

**Case Report**

# Biological Basis for a Relationship between Parkinson's Disease and Essential Tremor Elderly Identical Twins: One with PD and the Other with ET

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## Abstract

**Background/Objectives:** The two major "diseases of tremor" are Parkinson's Disease (PD) and Essential Tremor (ET). There is disagreement as to any linkage of these two entities. This report focuses on "elderly identical twins" wherein one twin manifests PD and the other one manifests ET.

**Design:** Blood samples from each twin were studied in our medical school's genetics laboratory. Pleasingly the genetic identity of the sisters was 99.9%.

**Setting:** One twin resided for many years at a teaching nursing home because of her disabling PD. The other twin lived independently in an apartment a few moments from the nursing home and visited her sister daily. Ultimately, the healthier twin, for convenience, also moved within a room at the teaching nursing home.

**Participants:** These identical twins were born in England. Their migration to America brought them to New York City and ultimately to the more disabled twin came under our care at our "teaching nursing home." Intervention: The ill twin was under the continual care of an associate professor of neurology at the Mount Sinai School of Medicine. The healthier community residing twin was evaluated by the "Professor of Medicine/Geriatrics" of our teaching nursing home. Traditional therapy for PD was administered. The twin with PD experienced some deterioration.

**Measurements:** Traditional neurological evaluations were done repeatedly and blood samples from both sisters were analyzed for their genetics.

**Results:** The genetic testing showed 99.9% concordance of the twins. The twin with PD continued to experience neurological deterioration. The healthier twin, after several years in her own apartment near the teaching nursing home, found it necessary to reside permanently at the teaching nursing home. She never demonstrated PD.

**Conclusion:** The simultaneous appearance of PD and ET in genetically proven identical twins strongly suggests a biologic linkage of these two diseases of tremor (PD and ET).

**Keywords:** Parkinson's disease; Essential tremor; Identical twins

## Introduction

Much has been written about Parkinson's disease (PD) and Essential Tremor (ET) and their possible relationship.

The PD tremor diminishes with effort or stops for a brief while once an action is initiated. This pause was long enough to have allowed the late Mohammed Ali, with his advanced Parkinson's, to ignite the Olympic torch inaugurating the 1996 Olympics in Atlanta, Georgia.

Seeking to combine the two tremor diseases, Louis and Ottman proposed a straight link from ET to PD [1]. Similar to Yahr et al. study [2], we propose a simultaneous beginning to PD and ET *via* the control of both through a single, unified genetic modification as seen in our identical twins, having PD in one and ED in the other.

The usual factors employed to support the non-relationship between them are as follows:

- In ET, the absence at autopsy of increased number of Lewy Bodies.
- Alcohol in small amounts may noticeably reduce an essential tremor but has no such effect upon the tremor of PD.
- Essential tremor may affect the head and voice, but this is usually not the case with PD.
- Non-response by ET patients to medications that do reduce the tremor of PD patients.

- Neuro-imaging abnormalities found in PD are not usually found in ET (Adler, CH Shill. HA Beach, TG).
- The overall prevalence of ET is much greater than that of PD.

Those who do support the relationship of PD and ET usually theorize that ET ultimately results or leads to PD. We present a novel piece of dual clinical history, suggesting a biological relationship between PD and ET with both illnesses apparently starting simultaneously at birth *via* genetic inheritance.

## Methods

To be sure that the sisters were "identical" twins, zygosity testing was performed using the AmpF/STR Identifier Kit from Applied Biosystems. The sisters were identical for all 15 loci examined. The probability that the sisters are monozygotic is >99.99%.

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## Case study: Identical Twins and Potential Links between PD and ET

The manifestation of the clinical entity is obviously profound in PD and minimal in ET. At the time of study at 88 years old, they have experienced these two diseases of tremor (PD and ET) at a simultaneous moment in their lives. The ET twin still has no evidence of PD at the time of this writing.

One sister, is white, single, childless and has advanced Parkinson's disease is bedridden after years of classic PD symptoms. The other sister is ambulatory having lived alone in a Manhattan apartment until the age of 88.

The twin sister with PD is now rigid in all four extremities and shows a severe cognitive impairment whereas her identical twin sister has no cognitive impairment. To our knowledge, this is the first report of identical twins, each manifesting one of the two widely occurring diseases of tremor.

## Results

This dual expression of ET in one twin and PD in the other tends to support the argument that there is a biologic/genetic relationship between PD and ET. Rather than believing in the "coincidence" of the two tremors, we present observations of a single simultaneous genetic defect leading to very different clinical expressions. While one twin possesses a mild cosmetic tremor, the other twin afflicted with PD suffers from an advanced socially impairing tremor and neurodisability necessitating institutional care for most of her adult life.

## Discussion

This duality deserves more study seeking even greater insight into etiology, causality, clinical guidance, prevention and treatment. Though "chance random events" could explain this dual occurrence of ET and PD in identical twin sisters, it is conceivable and likely that a genetic commonality has co-produced these simultaneous diseases of tremor. Thus, we see PD and ET in these identical twins as biologically related neurological disorders.

It is likely that a single genetic abnormality produces these diseases of tremor. Important is the discovery of SNP abnormalities. The genetic abnormality is probably "autosomal," and as in some other diseases, the autosomal abnormality has only partial penetrance in the case of ET patients. We hypothesize a "modifier" gene having some quantitative

effect on the level of expression of this motor disorder. Further genetic studies of these identical twins were not performed.

Presented is an unusual opportunity to consider the PD-ET possible relationship *via* identical twins, whom individually have PD and the classic ET. These twins emphasize the likely genetic nature of both PD and ET. We are stimulated not to embrace the linkage as only occurring in a straight line going from ET toward PD, but rather to consider something more. Further genetic studies are warranted in the hope that the despairing impact of PD could be modified through knowledge as to how the same genetics have produced such benign impact in ET compared to the distressing impact of PD.

This report continues the Geriatrician- author's long-time embrace of the diseases of tremor in older persons [3-9].

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