribution could be understood by a simultaneous reduction of the wash-in and wash-out allowing brain accumulation of IMP whereas lack of redistribution could be explain by a great wash-in diminution or a great wash-out acceleration.

In conclusion, late imaging of IMP related to brain kinetics of the tracer reflects a qualitative functional imaging of brain tissue. The RA could be closely related to subsequent improvement of clinical status at the end of 3 months. Thus, late imaging of IMP could be an index of prognosis in patients after cerebral ischemic attack which could be of real clinical interest in Stroke patients particularly concerning thereapeutics, nursing-care and re-habilitation decisions.