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# The capsular warning syndrome: Pathogenesis and clinical features

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**Article abstract**—Transient ischemic attacks (TIAs) are not homogeneous and may consist of subsets with mechanisms as varied as their stroke counterparts. We describe a form of TIA in 50 patients where crescendo episodes of ischemia were restricted to the region of the internal capsule, usually causing symptoms affecting face, arm, and leg. These patients composed 4.5% of a consecutive series of patients admitted with TIAs over a 15-year period and 33% of all TIAs classified as subcortical. We believe that the ischemia was most often due to hemodynamic phenomena in diseased, single, small penetrating vessels. When cerebral infarction developed, it was usually lacunar and involved a single penetrating vessel, although occasionally striatocapsular or anterior choroidal artery territory infarction occurred. There was no evidence of artery-to-artery or heart-to-artery embolism. Resistance to various forms of therapy, including hemodiluting, anticoagulant, and thrombolytic agents, was common. Because of dramatic and easily recognizable clinical presentation, apparent specific pathophysiologic mechanism, and the development of early capsular stroke in a high proportion of cases (42%), we have termed this the “capsular warning syndrome.”

NEUROLOGY 1993;43:957-962

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Transient ischemic attacks (TIAs) have been defined as brief, focal neurologic events of 24 hours' duration, or less. Only a limited classification of TIAs into subtypes has occurred so far; most clinicians recognize TIAs in the carotid and vertebrobasilar territories, but little further refinement of classification exists. More importantly, it has been difficult to relate the clinical features of TIA to pathogenesis. However, it is reasonable to assume that the pathogenesises of TIAs are as varied as their stroke counterparts and may reflect similar mechanisms. We described earlier a particular pattern of TIA consisting of repeated bursts of focal neurologic events due to ischemia in the region of the internal capsule.<sup>1-4</sup> This form of TIA is relatively easy to recognize and is pathophysiologically distinct. In many instances, the patients were examined during the attack, thus improving the reliability of our observations. The ischemia is probably due to in situ small penetrating vessel disease, with no evidence to suggest artery-to-artery or heart-to-artery emboli. We have termed this sequence the “capsular warning syndrome” because of its dramatic clinical presentation and high probability of early capsular stroke. In this study, we expand on our original observations in a series of 50 consecutive patients.

**Methods.** Patients with clinical features suggesting transient cerebral ischemia in the region of the internal capsule have been prospectively studied during Stroke

Unit data collection from 1977 to 1991. For the present study, all patients with TIA were also retrospectively categorized into groups depending on the presumed site of transient cerebral ischemia based on the following criteria:

1. *Probably subcortical.* Motor, sensory, or sensorimotor symptoms affecting face, arm, and leg simultaneously, with no cortical signs such as neglect, dyspraxia, or dysphasia; involvement of face and arm or arm and leg was accepted if also: (a) the patient was examined during the event, (b) a fresh infarct was seen in subcortex appropriate to clinical findings, or (c) ischemia was in the left hemisphere and patient spoke with no evidence of dysphasia (dysarthria may be present in cases where ischemia affects either hemisphere).

2. *Probably cortical.* Typically, the presence of cortical symptoms such as dysphasia, neglect, or dyspraxia with or without hemiparesis involving face, arm, and leg, or: (a) brachiofacial weakness with or without sensory involvement, (b) monoparesis with or without cortical signs, (c) patient examined during the event and cortical signs documented, or (d) amaurosis fugax occurred within the study period in the same vascular territory.

3. *Probably vertebrobasilar.* Evidence of brainstem involvement by documentation of more than one of the symptoms of diplopia, visual blurring bilaterally, dysarthria, alternating hemiparesis, crossed hemisensory loss, vertigo, nausea, vomiting, or examination during the event confirming these findings.

4. *Retinal.* Obscuration of vision in one eye, typically vertically like a “blind” and sudden and complete with no directional onset or with a more generalized blurring.

