Interobserver Agreement for the Diagnosis of Transient Ischemic Attacks

C. L. KRAAIJEVELD, M.D.,* J. VAN GIN, M.D.,* H. J. A. SCHOUTEN, PH.D.,† and A. STAAL, M.D.*

SUMMARY The interobserver agreement for the diagnosis of a cerebral transient ischemic attack (TIA) was investigated in a pool of eight senior and interested neurologists from the same department. They interviewed 56 patients in alternating pairs. The diagnosis was based on internationally accepted criteria. The agreement rates were corrected for chance (kappa statistics). Both neurologists agreed that 36 patients had a TIA and 12 had not, but they disagreed about 8 patients (kappa = 0.65; for perfect agreement kappa would be 1.0). The vascular territory (carotid or vertebrobasilar) was agreed upon in only 24 of the 36 patients in whom both diagnosed TIA's (kappa = 0.31). We concluded that currently the diagnosis of a TIA, made by a single neurologist, is a poorly defined entity.

CEREBRAL TRANSIENT ISCHEMIC ATTACKS (TIA's) are an important risk factor for the occurrence of stroke and vascular death.1 2 The recognition of these attacks has important implications for further management.3 However, the diagnosis is exclusively based upon the patient's history and can only in this way be distinguished from other paroxysmal disorders such as migraine, syncope, hyperventilation or epilepsy.

Little is known about the variation of the conclusions between physicians in this diagnostic process. Criteria for TIA's exist,4 but these are phrased in diagnostic terms, and the actual difficulty may be the earlier decision whether the patient's account should be interpreted as, for instance, hemiparesis or amaurosis fugax. Previous studies have shown some differences between observers in the assessment of isolated elements of the history.5-7 It has not been investigated, however, to what extent these differences affect the main conclusion. Moreover, chance agreement8 has not been taken into account in these studies.

Our study was undertaken to measure the interobserver agreement on the final decision whether patients had a TIA or not. We also measured the agreement on the vascular territory of presumed TIA's, since this decision may lead to performing carotid angiography and subsequent endarterectomy.

Patients and Methods

The design of the study was that each patient would, within two days, be interviewed independently by two senior neurologists from a chosen group of eight. These eight specialists belonged to the same University department of neurology, in which the diagnosis and management of patients with TIA's had been discussed at length. Common guidelines had been adopted since 1979. The combinations of two neurologists alternated in such a way that everyone would twice be paired with each of the seven others, once as the first investigator and once as the second (56 combinations).

During the study period (May–September 1982), we aimed at including all patients in whom a diagnosis of TIA was considered by the referring physician or by one of the residents of the department of neurology. Patients with slight residual deficits were also eligible if the history could not be biased by obvious handicaps such as weakness or aphasia. Seventy-four patients fulfilled the criteria, but 18 could not be included for the following reasons: one or both neurologists not available (11), unreliable history because of low intelligence (3), refusal to co-operate (3), or patient already known to the investigators (1). Of the final 56 patients in the study, 38 were men (mean age 60 years) and 18 were women (mean age 57 years).

After completing the history and writing a short summary, the neurologists had to answer the following questions on a standard form: 1) TIA, yes or no? 2) If yes, which territory? (carotid, vertebrobasilar, either, or both). Also, each conclusion was qualified as firm or doubtful. The following criteria were used:

A. Time course of TIA's: The symptoms should have developed within a few seconds and, if multiple, at the same time, without a 'march'; the disappearance of symptoms should be complete or almost complete within 24 hours.

B. Symptoms of carotid TIA's: Hemiparesis, aphasia and amaurosis fugax.

C. Symptoms of vertebrobasilar TIA's: Bilateral, basilar, or alternating weakness or sensory symptoms, transient global amnesia. Vertigo, diplopia, dysphagia, ataxia and drop attacks were accepted only if two or more of these symptoms occurred together.

D. Symptoms of uncertain arterial territory: Hemianopia and dysarthria.

E. Symptoms explicitly not acceptable as TIA: Unilateral sensory symptoms, syncope, loss of consciousness or confusion, convulsions, incontinence of urine or faeces, dizziness, focal symptoms associated with migrainous headache (also in the past), scintillating scotoma.

The degree of agreement between the two investigators was measured by kappa statistics.8

Kappa = (Po - Pe)/(100 - Pe),
where Po is the observed percentage of agreement, and Pe is the percentage of agreement that is to be expected by chance when judgments are statistically independent. Kappa = 0 when there is just chance agreement and kappa = 1 when there is perfect agreement.

**Results**

In answering the question ‘‘TIA or not?’’ the observers agreed on 48 of the 56 patients: 36 were considered by both to have had a TIA, and in 12 they agreed that the diagnosis was not TIA.

In 8 patients the conclusions were different, and in 4 of these cases both observers had marked their opinion as certain. From the written histories it seemed that the disagreements were not related to the nature of the symptoms that had been described by the patients (with one notable exception), but rather to the mode of onset or to accompanying symptoms such as migrainous headache. Expressed as the kappa value, the agreement rate between the two neurologists was 0.65 (table 1).

