this condition. Moreover, in the later stages of Parkinson’s disease, a debilitating confusional state with psychotic features is common. Although in some cases this parkinsonian dementia overlaps SDAT, there persists a high incidence of pure Lewy body dementia in parkinsonian patients with dementia. As anticholinergic drugs have mild antiparkinsonian effects, however, it is likely that not all neurologists will instinctively think that a procholinergic drug will worsen the rigidity.

We report here the results of a pilot study on the use of tacrine in patients with parkinsonian dementia. Seven patients were selected for the study (five men and two women, age range 66 to 82, mean 73.9 years). Patients were selected according to the following criteria: (a) diagnosis of Parkinson’s disease prior to the onset of dementia; (b) rigidity that had initially responded to levodopa; (c) a confusional state incorporating visual hallucinations and exacerbated by dopaminergic drugs; (d) a normal brain MRI or CT within two months of the study, to exclude multi-infarct dementia and reduce the possibility of concurrent SDAT.

All patients had carried the diagnosis of Parkinson’s disease for several years before the onset of dementia (mean 7.6 range 3–18 years). The diagnosis was made in each case on the basis of a syndrome of progressive rigidity and handwriting dyskinesia. Four patients also had a mild resting tremor at the time of diagnosis. In each case these presenting symptoms had initially responded well to levodopa, and all patients were taking levodopa at the time entry in the study. No patient had exhibited dyskinesia as a result of treatment with levodopa. None was currently using dopamine agonists, although four had previously used such drugs but had discontinued them because of worsening confusion. Selegiline had also been used in all patients before the study, and in all patients this drug had been discontinued for the same reason. None had used selegiline within four months of the start of the study. Four subjects had severe motor disability (Hoehn and Yahr stage 5) and were confined to a wheelchair or bedridden. Two were stage 4, and could walk with assistance, and one was stage 3, but had had a recent series of falls. Patients had baseline serum glutamic oxaloacetic transaminase and glutamic pyruvic transaminase studies and were started on tacrine at 10 mg four times daily. Liver function tests were obtained on a weekly basis. After two weeks, if transaminase concentrations remained stable, the dose was increased to 20 mg three times daily and maintained at that level for at least two months. All patients underwent Folstein (mini mental state) testing immediately before treatment, and again after two months of treatment. Unified Parkinson’s disability rating scale (UPDRS) scores were also obtained before and after treatment, the motor categories by direct examination, and the daily activity scores by interview of the spouse or care giver. All patients were maintained on levodopa without change during the trial.

In all cases the frequency of hallucinations was greatly reduced after treatment, and in five cases hallucinations were essentially eliminated. All seven patients showed much improvement in both Folstein scores and UPDRS scores (range 13 to 13, P < 0.0001) and UPDRS scores (items 1–31; mean score before treatment 79.3, mean score after treatment 29.6, P < 0.0001). The table shows these results. Although there was no characteristic pattern of mental changes, improvements were seen mainly in the categories of orientation, attention (serial 7s), and visuospatial awareness (copying a geometric figure). In addition, all patients were able to walk independently, improvements in gait corresponding roughly to improvements in mentation. There was no characteristic pattern of motor improvement, and in most patients improvements were seen in most categories of the UPDRS.

Patient (No 2) showed further improvements, according to her family, and underwent repeat Folstein and UPDRS testing seven months after initiation of treatment. At this time the Folstein score had risen to 28/30 (compared with 15/30 before treatment), and the UPDRS had shown a further reduction from 25 to 8. No further improvements were noted in any of these patients by their families, and no other patient was restudied. On the other hand patient No 4, who had the longest history of Parkinson’s disease (15 years), started to decline after six months of treatment with tacrine, indicating possible limits to the duration of benefit in some patients.

