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Clinical and instrumental characterization of GBA-related Parkinson's disease: focus on cardiovascular and sudomotor autonomic dysfunction and other non-motor features. Does the type of mutation matter?

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Background and aims: Some non-motor features (e.g. dementia) present more frequently in glucocerebrosidase-associated Parkinson's disease (GBA-PD). What is the autonomic profile in GBA-PD compared to PD non-carriers (iPD)? Is there any difference between carriers of severe (GBA-SM) *vs.* mild (GBA-MM) mutations?

Methods: Motor and non-motor features, including instrumental evaluation of cardiovascular and sudomotor autonomic functions, were compared between 21 GBA-PD (11 GBA-SM, 10 GBA-MM) and 24 iPD of similar sex, age and disease duration. Autonomic tests were additionally compared those of Dementia with Lewy Bodies (DLB, n=7).

Results: GBA-PD had greater motor complications and worse non-motor symptoms (mainly GBA-SM) than iPD, including orthostatic hypotension, sweat disturbances, pain, and cognitive dysfunction (mainly attentive/executive tasks, verbal memory, visuo-spatial abilities). At cardiovascular autonomic testing: (1) heart rate variability and blood pressure (BP) responses during phase IV of Valsalva Maneuver were lower in GBA-PD; (2) BP response during isometric exercise was selectively impaired in GBA-SM; (3) the pattern of baroreflex dysfunction at tilt test overlapped between GBA-PD and DLB (occurring earlier in DLB) and differed from iPD; (4) GBA-PD had reduced sweat output at the Dynamic Sweat Test. The severity of cardiac denervation in GBA-PD was intermediate between iPD and DLB.

Conclusions: Our data support the notion that GBA-PD is characterized by a more widespread pathology than iPD, with a greater impairment of cardiac parasympathetic system and of cardiac, muscular and sudomotor sympathetic system. Concerning cardiac denervation, GBA-PD places midway in the continuum between iPD and DLB, with GBA-SM (mainly L444P) more similar to DLB.