

IS CONTINUOUS DOPAMINERGIC STIMULATION A CONCEPT OF RELEVANCE TO PARKINSON'S DISEASE: NO

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Based on studies in monkeys, continuous dopaminergic stimulation is a rather intriguing concept. The idea is to mimic normal dopaminergic stimulation in the brain which acts receptors irrespective of sedentary state or physical activity five times per second. Thus, the hypothesis has been established that tonic stimulation is physiologic.

Surprisingly, a closer look into the literature shows that we do not know exactly whether dopamine receptors are really stimulated continuously. It is more likely that there are boosts in situations when fast movements are performed or when a person gets up from sitting or even walks or runs. In addition, even short acting dopamine agonists such as lisuride and apomorphine prevent the development of dyskinesias in patients, and so far there is no convincing evidence that the verysuperlong plasma half lives of cabergoline, rotigotine or ropinirole extended release prevents dyskinesias more effectively than shorter acting drugs. It may just be too simple to assume that dopamine agonists with a long plasma half-life are continuously absorbed and transported to the brain where they have to pass the blood-brain barrier and finally stimulate dopamine receptors continuously. This goal may not be achieved in all cases. In addition, half-lives represent only one distinguishing factor between dopamine agonists and levo-Dopa. It might well be the case that the different stimulation is a prerequisite for less dyskinesia. Dopamine agonists normally do not stimulate D1 receptors to the same degree as levo-Dopa. In animals the short acting drug apomorphine caused less dyskinesia than the longer acting levo-Dopa. It is also interesting that the addition of a dopamine agonist to levo-Dopa, which should lead to a more continuous stimulation, often induces hyperkinesia. To solve the problem robust randomized clinical trials are required.