5. *Uncertain.* Hemiparesis involving arm and leg during which no cortical symptoms were documented or noted

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Received May 1, 1992. Accepted for publication in final form September 4, 1992.

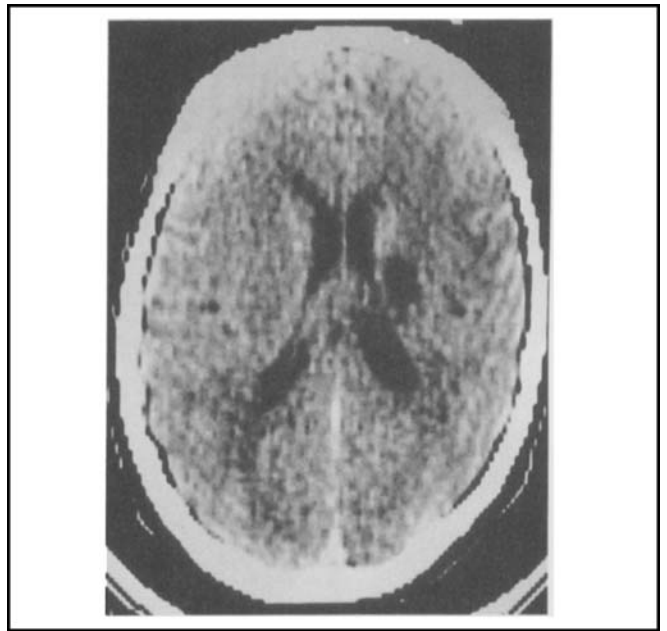
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by the patient. This involved mainly cases of ischemia in the right hemisphere or cases of left-hemisphere ischemia where the patient did not speak (right handed) or the nature of the speech disturbance was unclear.

Patients were recognized as having the capsular warning syndrome if the region of ischemia was classified as being subcortical and if repetitive neurologic events occurred at presentation. The time frame during which these events occurred was usually quite brief (most often within 72 hours), but for the purposes of this study those in whom three or more events occurred within 24 hours were identified to provide a benchmark for study entry. Hypertension was defined as two readings of diastolic blood pressure >95 mm Hg after the cerebral event had settled and antihypertensive treatment was then needed, or antihypertensive treatment was already being taken prior to admission. CTs were performed within 48 hours of admission and in most cases repeated between days 7 and 14 if the initial scan was negative. Carotid angiography was performed in patients where minimal or no clinical deficit was present and where information gained was likely to contribute to clinical management. Treatment was not systematized in any way, and selection of treatment type was based on the individual preference of the managing neurologist.

**Results.** During the period of study from 1977 to 1992, 4,950 patients were admitted to the Stroke Unit and 1,093 (22%) were classified as having TIAs. One hundred fifty-three (14%) of the TIAs were classified as probably subcortical, 429 (39%) as probably cortical, 114 (10%) as probably vertebrobasilar, and 124 (11%) as retinal; in 273 (25%) patients the location of ischemia was uncertain. Fifty-seven of these had features consistent with the capsular warning syndrome, and 50 (33% of patients with subcortical TIAs and 4.5% of all TIAs) of these had three or more events within 24 hours. Of the 50 patients, 31 were men and 19 were women; mean age was 63 years (range, 26 to 84). Twenty-seven of the patients (54%) with capsular warning syndrome were examined during the event, thus increasing the precision of clinical localization of the ischemic event to the region of the internal capsule.

