Attentional and Perseverative Impairment in Two Cases of Familial Fatal Parkinsonism with Cortical Sparing

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ABSTRACT: The neuropsychological findings in twin brothers with familial fatal Parkinsonism are reported. Post-mortem examination had shown extensive pathology in basal ganglia and brainstem, but not in the cerebral cortex. Although both showed average intelligence three months prior to death, they had impairment on a sorting task and in serial attention span. Some possible neural mechanisms are discussed.

METHODS AND RESULTS

One brother was assessed only once, and the other three times. Both had fairly complete assessments approximately 3 months before death, and these are the assessments which will be emphasized, because they a) provide a good picture of abilities fairly close in time to the post-mortem findings, but before general fatigue was an acute problem, and, b) permit comparisons to be made between the two cases, thus providing a more reliable picture of which abilities were affected in this disorder.

Patient 1 (deceased 20 October, 1976). This patient was first seen by the Neurology service at University Hospital when he was 46 years old. He was diagnosed as having Parkinson's disease and was started on L-Dopa therapy.

He was first assessed by the neuropsychology service at age 47, on 5 December, 1975, about 9 months prior to his death. His intelligence at this time, measured by the Wechsler Adult Intelligence Scale, was in the average range, with no significant discrepancy between the Verbal IQ (97), measuring verbal skills, and the Performance IQ (91) measuring nonverbal skills. Memory function, as measured by the Wechsler Memory Scale (Form I), was above average, and all subtests were at least average. Tests of attention span (described below) were also satisfactorily performed at this time. In fact, the only significant deficit on this occasion was a difficulty with the Wisconsin Card Sorting Test, on which the patient achieved zero categories (maximum = 6). He sorted all 128 cards according to matching forms, and thus received a perseverative error score of 95. This is remarkably poor performance in a person otherwise so intellectually intact.

The second (and last complete) assessment took place on 16 July, 1976, three months before death (see Table 1). By this time the Parkinson signs had accentuated, as had the shortness of breath and erratic breathing. He was nevertheless still co-operative and testable.

At this second assessment, the Full Scale IQ of 99 (tested by the alternate form of the WAIS, the Wechsler-Bellevue Scale, Form II) was still in the Average range. The Verbal IQ was 93, and the Perfor-
of previously presented words, as measured by the score on a Recur­
ning Words task, was also affected in this patient.

The consistent findings in both cases are 1) impaired perfor­
ance on tests of serial attention span (Modified Knox Cubes, Digit Span) and 2) highly perseverative behaviour on the card
sortig task.

Summary of Neuropathological and Biochemical Findings

These were reported in detail in the original paper, and will therefore be reviewed only briefly.

Post-mortem examination of the brains in both cases revealed a severe neuronal loss in the substantia nigra and the head of the caudate nucleus, with milder loss in the globus pallidus. The brainstem showed gliosis of the motor nucleus of X, n. tractus solitarius and adjacent reticular formation, with lesser gliosis in n. ambiguus. The cortex and cerebellum showed no abnormalities. Thus, there were extensive changes in the corpus striatum and in the medulla, but minimal changes elsewhere.

Biochemical assays revealed no deficiency in GABA, some deficiency of glutamic acid decarboxylase relative to normal, but not relative to other Parkinson patients. There were extremely low levels of tyrosine hydroxylase in all areas of the brain, but particularly in the caudate, putamen and substantia nigra. Patient 1 was on L-dopa medication at the time of death, but dopamine levels were nevertheless subnormal in both brothers, and in Patient 2 was low even relative to other Parkinson patients. Thus, there was clear evidence of degeneration of the nigrostriatal dopaminergic systems. No assays for norepinephrine were done.

**DISCUSSION**

The most salient findings in both cases were the presence of perseverative responding on a sorting task, and the presence of an attention-span deficit. Perseverative tendencies have been previously reported on category tasks in patients with Parkinson’s disease, with one exception. Perseverations have generally been attributed to associated pathology, in such patients, of the caudate nucleus or the frontal lobes. Since there is no report of neuronal loss in the frontal lobes in our two cases, direct frontal pathology may not be a prerequisite for the perseverative responding which Sandson & Albert call “stuck-in-set perseveration”.

The two patients presented here were even more perseverative (100% and 85% perseverative errors) than our other Parkinson patients who had been given the card sorting task (N = 8, mean perseverative errors — 45.4/60.5 errors or 75.6%). They are also more perseverative than our comparably-aged patients with frontal damage (n = 16, mean perseverative errors — 33.7/47.7 errors or 71%).

Our data would be compatible with suggestions that caudate damage itself may mimic the effects of frontal-lobe damage,
through frontal-caudate connections, but since striatal damage was extensive in our two patients, the evidence for specific caudate involvement is not strong. Moreover, in reviewing four of our cases with Huntington’s chorea and with CT scan evidence of caudate atrophy, who had been administered the card sorting task, performance was characterized by perseveration in only one case of the four. The perseverative behaviour previously reported in Parkinson cases may therefore be attributable to damage to other parts of the basal ganglia.

It is difficult to evaluate the effects of the periodic apnea. The original report on these patients stated that no anoxic changes were seen in the brains. Lasting hypoxia is reported to result in disorders of learning and memory, yet the two cases reported here have Memory Quotients comparable to their intelligence level. Delayed recall of material from the Wechsler Memory Scale, which is even more sensitive to memory disorders than the initial recall, is not consistently impaired either.

The other major finding of interest was that the serial attention span was impaired in both patients, and this was true for both verbal and nonverbal material. Thus, digit span was considerably lower than would be expected at this age level, and repetition of the cubes sequence was poor. This is despite normal memory function in one case, and only moderate disturbance in the other. The presence of deficits in immediate attention span in the absence of other memory difficulties has been previously documented in patients with idiopathic epilepsy. In contrast, patients with severe global amnesia often have intact immediate span. Patient 1 in fact showed some spike-wave activity on the electroencephalogram, similar to that seen in idiopathic epilepsy, but Patient 2 had merely a generalized dysrhythmia. It seems unlikely, therefore, that the attentional deficit is directly attributable to subclinical episodes of the “absence” variety. Impairment of serial attention span has been attributed to dysfunction of upper brain stem or other non-specific neural systems presumptively involved in “attention”, the latter is usually assessed by the immediate store of serially-ordered material.

The impairment of serial span in the present two cases is paralleled by a deficit in other patients we have seen with Parkinson’s disease and in Huntington’s chorea. It is therefore possible that the serial attention span deficit is related to neuronal loss in either the basal ganglia or the brainstem. It has been suggested that another aspect of attending, akin to vigilance, may be dependent on norpinephrine systems, and is consequently reduced in patients with Parkinson’s disease. Unfortunately, we have no information about norpinephrine levels in the brains of our two subjects.

The significant contribution of these two cases lies in the fact that the cortex appeared to be spared, while basal ganglia and other subcortical structures were extensively affected. They provide strong support for a subcortical contribution to serial attention span mechanisms, and cast doubt on suggestions that primary frontal-lobe pathology is a necessary prerequisite for perseverative responding.