Pharmacotherapy for Akinesia Following Anterior Communicating Artery Aneurysm Hemorrhage

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The dopamine system may be involved in three situations: the nigral projection to the basal ganglia, the mesocortical projection to the anterior cingulate gyrus, or the medial forebrain bundle projection to cortical and limbic sites. Because of the close association of dopamine systems with the known neurological syndromes of akinesia, we elected to treat a patient with akinesia due to rupture of anterior communicating artery (ACA) aneurysm with the dopamine agonist, bromocriptine. This case has important implications for the understanding of brain/behavior relationships as well as for the development of new therapies for patients who have sustained neurological injury.

Key words: Dopamine agonist, Bromocriptine, Head injury

Dopamine is a neurotransmitter that has long been known to affect motor system function through the nigrostriatal pathway (1). Dopamine also influences other neurological systems. Through its effect on limbic system function, for example, dopamine has been implicated in the expression of psychotic (2) and affective (3) symptoms. Albert et al (4) and Bachman and Morgan (5) recently suggested that damage to mesocortical dopamine systems may be responsible for certain features of aphasia and have demonstrated that the dopamine agonist, bromocriptine, may effectively alleviate selected aphasic symptoms.

Akinesia may occur as the result of lesions of the basal ganglia or nigrostriatal system, as in Parkinson's disease, lesions of the anterior cingulate region (6, 7), pressure on the walls of the third ventricle secondary to tumor (8), or lesions of the midbrain/diencephalic junction (9). The dopamine system may be involved in all three situations: the nigral projection to the basal ganglia, the mesocortical projection to the anterior cingulate gyrus, or the medial forebrain bundle projection to cortical and limbic sites. Because of the close association of dopamine systems with the known neurological syndromes of akinesia, we elected to treat a patient with akinesia due to rupture of an anterior communicating artery (ACA) aneurysm with the dopamine agonist, bromocriptine.

REPORT OF A CASE

The patient was a 48-year-old, right handed, veteran who presented with acute onset of a severe headache. A CT scan was consistent with subarachnoid hemorrhage. He developed acute hydrocephalus requiring bilateral ventriculostomies 10 days later. Approximately 4 wk later, he underwent clipping of an ACA aneurysm via a right frontotemporal craniotomy. Immediately following surgery, he was extremely abulic. He was transferred to the Boston VA Medical Center 3 months after surgery for further care.

At the time of admission he would sit motionless in his chair for hours. There was virtually no facial expression. Fluctuations in arousal were prominent. There was mild rigidity throughout but no tremor,
cogwheeling, or weakness. Deep tendon reflexes were brisk, but there was no clonus, and Babinski reflexes were absent. He would only stand or walk when coaxed and assisted. He tended to shuffle and, because he seemed to walk on his toes, also was unsteady.

He was unable to cooperate with testing for more than 15 to 20 min and even then required frequent prompts and cues. Response style was notable for long latencies with minimal responses. In addition, he frequently had difficulty in initiative responses. He had no appreciation of his situation and at times confabulated that he was at work. Distractability, pull to stimulus, and perseveration characterized all task performances. Utterances were grammatical but monotonous and laconic. There was no evidence of impaired confrontational naming or auditory comprehension. Visuospatial function was intact for copying except for pull to stimulus and perseveration. He could carry out 1 and 2 step commands but refused to perform more complex commands.

A trial of bromocriptine was instituted. Bromocriptine was begun at a dose of 2.5 mg a day and was gradually adjusted upwards to a total daily dose of 15 mg a day over 10 days. No significant side effects were encountered. During treatment there was a marked change in the patient’s overall behavior. He now frequently initiated conversation and would develop a lengthy reply in response to questions. Movements were quicker and a more normal facial affect was apparent. On the Boston Naming Test (10) there was a slight improvement in the overall score with a significant decrease in perseverations and response latencies. Unfortunately, he remained extremely amnestic and inattentive. Spontaneous initiation of confusional behavior on the ward became disruptive. When the bromocriptine was gradually discontinued, his initiation of movement and speech was slightly worse but disruptive behaviors continued for a number of weeks afterwards. These behaviors also gradually abated.

**DISCUSSION**

The absence of tremor, cogwheel rigidity, or characteristic posture makes the diagnosis of parkinsonism unlikely in this patient. His clinical response to treatment with bromocriptine was characterized by significant improvement in akinesia (both cognitive and motor) as well as arousal. Other clinicians also have reported clinical improvement in patients with non-parkinsonian akinesia treated with agents that enhance dopamine system function. Ross and Stewart (11) reported the case of a 36-year-old man with akinesia due to an anterior hypothalamic tumor who responded to treatment with bromocriptine but not to carbidopa/L-dopa or methylphenidate. As reported above, Albert et al (4) and Bachman and Morgan (5) have shown that symptoms of impaired speech initiation and hesitations, typical of transcortical motor aphasia, may respond to treatment with bromocriptine. Other clinicians have described patients with akinesia and/or hypoarousal due to structural neurological lesions who improved after treatment with methylphenidate, dextroamphetamine, dopamine agonists, or dopamine precursors (12–14). These clinical observations suggest that dopamine may play a role in activation of aspects of cognition and behavior aside from dopamine’s well established role in motor function. The cognitive and affective aspects of dopamine function may be mediated by the dopaminergic mesocortical and mesolimbic systems, respectively (3).

This single case report, although not validated by a double-blind assessment or a placebo control, suggests that dopamine agonist therapy may alleviate some of the motoric and behavioral features associated with an anterior, medial frontal lesion. The ACA aneurysm hemorrhage may have interrupted ascending mesocortical dopamine projections destined for mesofrontal cortex and anterior cingulate gyrus. This hypothesis is consistent with this patient’s follow-up CT scan which showed bilateral, symmetrical focal frontal lobe encephalomalacia. The fact that this patient responded to pharmacotherapy at all implies that the postsynaptic receptors within these target areas must have been relatively spared. If true, this would suggest that some focal lesions may exert their clinical effect by interrupting broadly organized neurotransmitter systems at critical loci. This finding has important implications for the understanding of brain/behavior relationships as well as for the development of new therapies for patients who have sustained neurological injury.
REFERENCES