

A new approach to Parkinson's disease combining caffeine, methylphenidate, and anticholinergic agents: case histories, pharmacological data, and a conceptual framework from traditional Chinese medicine

To the Editor—Sedation is a common side-effect of drugs used to treat Parkinson's disease, especially anticholinergic and dopaminergic drugs. Caffeine and methylphenidate may alleviate this sedation and improve the treatment of Parkinson's disease.

Two case histories provided the initial basis for this idea. The first patient was a healthy adult who occasionally needed diphenhydramine for allergies but would consequently be lethargic and ataxic for several hours thereafter. On one occasion, he took diphenhydramine with two cups of coffee and was able to function normally that day, with no lethargy or ataxia. The second was an elderly man with Parkinson's disease and severe depression. He was chronically somnolent after each dose of levodopa/carbidopa, and was prescribed methylphenidate for depression. His somnolence markedly improved over a 2-month period when I saw him in a geriatric clinic. Pharmacological studies have shown that caffeine and methylphenidate can increase mental acuity, in direct opposition to anticholinergic drugs such as diphenhydramine. Subjects given 200 mg of caffeine and 25 mg of diphenhydramine on different days demonstrated improved performance on a visual vigilance task with caffeine and worse with diphenhydramine.¹ Auditory-evoked cortical potentials were recorded during performance of the visual task. Caffeine lowered amplitudes of the evoked cortical potentials, and diphenhydramine increased amplitudes.¹ Caffeine suppressed an auditory distraction and diphenhydramine made subjects more susceptible. A comparable effect could be shown with methylphenidate and diphenhydramine.² Pharmacological studies also suggest that caffeine and methylphenidate show promise as anti-Parkinsonian agents in and of themselves. A positron emission tomographic scan study has demonstrated that caffeine stimulates D2 dopamine receptors and potentiates the release of dopamine.³ Methylphenidate has been shown to raise dopamine levels in the basal ganglia by inhibiting dopamine transporter reuptake.⁴ Consistent with these mechanisms, caffeine potentiates the anticholinergic agent trihexyphenidyl in reversing haloperidol-induced catalepsy in rats.⁵ Methylphenidate improved speed of finger tapping and initiation of activity when given to a group of Parkinsonian patients.⁶

I suggest that a combination of caffeine, methyl-

phenidate, and an anticholinergic agent may have therapeutic benefits in early Parkinson's disease and may delay the need for more expensive drugs, especially if such benefits can be augmented by other approaches. By this, I am referring to the use of traditional Chinese medicine that has proven efficacy for Parkinson's disease and provides a conceptual model of deficiency in Ben (root) and excess in Biao (branch).⁷ Could one think of caffeine, methylphenidate, and an anticholinergic agent as restoring the balance of Ben and Biao? Do Chinese herbal preparations used for Parkinson's disease already have anticholinergic, dopaminergic, or methylxanthine (caffeine-like) activity? Would acupuncture enhance the effects of caffeine, methylphenidate, and anticholinergic agents? Clinical trials and further investigation might be particularly productive in China. I hope these ideas will stimulate research and new treatments for patients with Parkinson's disease.

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