**Representative case reports. Patient 1.** A 52-year-old, right-handed chauffeur with a history of untreated hypertension developed sudden onset of left face, arm, and leg weakness while driving on July 4, 1977. A dull, generalized headache had preceded the onset of symptoms. Complete recovery occurred in approximately 5 minutes, but two more episodes quickly followed lasting 45 minutes and 30 minutes. He drove to the emergency department where examination was normal. An intravenous dextran plasma expander was commenced and he was admitted to a general medical ward. Another episode occurred the next day. Blood pressure was 160/90, pulse regular, and he was started on a diuretic. Four-vessel arteriography was normal. A further episode occurred 3 days later, four episodes the day after, and an unknown number on the following day, with complete recovery between each event. A psychiatrist was consulted, who felt that these might have been functional. On July 11, 1977, further events occurred during continuous EEG monitoring. After forward head flexion the patient stated, "I can feel it coming on," and over the next 30 seconds he developed a dense pure motor



*Figure 1. CT of a 52-year-old man (pt 1) with repetitive episodes of left hemiplegia that culminated in lacunar stroke 11 days later. Scan shows a right internal-capsule lacune.*

hemiplegia of the left face, arm, and leg. His speech was slurred, there was no visual or sensory neglect or eye deviation, and he was able to recognize objects placed in his left hand. Left toe was extensor. The hemiplegia lasted for approximately 10 minutes, during which the EEG was normal. Recovery occurred over 30 seconds. The next day, a slight left facial paresis and extensor left plantar response were noted; 3 days later he developed a left pure motor hemiparesis (2/5 face, 2/5 arm, and 3/5 leg). A head CT was normal. He returned to work in October 1977 in a clerical capacity. CT was performed a year later and showed a lacune in the posterior limb of the capsule in the right paraventricular region (figure 1). He later developed ischemic heart disease and hypercholesterolemia but had no further neurologic events. He suffered a presumed cardiac death at a railway station in 1983.

**Patient 2.** A 56-year-old, right-handed woman with a history of untreated hypertension was seated at her kitchen table at 9:30 AM on October 20, 1983, when she noted the sudden onset of weakness and numbness of her right face, arm, and leg. She slipped to the floor and lay there for some time before crawling to the telephone. Her speech was slurred but there was no malapropiation of words. Seventy-five minutes later, a rapid resolution occurred over seconds. At 11:30 AM the symptoms returned, but this time they only lasted for 45 minutes. A 15-minute episode occurred at 12:30 PM. At 1:30 PM, while in the emergency department lying on a couch, she again developed a dense right hemiplegia involving face, arm, and leg. She was dysarthric, and a complete motor and sensory loss involving right face, arm, and leg was present; reflexes were symmetric, but right plantar was extensor. Sensory signs cleared over the next hour but the hemiplegia remained. No visual or sensory inattention was present. General examination revealed no cardiac abnormalities and no cervical bruits. Blood pressure was 240/130, pulse 82 beats per minute and regular. Hypertension was treated with an oral beta blocker.

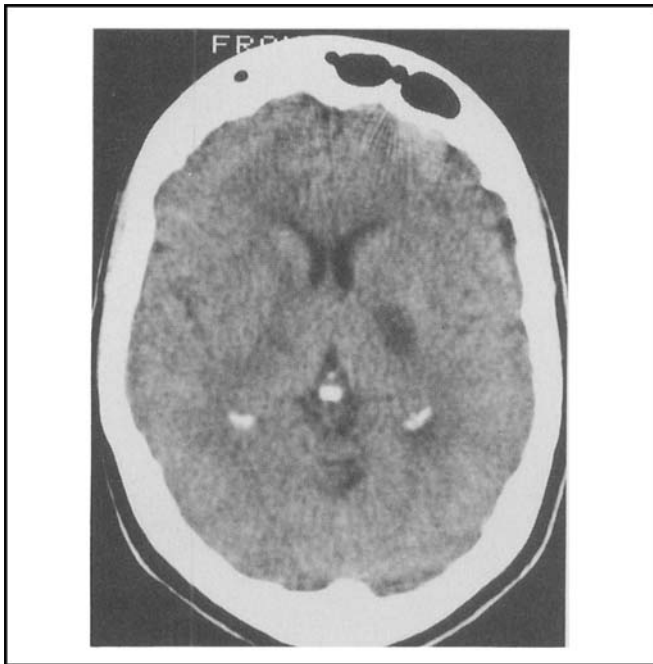


Figure 2. CT of a 56-year-old woman (pt 2) who presented with repetitive episodes of right hemiparesis and developed a capsular stroke. Scan shows an infarct involving more than one penetrator in the territory of the left anterior choroidal artery.

