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Small fiber neuropathy in Parkinson's disease explored by the sudoscan

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ABSTRACT

Small fibers function was evaluated by the electrochemical skin conductance (ESC) in 67 consecutive PD patients and 66 age-matched controls using sudoscan technology. There is no significant reduction in ESC in PD patients compared with controls. We found a weak correlation between feet ESC and modified Hoehn and Yahr Scale.

1. Introduction

The early diagnosis of sudomotor dysfunction in Parkinson's disease patients could be effective to detect small fiber neuropathy [1]. Among the functional tests which evaluate sudomotor function are the assessment of the electrochemical skin conductance (ESC) using sudoscan procedure [2]. To this end, we looked for a possible dysfunction of SFN in PD patients by sudoscan. Sixty-seven (67) outpatients with idiopathic PD were sequentially evaluated between May 2015 and September 2017 at the Victor Pauchet Clinic, Amiens, France. The study participants have mH&Y stages ranging from 1 to 3, an equilibrate sex rate, men/women = 34/33, age ranging from 59 to 88 years (mean 74.13). The Sudoscan device (Impeto Medical, France) undergo the assessment of sudomotor function by the electrochemical sweat conductance (ESC) [2].

2. Standard protocol approvals, registrations, and patient consents

All participants provided their written informed consent prior to the study which was approved by the local Ethical Committee. The quantitative data used to support the findings of this study are included within the supplementary information files (Table 1). Statistical analyses were performed with the open source software "R" (version 3.5.1.). We used analysis in main components (ACP), hierarchical classification main on components (HCMC) and inferential methods.

3. Results

In the group of patients, regression on ESC_F: R^2 of 0.59 is obtained on 100 samples bootstrap. The five variables that can best account for ESC_F are ESC_H, Hoehn and Yahr scale, age_rec and age. The coefficient not parametric rho of Spearman is 0.88 and p-value lower than 2.10^{-16}, thus the relation between observed and predicted values is significant.

Using the test not parametric of Mann-Whitney for ESC-F, U = 2006, p = 0.3557, was noted that the difference between both groups is not significant.

According to the analysis in main components (ACP) of clinical characteristics including age, BMI and skin electroconductances there are no discrimination between patients and controls but there are a clear age gradient, the oldest subjects have lower ESC_F and ESC_H.

Using, the inferential methods the value of ROC never exceeds 0.66 on average on 100 sample bootstrap. ESC_H, gender and ESC_F discriminate at best between patients and controls.

Fig. 1 shows receiver-operator characteristic curve (ROC) of ESC_H and ESC_F which reflect the risk of neuropathy. The area under the curve = 0.661, $p < 0.0001$ indicates a distribution between the patients and controls only slightly different from the distribution at random.

4. Discussion

This study reports the assessment of peripheral neuropathy by sudoscan in PD patients. There is no significant reduction of ESC in PD patients versus age-matched controls. First, the assessment of skin electroconductances looked only at small fibers impairment. Second, the inadequate sensitivity of the sudoscan method even though it was ranked the second as efficacy among five neurophysiological tests [3]. In this study, receiver operating characteristic (ROC) didn't exceed 0.661. Third, the significant decrease of ESC in some controls could be due to glycemic dysfunction, more than half of the patients with diabetic neuropathy is asymptomatic [4]. Recently, published data by Xu and colleagues [5] evaluating 43 hospitalized patients in the later stages of PD found significantly lower skin electroconductances of the limbs in PD patients than in controls. With regards to our findings, most of the subjects are in the moderate stages of the disease with an average Hoehn and Yahr scoring very close to 2 therefore less debilitating than the Chinese cohort. In our case, the multivariate analysis shows a statistical relationship between ESC_F and UPDRS which could underlie the nigrostriatal degeneration process at sudomotor dysfunction. There are phenotypic differences of PD patients with tremor-dominant versus axial dominant phenotype as distinct PD subtypes with different rates of progression. The PD patients with UPDRS score exceeding 30 and severe comorbidities have an increased propensity to SFN.

Conclusion. From this study, there was no strong association between skin electroconductances and functional stages of PD suggestive of a diversified contribution of the different comorbidities. Overall, the findings from this study suggest that SFN involvement is more linked with age, disease severity and vascular co-morbidities.

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Table 1
Demographic and clinical features in Parkinson's disease patients.

