

Appendix 7 (as supplied by the authors): Emerging therapies in Parkinson disease

Intranasal Levodopa

Because of its low bioavailability (30%) when levodopa is taken orally¹, there is a growing interest in other modes of levodopa delivery. Intranasal delivery of levodopa via nanoparticles has the advantage to bypass the peripheral metabolism and the blood-brain barrier, and is easy to administer. The drug delivery to brain is through the olfactory and trigeminal nerve pathway.² Animal studies have shown convincing results but it is still in the experimental phase.^{1,2}

Botulinum toxin for tremor

Injection of botulinum toxin has been shown to reduce tremor severity and improvement in functional rating scores.^{3,4} This treatment has not yet been widely adopted because visual assessment of upper limb tremor is restricted by the difficulty to separate multi-joint movements.⁵⁻⁷ Our group has shown that kinematically-guided muscle selection for upper limb tremor injection of incobotulinumtoxinA results in significant reduction in severity of tremor.^{6,8} We are currently completing a larger open-label study of PD patients treated with incobotulinumA toxin for tremor using kinematic guidance.

Transcranial magnetic stimulation

Repetitive transcranial magnetic stimulation (rTMS), placed on the scalp over the primary motor cortex, has shown promising results in short-term (1 day) and long-term (1 month) motor improvement in PD patients, but further studies are required to confirm efficacy prior to routine clinical use.⁹

Nilotinib

In an open-label phase 1 study of 12 patients with synucleinopathies studied over 6 months, the chemotherapeutic drug, nilotinib, a tyrosine kinase inhibitor used in chronic myelogenous leukemia, led to statistically significant reductions in cerebrospinal fluid levels of alpha-synuclein, and reported cognitive and motor improvements in 11 of 12 patients. We advise caution in interpreting these results, as this was a nonblinded study in few carefully selected patients for which we do not have all the details. A double-blind, placebo-controlled phase 2 clinical trial is planned for 2016. (Society for Neuroscience (SfN) 2015 Annual Meeting. Abstract 12.01)

Others

Few promising drugs undergoing clinical trials for neuroprotection in PD¹⁰ include inosine¹¹, deferiprone¹², isradepine¹³, transdermal nicotine patch (clinicaltrials.gov/ct2/show/NCT01560754), and alpha-synuclein immunotherapy (clinicaltrials.gov/ct2/show/NCT02157714).¹⁴ Trials involving spinal cord stimulation for postural instability and gait dysfunction in PD are currently underway (clinicaltrials.gov/ct2/show/NCT02539784 and clinicaltrials.gov/ct2/show/NCT02388204). Other alternate methods for continuous levodopa delivery are being studied to treat motor fluctuations, including subcutaneous levodopa (clinicaltrials.gov/ct2/show/NCT01883505).

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