EEG, hematologic study, and liver and renal functions were all normal. CT showed an infarct involving more than one penetrating vessel in the territory of the left anterior choroidal artery (figure 2). She later was noted to be acromegalic, and a pituitary tumor was removed transphenoidally on November 17, 1983. Postoperatively, she became dysphasic for about 18 hours. Carotid angiography revealed a 30% stenosis of the left internal carotid artery, and subsequent endarterectomy revealed a calcific plaque extending up the anteromedial wall for 2 cm. Some pits within the plaque were seen but no evidence of hemorrhage or ulceration was present. Modest gains ensued over the next 2 years, but functional weakness persisted. No further neurologic events occurred.

**Patient 3.** A 75-year-old widow awoke at 4:00 AM and found that she was unable to get out of bed because of inability to move her left side. Her speech was slurred. After about 15 minutes the weakness suddenly resolved. She got up and went to the kitchen where again left-sided weakness developed, this time including her face, which resolved in 10 minutes. Two more brief episodes (minutes) occurred prior to her arrival at the hospital that morning. History included coronary artery bypass grafting, and at the time of coronary angiography a left carotid stenosis (uncertain degree) was noted. There was no history of hypertension, and she was a nonsmoker. A left cervical bruit was heard at the angle of the jaw, and blood pressure was 160/90 with pulse 70 beats per minute and regular. Neurologic examination was normal, but when she was stood to examine her gait at about midday she again developed weakness involving her left arm (2/5) and leg (2/5) over a period of seconds. No sensory change was experienced, reflexes were symmetric, but left plantar was extensor. There was no visual or sensory neglect. Intravenous plasma expander was commenced. Blood pressure was 180/90 during this event. She had

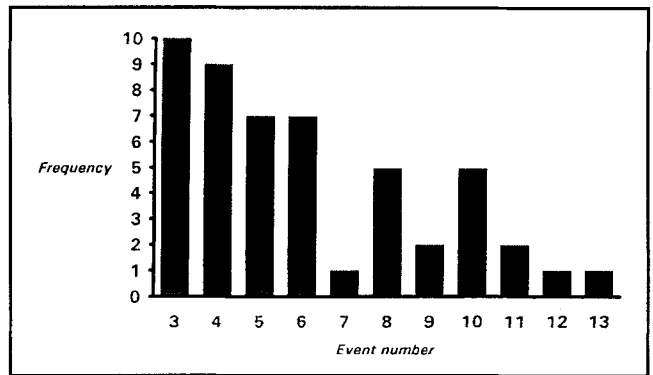


Figure 3. Frequency of neurologic events among 50 cases of the capsular warning syndrome.

**Table. The distribution of motor and sensory symptoms in 50 cases of the capsular warning syndrome**

| Symptoms                   | No. of patients |
|----------------------------|-----------------|
| Motor                      |                 |
| Face/Arm/Leg               | 16              |
| Face/Arm                   | 1               |
| Arm/Leg                    | 5               |
| Sensory                    |                 |
| Face/Arm/Leg               | 1               |
| Face/Arm                   | 0               |
| Arm/Leg                    | 1               |
| Sensory/Motor              |                 |
| Face/Arm/Leg               | 14              |
| Face/Arm                   | 2               |
| Arm/Leg                    | 9               |
| Dysarthria/Motor/Sens. Arm | 1               |
| Total                      | 50              |

recovered except for mild left leg weakness the next day. Right carotid angiography was normal as was CT. During the same night she again developed dysarthria and left-sided weakness. By morning she was unable to move her left arm or leg and had a profound left facial weakness with dysarthria. There were no sensory or cortical signs. CT performed 10 days later showed a right striatocapsular infarct<sup>5,6</sup> (films since destroyed). EEG showed increased slow activity over the right hemisphere, and neuropsychological examination did show some visuospatial difficulties. She made a gradual recovery over the next few months.

