The Continuing Saga of GDNF

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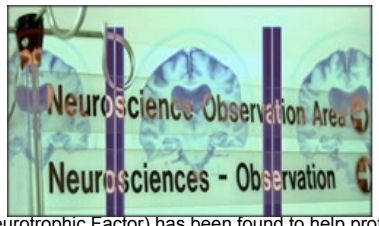

Anatural substance known as GDNF (Glial cell line-Derived Neurotrophic Factor) has been found to help protect and maintain the health of the brain. In May 2003, an article appeared in the prestigious journal Nature Medicine, titled "Direct Brain Infusion of Glial Cell Line-Derived Neurotrophic Factor in Parkinson's Disease," citing a study conducted by groups in Bristol, England and the University of Wisconsin in which five people with Parkinson's disease received GDNF directly into their brains, slowly and continuously through a thin tube.A lead author of the study, Dr. Clive Svendsen, recently discussed his findings at Eisenhower's Phillip and Carol Traub Parkinson's Center.

According to Dr. Svendsen, the subjects receiving GDNF experienced improvement in many areas: mobility increased and "off " times decreased; dyskinesia (uncontrolled movements) was reduced; non-motor symptoms such as sense of smell and libido improved; and PET scans showed increased dopamine activity, suggesting GDNF caused brain cells to sprout and make new replacement connections.

Based on these encouraging results, Amgen®, the company that provided GDNF, organized a 48-person trial conducted in a double-blind, placebocontrolled fashion. To the surprise and dismay of all involved, the participants who received the GDNF did not exhibit any greater benefit than those who received the placebo.

Possible reasons for this discrepancy include dosage and delivery differentiations between the Amgen trial and the England/Wisconsin study. It is also possible that the England/ Wisconsin subjects were simply demonstrating a placebo effect, which is known to have a substantial impact in clinical trials, particularly in Parkinson's disease. The placebo effect may be created by dopamine changes in the brain…when people expect to improve, dopamine levels may raise temporarily. An argument against the placebo effect in the England/ Wisconsin trial is that the benefit has been sustained for a two-year period; whereas, improvement from a placebo will typically wane after a few months.

Svendsen and colleagues published follow-up data in February 2005, again showing substantial improvement in the five subjects, with one person able to completely discontinue levodopa. A second group led by Donald Gash at the University of Kentucky found results similar to Svendsen.

Findings of the England/Wisconsin collaboration and Kentucky study suggest GDNF may become an innovative method of therapy for Parkinson's disease. However, Amgen has indicated GDNF produced brain damage in two monkeys and antibodies in the blood.The cerebellum damage has not been observed by researchers, and the significance of the antibodies, if any, is unclear. Based upon their human trial of GDNF and the monkey study data, Amgen has decided not to proceed with further human testing. Amgen holds the worldwide rights to GDNF.

The ongoing saga of GDNF is far from over, however. It may be possible to deliver GDNF, or a similar substance, in a safer manner than placing a tube permanently into the brain. One proposal is to program stem cells to manufacture GDNF, plant them into the brain, and then switch them on/off by taking a pill. The technology exists, and plans are underway.

EVENTS Call 760-773-1480 for information and reservations. Nutritional Counseling for Parkinsonians By appointment Sarah Gaete, Registered Dietician 1-hour consultation $65; follow up $45 PD in Motion T TH, 9 to 10 a.m. Lisa Manning, CET Cost is $40 per month