The agreement on the vascular territory was studied for the 36 patients in whom both observers agreed on the diagnosis of TIA. For practical purposes the conclusions were grouped according to whether carotid angiography would have to be considered. Thus, ‘‘carotid territory’’ and ‘‘carotid plus vertebrobasilar territory’’ were taken together and also ‘‘vertebrobasilar territory’’ and ‘‘territory uncertain’’. The observers agreed on this dichotomous choice in 24 patients, with a kappa value of 0.31 (table 2).

**Discussion**

In all studies on the incidence, causes and treatment of patients with transient ischemic attacks it has been tacitly assumed that a precise diagnosis of these attacks was ensured by strict definitions. In our study, such definitions prompted the first as well as the second tacitly assumed that a precise diagnosis of these attacks was not a TIA. Likewise, both would have concluded in 8% that the group as TIA, they would still have agreed on 59%.

For practical purposes the consensus may not necessarily increase the accuracy of the diagnosis, but in the absence of objective criteria for TIA’s a pragmatic approach should be adopted. A second step towards a common concept of TIA’s could be to ‘‘translate’’ the definitions from abstract diagnostic terms into plain language. In this way the patients’ symptoms would need less interpretation.

We conclude that future studies about patients with TIA’s should explicitly mention the diagnostic procedure, that is the methods used in acquiring and interpreting the patient’s history.

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**TABLE 1**

<table>
<thead>
<tr>
<th>First investigator</th>
<th>Yes %</th>
<th>No %</th>
<th>Total %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>36 (64)</td>
<td>4 (7)</td>
<td>40 (71)</td>
</tr>
<tr>
<td>*C</td>
<td>51</td>
<td>C</td>
<td>20</td>
</tr>
<tr>
<td>No</td>
<td>4 (7)</td>
<td>12 (22)</td>
<td>16 (29)</td>
</tr>
<tr>
<td>C</td>
<td>20</td>
<td>C</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>40 (71)</td>
<td>16 (29)</td>
<td>n = 56</td>
</tr>
</tbody>
</table>

kappa = 0.65 (SE = 0.11).

* C = percentage expected by chance.

**TABLE 2**

<table>
<thead>
<tr>
<th>Territory of the Cerebral Circulation was Involved</th>
<th>First investigator</th>
<th>Second investigator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carotid &amp; vertebrobasilar %</td>
<td>4 (11)</td>
<td>8 (22)</td>
</tr>
<tr>
<td>Vertebrobasilar %</td>
<td>4 (11)</td>
<td>8 (22)</td>
</tr>
<tr>
<td>or uncertain %</td>
<td>19</td>
<td>15</td>
</tr>
<tr>
<td>Total</td>
<td>24 (67)</td>
<td>12 (33)</td>
</tr>
</tbody>
</table>

kappa = 0.31 (SE = 0.16).

* C = percentage expected by chance.
References
6. Tonassello F, Mariani F, Fieschi C et al: Assessment of Inter-

Demonstration of Adenosine Receptors on Mouse Cerebral Smooth Muscle Membranes
DAVID W. BECK, M.D., HARRY V. VINTERS, M.D., STEVEN A. MOORE, M.D., PH.D., MICHAEL N. HART, M.D., FRITZ A. HENN, M.D., PH.D., PASQUALE A. CANCELLA, M.D.

SUMMARY Adenosine receptors have been identified on brain cortical membranes and microvascular preparations. However, they have not been demonstrated on specific microvascular elements in isolation. 2-3H-chloroadenosine was used as a ligand to investigate the presence of adenosine receptors on isolated mouse cerebral smooth muscle membranes. The binding studies reveal the presence of a high affinity binding site with a Kd value of 33.3 nM and a maximal binding capacity (Bmax) of 283 fmol/mg protein. These findings demonstrate that there is an adenosine receptor on cerebral smooth muscle membranes.

ADENOSINE has been proposed as a neuroregulator of cerebral blood flow because of the rapid rise in brain adenosine levels following hypotension, ischemia, seizures, and hypoxia and because adenosine is a potent vasodilator. In its proposed role of regulating cerebral blood flow it is speculated that adenosine may be present in the glial foot process via 5' nucleotidase, released into the extracellular space, and bound to cerebral smooth muscle membranes resulting in relaxation of the vessel. There is some evidence to support this hypothesis. Adenosine receptors A1 and A2 have been identified on brain membranes and are associated respectively with a decrease and an increase in cyclic AMP production. Furthermore, increased smooth muscle cyclic AMP has been associated with vessel relaxation. Adenosine receptors on cerebral smooth muscle membranes, however, have never been demonstrated. Palmer, et al have shown adenosine receptors in capillaries of rat cerebral cortex coupled to adenylate cyclase. However, these microvessel preparations are impure, in that they contain several microvascular elements such as glia, endothelia, smooth muscle, and pericytes.

If indeed adenosine regulates cerebral blood flow via action on cerebral smooth muscle membranes, then receptors on specific microvascular elements need to be demonstrated in isolation. We report the results of binding studies of 2-3H-chloroadenosine with isolated mouse cerebral smooth muscle membranes. Our results show a high affinity receptor for 2-3H-chloroadenosine is present on cerebral smooth muscle membranes.

Methods
Cell Cultures
Isolation of mouse cerebral microvessels and derivation of cerebral smooth muscle cells and cerebral endothelial cells in tissue culture have previously been described from our laboratory. Cerebral smooth muscle cells are characterized by their broad, polygonally shaped morphology and possess many characteris-
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