*Clinical features.* The definition of this group specifies at least three clinical events within 24 hours, and the number of events ranged from three to 13 (figure 3). Characteristically, the onset tended to occur over seconds; several patients described a feeling of the weakness "coming on" rather than presenting abruptly (see patient 1). Pure motor hemiparesis was the most common presenting symptom (table), although the onset was often accompanied by sensory symptoms that usually cleared quickly before the motor symptoms resolved.

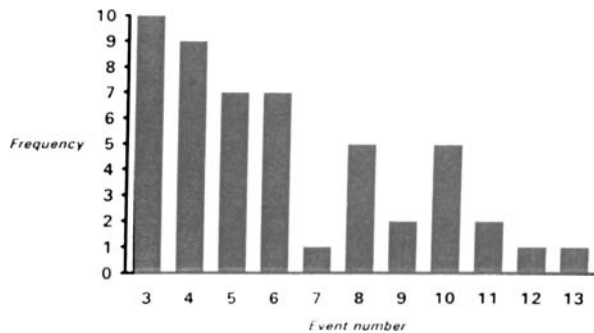


Figure 4. Duration of neurologic events among 50 cases of the capsular warning syndrome.

The mean duration of events was quite brief at 6.1 minutes (figure 4) and ranged from 2 minutes to 4 hours. The episodes were usually clustered within a relatively narrow time frame, for example, five episodes within 3 hours in one patient, although the range of the completion of the burst of clinical events was from 1 hour to several bursts over 5 days. The maximum documented number of events was 13, and this occurred over a 4-day period. However, often the events were so frequent and close together that the exact count was lost by both physician and patient. The presentation was so spectacular in two patients with such sudden and complete resolution, that prior to neurologic consultation the symptoms were considered to be hysterical in nature. Headache was not a feature of the presentation, although a small number complained of mild cranial ache of a nonspecific nature.

**Risk factors.** Forty-two patients (84%) had either preexisting hypertension or hypertension was diagnosed upon admission. Nineteen (38%) were current smokers, nine had a history of hyperlipidemia, five were diabetic, 10 had a history of myocardial infarction, one had valvular heart disease, and one patient had atrial fibrillation.

**CT.** All patients had CTs at the time of initial assessment. Twenty-five showed ipsilateral small deep infarcts, and the remaining scans were normal. Seven patients had relevant infarcts on CT but no fixed neurologic deficit. In 18 of 21 patients with subsequent stroke either during inpatient stay or prior to admission, the side of the infarct was confirmed as being in the clinically relevant internal capsule. In 15 of the 18 patients with relevant infarcts, the infarct was in the territory of a single small penetrating vessel (eg, patient 1), in two patients striatocapsular infarction was seen (eg, patient 2), and in another, infarction in the territory of the anterior choroidal artery (patient 3).

**Angiography/ultrasonography.** Twenty-seven patients underwent angiographic study, and six had duplex ultrasound scanning of internal carotid arteries. In 30, the study was normal or minimal change was demonstrated at the origin of the ipsilateral internal carotid artery. Three patients had significant change (50% stenosis in one and 20%

stenosis in two). One patient had high-grade stenosis of the ipsilateral middle cerebral artery.

**Treatment.** During the clinical episodes, plasma expanders (10% dextrose in 500 ml over 1 hour and then 500 ml over 6 hours in each 24 hours for the next 72 hours) were used in 25 patients, but the episodes continued. In eight of these, subsequent stroke occurred (eg, patient 1). Three patients were given intravenous heparin, one of whom developed a stroke. Thirty-six patients were commenced on aspirin and were taking this medication on discharge. Four patients were discharged on warfarin. Carotid endarterectomy was performed in three patients, but in no patient was active ulceration with or without clot formation found.

