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Therapy found for Parkinson's disease dyskinesia

Researchers may have found a way to treat the disabling dyskinesia frequently induced by treatment of Parkinson's disease with levodopa. Working in a monkey model of the disease, Erwan Bézard (Université Victor Segalen, Bordeaux, France) and colleagues report that levodopa-induced dyskinesia can be greatly attenuated by treatment with a partial dopamine D₃ receptor agonist.

In Parkinson's disease, which is caused by a lack of the neurotransmitter dopamine, replacement therapy with levodopa initially improves motor symptoms. However, many patients develop dyskinesia after extended treatment and the uncontrolled and random movements of severe dyskinesia, says Bézard, "can be more socially disruptive than the Parkinson's disease itself".

Little can be done at present to reduce dyskinesia, says Peter Jenner (King's College, London, UK). "For example, reducing the dose of levodopa provoking the movements can reduce their intensity but usually at the expense of antiparkinsonian activity and amantidine can suppress dyskinesia in some patients." But, says Bézard, this latter drug can cause side-effects such as psychosis. Bézard and colleagues

turned to an animal model of Parkinson's disease to look for other treatments for dyskinesia. They report that dopamine D₃ receptor expression is decreased in monkeys treated with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, a compound that induces parkinsonism. However, in those monkeys that developed dyskinesia after extended levodopa treatment, D₃ receptor expression increased.

The researchers postulated that, if the fluctuations in the function of this receptor could be limited, levodopa-induced dyskinesias could be attenuated without losing levodopa's beneficial effects.

To test this idea, the researchers treated their monkeys with BP 897, a partial D₃ receptor agonist. BP 897, explains Bézard, "slightly promotes the action of levodopa when there is a small amount of the drug in the system but acts as an antagonist when there is too much levodopa as in dyskinesia". As hoped, the partial agonist normalised D₃ receptor function and thus attenuated the side-effects of levodopa treatment (*Nat Med*; published online May 12; DOI 10.1038/nm875).

"Although I would like to see more data on different drug doses, the implications of this study are that in patients who have developed dyskinesia as a result of levodopa treatment, a D₃ receptor partial agonist at the right dose should decrease involuntary movement while having no adverse effect on the beneficial actions of levodopa", comments Jenner. But, he warns, "whether this can be achieved in practice is a different story".

A phase 2A clinical trial already initiated in France should start to address this reservation.

Jane Bradbury

Coronavirus confirmed as cause of SARS

An international team of researchers has completed the final proofs that severe acute respiratory syndrome (SARS) is caused by the primary suspect—SARS-associated coronavirus (SCV). Health officials hope that the confirmation will make the task of containing the epidemic more manageable.

Tests done over the past 2 months have shown that SARS-associated coronavirus fulfils three of Koch's six postulates that must be satisfied to establish a virus as the cause of a disease: isolation from the host, cultivation in host cells, and filterability.

New research has shown that the virus fulfills the three remaining criteria: production of similar disease in the host species or a closely related species—in this case macaques; reisolation of the virus from infected test individuals; and detection of an immune response to infection with the virus (*Nature* 2003; 423: 240).

Lead researcher Albert Osterhaus (Erasmus Medical Centre, Rotterdam, Netherlands) said that the confirmation of the role of the virus was a tremendous collaborative effort. "Confirmation of the causative role of SCV in the macaque experiment came within 3 weeks after the virus had first been found and implicated as the possible cause of SARS", he said. "This rapid turnaround was made possible by the exemplary coordination of all the scientific efforts through the WHO network of laboratories involved."

Trish Perl (Johns Hopkins School of Medicine, Baltimore, MD, USA) compared the speed with which SCV was confirmed as the cause of SARS to the time it took to confirm HIV as the cause of AIDS—nearly 2 years in the latter case. "The rapidity of discovery, identification and fulfillment of

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Koch's [postulates] is astonishing", said Perl.

The confirmation of SCV's role in SARS will have a substantial effect on efforts to control the disease, said Alison Galvani (University of California, Berkeley, CA, USA). "The identification and genetic sequencing of the causative agent of SARS does have implications for the control of this disease both in the short term and in the long term", she said. "The PCR assay can be used as a diagnostic test to identify people who are incubating the disease but are not yet symptomatic. This will enable us to develop much more efficient quarantine procedures of only the people who have been infected, rather than everyone who may have been exposed."

David Lawrence