

Treatment and Causes of Parkinson's Disease

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Abstract

Parkinson's is a common neurological disease most commonly found in adults and the elderly whose symptoms include loss of motor control. For many years scientists have researched cellular replacement to alleviate the symptoms of this disorder. Though there are various methods of cell transplants, including the use of stem cells and alternative dopamine-producing cells, many raise either ethical issues or health concerns. Causes of the disease have also been a major area of research- scientists have emphasized on an apparent abundance of α -synuclein, a protein that blocks neuron chemical signaling when accumulated, in brain tissue.

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In 1817 James Parkinson published the first description of Parkinson's disease, although the symptoms of this condition have been known far back into history. Characteristics of Parkinson's are described as uncontrollable shaking and loss of motor control that progress until the patient is completely paralyzed. Diagnosis normally begins after the age of 50, and reported cases increase as the age of the population increases. The disease is now known as a neurological condition that is suspected to be a genetic trait, though there are many apparent causes. Research has shown that most of the symptoms are apparent when nerve cells in the substantia nigra, cells that produce chemical signaler dopamine, are damaged or die. Recent research in terms of treatment and causes center around two ideas: cell replacement and the negative effects of α -synuclein protein.

The idea of transplanting brain cells from fetal cadavers has been practiced experimentally using primarily rodents for the past 20 years. Implanting working brain tissue into a subject with Parkinson's disease compensates for the insufficient dopamine concentrations in the brain. However, rodent brains differ greatly in terms of biochemistry, size, organization, and other factors compared to human brains. Redmond (2002) stresses the need for more research on procedural effects on primates, as "direct assessments of cell morphology ... and regional biochemistry can rarely be performed on humans" (p. 460). Primate's brains are significantly more similar to human brains in terms of complexity to those of rodents.

In terms of research on human subjects, more questions than solutions have been found. According to Redmond (2002), Millar, and Federoff (2005), though transplant procedures are reasonably safe and demonstrate functional effects, outcomes are highly

variable (p. 472). Studies show that the younger the recipient is the more beneficial the transplants- increased age results in decreased cerebral flow and oxygen consumption, which lessens the effects. While the effects of aging are difficult to compensate for, other problems have suggested solutions that require more research.

A common problem with transplanting brain tissue is the survival rate of the transplanted tissue. Most of the cells die within the first few days due to many reasons, such as trauma, disruption of position, and loss of cell-to-cell contact, which stimulate cell apoptosis- a natural death of the cell. Transplanting larger quantities of cells did not lead to an increased rate of survival as hoped, but a wide-spread distribution was found to be highly beneficial to dopamine concentration. Tenascin, an antibody, was found to compensate for the cell-to-cell contact that is lost during transplant procedure and increase survivability.

Other than solving problems due to early death of implanted brain cells, a source for alternative replacement cells is being investigated. Fetal cells bring up political and ethical controversy that suspends research. Genetically modified cells as well as animal cells have been suggested, but that brings the potential for new problems with biosafety. Redmond (2002) writes that other dopamine-producing cells from the carotid body, bone marrow, tumor cells, and adult stem cells may avoid stimulating apoptotic signals (p. 479). However, those cells may have reduced plasticity or the same genetic defects that the patient is trying to alleviate. Olanow (2005) writes that ideally stem cells could be induced to become dopamine producing cells and integrated with non-dopamine producing cells, however survival rates of those cells are small and “complications such as tumor formation” are problematic (p. 617).

Chan and Meier (2002) state that “recent studies have implicated mitochondrial dysfunction and oxidative stress in the pathogenesis of various neurodegenerative diseases as well as in the aging process” (p. 325). Oxidative stress is a result of the many reduction-oxidation reactions throughout the brain. Iron (II) ions, which are common reactants of these reactions, are suspected facilitators of Parkinson symptoms. Iron is the most abundant metal in the body, particularly in the brain and the liver where it partakes in many important reactions. However, Wolozin and Golts (2002) state that in the brain iron (II) ions are found to promote the aggregation of α -synuclein proteins, which are found in structures in neurons known as Lewy bodies (Baptista, Cooker, & Miller, 2004, p. 63). While it is normal for metals such as iron to catalyze reactions and bond to amino acids, patients with Parkinson’s have elevated levels of iron. This protein aggregation is toxic to cells and results in “loss of cellular activity as well as inhibition of organelle function” (p. 22). The further accumulation of the damaged proteins further damages brain cell tissue. Whether iron induces this accumulation of α -synuclein or α -synuclein attracts free iron atoms is not yet known (p. 27). However, Wolozin and Golts (2002) believe that pharmacists are able to inhibit α -synuclein gene expression, decreasing the accumulation of this damaged protein (p. 30).

Alpha-synuclein is also believed to have a detrimental effect on mitochondrial function (Baptista, Cookson, & Miller, 2004, p. 69) as it inhibits the pathways of the organelle. According to Betarbet and his colleagues, neurons rely on mitochondrial respiration to produce ATP, the cell’s chemical energy source, which is important for cellular homeostasis. The reduced quantities of ATP result in depolarization of the mitochondria, which inhibits chemical and energy production of the cell, killing the cell.

Impairment of the vital pathways also leads to abnormal cellular receptors, disrupting neuron signaling. Patients with Parkinson's express reduced mitochondria activity in brain tissue, which further links the disease with defects in the mitochondria as well as α -synuclein (p. 193-194).

The treatments and causes of Parkinson's disease have continuously been researched for the past 100 years. In combination of recent technology with discoveries, cellular transplants and examination of mitochondria pathway inhibition have been possible and are practiced today. As research continues, this neurological disease will continue to be studied and knowledge about it will expand, resulting in an increase in the understanding of what treatments are the most beneficial to the patients.

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