**Early prognosis.** Twenty-one patients (42%) had either developed a fixed deficit by the time they arrived at the emergency department or went on to develop stroke during their inpatient stay (mean inpatient stay was 17 days; range, 3 to 54 days). Of those patients with fixed deficit, 15 had pure motor hemiparesis, one dysarthria and clumsy hand syndrome, and five sensorimotor stroke<sup>7</sup>; two patients developed striatocapsular infarction and had a hemiparesis with predominant arm weakness and cortical signs typical of this syndrome,<sup>5,6</sup> and one had a pure motor hemiparesis with infarction in the territory of the anterior choroidal artery (patient 2).

**Discussion.** We have outlined the clinical features and pathogenesis of the capsular warning syndrome, a distinct form of TIA that may be clinically located to the region of the internal capsule and which leads to early capsular infarction in a high proportion of cases (42%). This expands upon our earlier descriptions of this condition<sup>1-4</sup> and other studies of subcortical TIAs.<sup>8,9</sup> While the majority of the infarcts that developed following the burst of clinical events were lacunar, this was not invariably so. Two patients developed striatocapsular infarction,<sup>5,6</sup> and one developed infarction in the region of the anterior choroidal artery territory. While internal capsular infarction was the only finding in those patients who developed permanent deficits, it is possible that in some cases of the capsular warning syndrome the area of ischemia may involve the pyramidal tracts below the capsule, perhaps in the area of single penetrators from the basilar artery. With the more widespread use of MRI, the frequency with which this occurs may be more clearly established. The pattern of frequent clinical events suggesting incipient vessel occlusion in other vascular territories has not yet been clearly defined.

The repetitive nature of clinical events leading up to capsular infarction has been noted earlier by both Marie<sup>10</sup> and Fisher and Curry.<sup>11</sup> Marie stated, "The multiplicity of episodes, with variable interval between them, is an essential characteristic of lacunar degeneration. Of my 50 cases, 32 had two or more previous episodes." Fisher and Curry noted, "In our experience, a burst of frequent hemiplegic

spells suggested the pure motor syndrome arising more likely in the capsule than in the pons." Similar premonitory events were noted by Helgason et al<sup>12</sup> in their series of patients with anterior choroidal artery territory infarction. Rothrock et al<sup>13</sup> described 47 patients with crescendo TIAs, nine of whom had repetitive symptoms suggesting the capsular warning syndrome. In our experience, the onset is not instantaneous, as in patient 2. More often, the patient could feel "the weakness coming on over a period of seconds," and its resolution was over a period of seconds or minutes.

The mechanism whereby such stereotypically repeated events occur within such a brief period of time is unclear. In general, it has been hypothesized that clinical patterns of this type have a hemodynamic basis. This is supported by the observation that incipient occlusion of the internal carotid artery may be accompanied by repetitive events, although usually with associated cortical signs.<sup>14</sup> In two of the cases of lacunar infarction reported by Waterson et al,<sup>15</sup> a hemodynamic basis was postulated based on the finding of ipsilateral internal carotid occlusion and the position of the small infarcts in the borderzone between deep and superficial penetrating arteries. These cases were not preceded by the capsular warning syndrome. We have not found any examples of ipsilateral severe carotid occlusive disease in this condition. Our own anecdotal experience would suggest that embolic artery-to-artery phenomena cause events more widely separated in time, and there was little angiographic evidence to support an embolic mechanism in our patients. Another possible mechanism would be artery-to-artery microemboli within the penetrating vessels themselves, but for much the same reasons cited above concerning the temporal behavior of emboli in general, this seems less likely. Similarly, cardiac embolism seems unlikely in view of the lack of cardiac abnormalities. The brevity of duration of TIAs has been positively correlated with the degree of carotid artery stenosis in two studies,<sup>16,17</sup> perhaps supporting the view that hemodynamic events are of shorter duration than embolic events from the heart allowed by more open carotid systems. Could these events relate to vasospasm? Friberg and Olsen<sup>18</sup> recently ascribed cerebrovascular instability, as documented by intra-arterial xenon-133 cerebral blood flow studies, to vasospasm in several patients with TIA and stroke, although perhaps on tenuous grounds given that vasospasm was not demonstrated angiographically. Vasospasm of retinal vessels occurs during episodes of amaurosis fugax when not in a migrainous setting<sup>19</sup> and repetitive clinical events occasionally occur in hemiplegic migraine. In spite of this indirect supporting evidence for this mechanism, we feel that hemodynamic factors secondary to structural arterial change such as atheroma or lipohyalinosis is the most likely mechanism in the majority of our cases.