In this pilot study the use of tacrine in parkinsonian dementia, considerable improvements were seen in all patients. The finding of motor improvement was unexpected. Before starting this investigation it was thought that even if the dementia ameliorated patients might become more rigid, as anticholinergic drugs have slight antiparkinsonian motor effects. Indeed there is at least one reported case in which rigidity is said to have been developed in a patient with Alzheimer’s disease treated with tacrine. In our study, on the contrary, patients became less rigid. This finding may perhaps be understood if the degenerating cholinergic neurons in Parkinson’s disease are not striatal interneurons but cortical projections, at least some of which are involved (directly or indirectly) in the generation of movements.

Central diabetes insipidus: a complication of herpes simplex encephalitis

Secondary diabetes insipidus occurs as a result of damage to the hypothalamic-neurohypophysial system due to opportunistic infections in AIDS, in neonates, and in children with acute bacterial meningitis. Diabetes insipidus after herpes encephalitis in adults is rare.

Five days before admission, a 42 year old woman developed a prodomal influenza-like illness with rapid onset of headache, behaviour disorder, and clouding of consciousness and became increasingly disoriented and lethargic. She was admitted to hospital because of a tonic-clonic seizure. Her temperature was 38.5°C. The Glasgow coma scale score was 12 and she had neck stiffness and bilateral Babinski’s sign. The CSF showed mononuclear pleocytosis (600 white cells/ml), 131 mg/dl protein, and 80 mg/dl glucose. The EEG suggested encephalitis. Head MRI CT showed hyperintense lesions in the left temporal and frontal lobes and insular cortex, a midline shift to the right, and involvement of the right temporal and frontal lobes highly suggestive of herpes simplex virus encephalitis. There was a significant rise in the titre of serum antibodies to acyclovir and also amikacin for a urinary infection. Brain MRI showed hyperintense areas corresponding to the lesions in the left temporal and frontal lobes and insular cortex, a midline shift to the right, and involvement of the right temporal and frontal lobes highly suggestive of herpes simplex virus encephalitis. There was a significant rise in the titre of serum antibodies.

Dementia and motor disability scores in patients with Parkinson’s disease before and after two months after treatment with tacrine

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>PD</th>
<th>Dementia</th>
<th>MMS</th>
<th>MMS</th>
<th>UPDRS</th>
<th>UPDRS</th>
</tr>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>pre-Rx</td>
<td>post-Rx</td>
<td>pre-Rx</td>
<td>post-Rx</td>
</tr>
<tr>
<td>1</td>
<td>82</td>
<td>4</td>
<td>1</td>
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<td>77</td>
<td>6</td>
<td>1</td>
<td>15</td>
<td>24</td>
<td>89</td>
<td>25 (8)*</td>
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<tr>
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<td>6</td>
<td>1</td>
<td>15</td>
<td>23</td>
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<td>31</td>
</tr>
<tr>
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<td>6</td>
<td>1</td>
<td>15</td>
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<td>86</td>
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</tr>
<tr>
<td>5</td>
<td>66</td>
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<td>0.5</td>
<td>15</td>
<td>21</td>
<td>86</td>
<td>28</td>
</tr>
<tr>
<td>6</td>
<td>74</td>
<td>4</td>
<td>0.25</td>
<td>19</td>
<td>24</td>
<td>103</td>
<td>41</td>
</tr>
</tbody>
</table>

PD = Parkinson’s disease duration; MMS = mini mental state score (Folstein) out of 30; UPDRS = unified rating scale (items 1–31); post Rx = before/after treatment; *at 7 months after initiation of treatment; §scored out of 29.

Definitive conclusions regarding the pathogenesis of this effect, however, must await confirmation and further study.

The psychotic confusional state seen in the later stages of Parkinson’s disease is a common and significant source of morbidity. Our results suggest that low dose tacrine is efficacious in its treatment. In our study population tacrine dispensed with the need for conventional antipsychotic medications, and was causing no motor improvements. Although these preliminary findings are highly suggestive, caution should be exercised in their interpretation until confirmed by a controlled study, preparations for which are underway.

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