

Letter to the Editor

Letter to the Editor: Is It Too Early to Underrate Genetics onto PD Pathogenesis? Reflections on History

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Sirs,

The precious contribution by Borgers, Bloem, and Den Heijer [1] aims at reinforcing the perception around the relatively modest influence of genetics onto the pathogenesis of Parkinson's disease (PD) and demonstrates, once more, the relevance of toxic environmental factors. The survey on recent twin studies showed, indeed, that the heritability estimates for PD, with presently available approaches, falls into the lower percentile.

However, I would suggest two main observations in order to insert their valuable notes into a more reliable scenario.

At first, they may suffer a sort of Eurocentric vision (actually, a mistake shared by all of us as western neurologists). Consistent literature emphasized the diagnostic capability of old "ayurvedic" Indian medicine around movement disorders. The paper by Ovallath and Deepa [2] composed an historical overview, with evidence about the clinical suspect of PD raised from centuries BC to late middle age; hence, long time before the eclectic Jamie Parkinson produced his essay. No question on his genial intuition despite the lack of diagnostic tools; but, likely, PD was envisioned well in advance (not mention-

ing Galen or the early description in ancient China). Even the popular Wikipedia states "The history of PD expands from 1817, but features were described since before Christ", and acknowledges the definition of *Kampavata* (sort of trembling in Sanskrit), which in fact recapitulated most PD signs, long before any industrial revolution took place. Of course, this reminiscence might suggest, unfortunately, the potential toxicity of *natural* organic compounds with worldwide distribution [3].

Further, are we confident on the fact that aging is not the core player? Life expectation has been solidly below 40s up to the end of 19th century. Authors claim that the growth of PD persists even after correction of the aging parameter; but the diagnosis itself has profoundly changed in recent decades! In contemporary era, we now capture the subtle PD non-motor spectrum, including gut dysbiosis [4] and utilizes effectively biochemical or electrophysiological biomarkers [5, 6] before any functional severe motor impairment occurs. Hence, if the "rapid growth" of PD is an undisputed reality, it might be attributable, in part, to more sensitive inclusion criteria. This change of paradigm applies to any age, including the so-called early-onset PD, when genetic

predisposition (through still obscure pathways) might be relevant.

In conclusion, I am aware that, from a mere epidemiological point of view, the prevalence of PD has been increased dramatically (one generation ago, we did estimate in 220,000 the Italian PD patients; now, 40% more at least!). Yet, whether this is attributable mostly to old (i.e., cycadaceae or trichloroethylene) or new environmental toxins (such as glyphosate) affecting our mitochondrial energy machine is far from established. Probably, genetic factors still exert some synergistic and seminal role through influencing intracellular cascades, simply not so easy to be catching.

Note: A reply to this Letter to the Editor is available [7].

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