Given that hemodynamic phenomena within a

single penetrating vessel appears to be the most likely mechanism of ischemia, how does this relate to the underlying pathology? The earlier studies of Fisher<sup>20-22</sup> have shown that lacunar infarcts may be caused by in situ disease of small penetrating vessels. This may include lipohyalinosis secondary to the effects of hypertension, atheroma within the penetrating vessel, or atheroma associated with a larger parent vessel. This latter change may be present in cases of middle cerebral artery stenosis, as found in two of our patients. It appears most likely that high-grade stenoses of penetrating vessels due to any of these pathologies may create the hemodynamic environment for the clinical expression of the capsular warning syndrome.

In spite of various treatment modalities, including anticoagulants, plasma expanders, or aspirin, it is uncertain as to whether these alter the natural history of the syndrome. Anecdotal reports of failed medical therapy (heparin) in progressing lacunar stroke suggest that this form of cerebral infarction may be therapeutically resistant,<sup>23</sup> although the complete recovery between episodes in cases of the capsular warning syndrome may suggest a slightly different situation than in progressing stroke *per se*. Because of the repetitive nature of the events and the relatively high incidence of subsequent ischemic stroke, this form of TIA may be ideal to formally test various therapies since relatively small sample sizes would be required.

## References

1. Donnan GA. A study of lacunar infarction syndromes. Melbourne, Australia: Melbourne University, 1980. Thesis.
2. Donnan GA, Tress BM, Bladin PF. A prospective study of lacunar infarction using computerized tomography. *Neurology* 1982;32:49-56.
3. Donnan GA, Bladin PF. The capsular warning syndrome: repetitive hemiplegic events preceding capsular stroke [abstract]. *Stroke* 1987;18:296.
4. Donnan GA, Bladin PF. Not all TIAs are equal [letter]. *Neurology* 1988;38:1659.
5. Bladin PF, Berkovic SF. Striatocapsular infarction: large infarcts in the lenticulostriate arterial territory. *Neurology* 1984;34:1423-1430.
6. Donnan GA, Bladin PF, Berkovic SF, Longley WA, Saling MM. The stroke syndrome of striatocapsular infarction. *Brain* 1991;114:51-70.
7. Fisher CM. Lacunar infarcts: a review. *Cerebrovasc Dis* 1991;1:311-320.
8. Hankey GJ, Warlow CP. Lacunar transient ischaemic attacks: a clinically useful concept? *Lancet* 1991;337:335-338.
9. Kappelle LJ, van Latum JC, Koudstaal PJ, van Gijn J. Transient ischaemic attacks and small-vessel disease. *Lancet* 1991;337:339-341.
10. Marie P. Des foyers lacunaires de desintegration. *Rev Med* 1901;21:281-289.
11. Fisher CM, Curry HB. Pure motor hemiplegia of vascular origin. *Arch Neurol* 1965;13:30-44.
12. Helgason C, Wilbur A, Weiss A, Redmond KJ, Kingsbury NA. Acute pseudobulbar mutism due to discrete bilateral capsular infarction in the territory of the anterior choroidal artery. *Brain* 1988;111:507-524.
13. Rothrock JF, Lyden PD, Yee J, Wiederholt WC. 'Crescendo' transient ischemic attacks: clinical and angiographic correlations. *Neurology* 1988;38:198-201.
14. Fisher CM. Occlusion of the internal carotid artery. *Arch*

