Medical Xpress

Expectations may affect placebo response in patients with Parkinson's disease

August 2 2010

Individuals with Parkinson's disease were more likely to have a neurochemical response to a placebo medication if they were told they had higher odds of receiving an active drug, according to a report in the August issue of *Archives of General Psychiatry*.

"The promise of symptom improvement that is elicited by a placebo is a powerful modulator of brain neurochemistry," the authors write as background information in the article. "Understanding the factors that modify the strength of the placebo effect is of major clinical as well as fundamental scientific significance." In patients with Parkinson's disease, the expectation of symptom improvement is associated with the release of the neurotransmitter dopamine, and the manipulation of this expectation has been shown to affect the motor performance of patients with the condition.

Sarah C. Lidstone, Ph.D., of Pacific Parkinson's Research Centre at Vancouver Coastal Health and the University of British Columbia, Vancouver, Canada, and colleagues studied 35 patients with mild to moderate Parkinson's disease undergoing treatment with the medication levodopa. On the first day of the study, a baseline positron emission tomographic (PET) scan was performed, participants were given levodopa and a second scan was performed one hour later to assess dopamine response. On the second day, patients were randomly assigned to one of four groups, during which they were told they had either a 25-percent, 50-percent, 75-percent or 100-percent chance of receiving active medication before the third scan; however, all patients were given

placebo.

Patients who were told they had a 75-percent chance of receiving active medication demonstrated a significant release of dopamine in response to the placebo, whereas those in the other groups did not.

Patients' reactions to the active medication before the first scan was also correlated with their response to placebo. "Importantly, whereas prior medication experience (i.e., the dopaminergic response to levodopa) was the major determinant of dopamine release in the dorsal striatum, expectation of clinical improvement (i.e., the probability determined by group allocation) was additionally required to drive dopamine release in the ventral striatum," the authors write. Both areas have been shown to be involved with reward processing; in patients with a chronic debilitating illness who have responded to therapy in the past, expectation of therapeutic benefit in response to placebo has been likened to the expectation of receiving a reward.

"Our findings may have important implications for the design of clinical trials, as we have shown that both the probability of receiving active treatment—which varies in clinical trials depending on the study design and the information provided to the patient—as well as the treatment history of the patient influence dopamine system activity and consequently clinical outcome," the authors conclude. "While our finding of a biochemical placebo response restricted to a 75 percent likelihood of receiving active treatment may not generalize to diseases other than Parkinson's disease, it is extremely likely that both probability and prior experience have similarly profound effects in those conditions."

More information: Arch Gen Psychiatry. 2010;67[8]:957-865.

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Provided by JAMA and Archives Journals

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