- Neurol 1951;65:346-377.
15. Waterson JA, Brown MM, Butler P, Swash M. Small deep cerebral infarcts associated with occlusive internal carotid artery disease. *Arch Neurol* 1990;47:953-957.
  16. Pessin MS, Duncan GW, Mohr JP, Poskanzer DC. Clinical and angiographic features of carotid transient ischaemic attacks. *N Engl J Med* 1977;296:358-362.
  17. Harrison MJG, Marshall J, Thomas DJ. Relevance of duration of transient ischemic attacks in carotid territory. *Br Med J* 1978;1:1578-1579.
  18. Friberg L, Olsen TS. Cerebrovascular instability in a subset of patients with stroke and transient ischaemic attack. *Arch Neurol* 1991;48:1026-1031.
  19. Burger SK, Saul RF, Selhorst JB, Thurston SE. Transient monocular blindness caused by vasospasm. *N Engl J Med* 1991;325:870-873.
  20. Fisher CM. The arterial lesions underlying lacunes. *Acta Neuropathol (Berl)* 1969;12:1-15.
  21. Fisher CM. Capsular infarcts: the underlying vascular lesions. *Arch Neurol* 1979;36:65-73.
  22. Fisher CM, Caplan LR. Basilar artery branch occlusion—a cause of pontine infarction. *Neurology* 1971;21:900-905.
  23. Dobkin BH. Heparin for lacunar stroke in progression. *Stroke* 1983;14:421-423.



# Olfactory testing differentiates between progressive supranuclear palsy and idiopathic Parkinson's disease

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**Article abstract**—Olfactory dysfunction occurs in most patients with idiopathic Parkinson's disease (PD). In this study, we sought to determine whether such dysfunction is also present in progressive supranuclear palsy (PSP), a condition which shares a number of motor symptoms with PD and is commonly misdiagnosed as PD. We administered the University of Pennsylvania Smell Identification Test, a standardized test of odor identification ability, to 21 PSP patients; 17 also received a forced-choice odor detection threshold test. We compared the olfactory test scores to those obtained from PD patients and normal controls matched to the PSP patients on the basis of age, sex, and smoking habits. Overall, the olfactory function of the PSP patients was markedly superior to that of the PD patients and did not differ significantly from that of the normal controls. There was no association in either the PSP or PD patient groups between (1) the olfactory test scores and (2) measures of motor symptom severity, disease stage, and medication usage. These findings demonstrate that patients with PSP and PD differ markedly in their ability to smell and suggest that olfactory testing may be useful in their differential diagnosis.

NEUROLOGY 1993;43:962-965

Progressive supranuclear palsy (PSP) accounts for nearly 5% of patients who manifest parkinsonian symptoms.<sup>1</sup> Although this syndrome is frequently characterized by bradykinesia and rigidity early in its progression, tremor is rarely present. The distinguishing feature of this disorder is vertical-gaze paresis (especially downgaze paresis) which can be overcome by the oculoccephalic maneuver. Another prominent feature of PSP is a slowing of thought

processes.<sup>2</sup> Because this disorder shares a number of motor symptoms with idiopathic Parkinson's disease (PD), it is commonly misdiagnosed as PD. Unlike PD, however, its parkinsonian features are less responsive to anti-PD medications.<sup>3</sup> Furthermore, PSP differs from PD in additional neuronal loss within the basal ganglia, cerebellum, and the upper brainstem<sup>4</sup> and more severe frontal lobe dysfunction.<sup>5</sup> A considerable body of evidence

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Supported by grant RO1 AG 08148 from the National Institute on Aging and grant P01 DC 00161 from the National Institute on Deafness and Other Communication Disorders.

Received July 8, 1992. Accepted for publication in final form September 30, 1992.

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*Neurology* 1993;43;957

DOI 10.1212/WNL.43.5.957

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