Patients	Sex	Age	Disease duration [1–5]	Hand ESC(μS)	Foot ESC (μS)	ESCR (%)	UPDRS	mH&Y	SEADLS (%)	Mean levodopa dose mg/day	DAT-scan putaminal depletion
P1	F	81	2	70	66	48	9	1,5	90	400	B,PR2,PL2,NCR1,NCL1
P2	F	84	2mo	83	76	54	41	3	70	700	ND
P3	F	60	1	73	73	32	21	1,5	80	820	B,PR3,PL1,NCR1,NCL3
P4	F	59	1	75	78	37	6	1	100	200	B,PR2,PL1
P5	F	61	3	76	88	30	10	1	100	200	B,PR3,PL2,NCR2,NCL1
P6	M	79	4	76	90	32	34	3	80	800	ND
P7	M	76	4	64	79	43	14	1	90	500	ND
P8	F	79	21/2	75	89	31	9	1	100	300	ND
P9	M	85	8	65	74	51	22	2	80	1000	ND
P10	M	79	5	65	84	41	12	1	100	150	ND
P11	M	66	2	67	85	34	17	2	80	400	B,PR3,PR2,NCR1,NCL1
P12	M	67	5	54	73	45	13	2	90	300	B,PR4,PL2,NCL3
P13	F	59	9	72	70	22	29	2,5	80	150	B,PR3,PL2
P14	F	75	2	76	87	34	16	1,5	90	300	B,PR3,PL2,NCR2,NCL1
P15	F	82	2	41	66	52	19	2	80	150	B,PL4,PR1
P16	F	75	1	70	81	40	26	3	80	400	ND
P17	M	82	7	78	86	55	8	1	100	900	ND
P18	M	68	1	55	77	51	6	1	100	150	ND
P19	M	73	2	33	56	54	24	3	70	1000	ND
P20	F	83	3	75	77	53	9	1	100	300	ND
P21	M	65	11/2	46	77	47	27	1,5	90	300	B,PR2,PL2
P22	F	74	6	62	83	36	21	1,5	80	300	ND
P23	M	73	1	80	81	38	8	1	100	150	ND
P24	F	65	1	78	89	19	21	1,5	90	500	ND
P25	F	72	6	72	74	54	16	1,5	90	300	B,PR3,PL1,NCR3,NCL1
P26	F	83	5	28	57	54	32	2,5	70	400	ND
P27	M	74	5	75	83	30	5	1	100	200	ND
P28	F	64	5mo	91	86	17	39	3	70	350	ND
P29	M	59	2	63	87	19	14	1,5	90	200	B,PR2,PL2
P30	M	80	5	51	76	47	44	3	70	600	ND
P31	M	71	8	68	85	40	7	1	100	600	ND
P32	F	69	5	77	81	27	11	1	100	300	ND
P33	F	64	5	85	88	17	10	1,5	90	400	ND
P34	F	78	2	53	75	44	6	1	100	150	ND
P35	M	73	3mo	64	78	46	16	1	90	150	B,PR2,PL2,NCL1
P36	F	86	3	41	43	56	20	2,5	70	300	ND
P37	M	69	1/2	60	86	35	12	2	90	300	B,PR4,PL3,NCR3,NCL3
P38	F	76	3	70	75	54	18	2	80	400	B,PR2,PR2,NCR1,NCL1
P39	F	79	6	69	90	48	18	1,5	80	100	ND
P40	M	68	5mo	46	78	39	5	1	100	150	B,PR3,PL1
P41	F	85	1	31	60	58	41	3	70	250	ND
P42	F	88	6	79	72	56	36	3	70	300	ND
P43	F	60	6	69	80	54	38	3	70	1000	B,PR3,PL3NCR1,NCL1
P44	F	77	10	80	79	52	42	3	70	500	ND
P45	F	87	8	57	63	50	39	3	70	300	ND
P46	F	74	8	61	81	34	33	3	80	400	ND
P47	M	73	5	65	86	29	43	3	70	1000	B,PR3,NCR2,NCL2
P48	M	75	1	62	85	37	37	2	80	300	B,PR3,PL3,NCR2,NCL2
P49	F	83	1	46	72	59	36	3	70	300	ND
P50	M	69	3	79	87	43	19	1,5	90	450	B,PR2,PL2,NCR1,NCL1
P51	M	79	4	38	60	41	23	1,5	90	200	B,PR2,PL4,NCR1,NCL1
P52	M	85	6	76	80	45	44	3	70	300	ND
P53	M	69	6	80	82	43	20	2	90	450	ND
P54	F	74	6	62	74	60	19	1,5	80	500	ND
P55	M	86	3	67	87	42	7	1,5	90	150	B,PR3,PL3
P56	M	83	4mo	45	74	56	15	1,5	90	300	ND
P57	F	83	4	78	71	50	12	1,5	90	500	B,PR2,PL2,NCR1,NCL1
P58	F	76	1	74	76	44	29	3	80	500	ND
P59	M	76	2	55	71	50	28	1,5	90	700	B,PR2,PL2
P60	M	60	21/2	66	86	19	13	2	90	300	B,PR2,PL2,NCR1,NCL1
P61	M	77	6	43	79	43	17	1,5	90	500	ND
P62	M	78	61/2	78	78	35	10	1,5	90	300	ND
P63	M	60	3	70	87	19	21	2,5	80	400	B,PR2,PL2
P64	M	82	61/2	69	81	45	42	3	70	700	ND
P65	F	66	71/2	67	84	24	9	1,5	90	400	ND
P66	M	70	11/2	42	77	46	16	2	80	400	B,PR3,PL3,NCR2,NCL2
P67	M	77	21/2	59	79	45	35	3	70	300	B,PR3,PL3,NCR2,NCL2

B = Bilateral dopamine depletion, P = Putamina, BP = putaminal bilateral dopamine depletion, PR = putaminal dopamine depletion predominant at right, PL = putaminal dopamine depletion predominant at left, CH = Caudate heads dopamine depletion, CHR = Caudate heads dopamine depletion predominant at right, CHL = Caudate heads dopamine depletion predominant at left, ND = scan not done. Mo = months. ESC (electrochemical skin conductance), mH&Y (modified Hoehn and Yahr Scale), SEADLS (Schwab and England Activities of Daily Living Scale), ESCR (electroconductance screening, risk of cardiac autonomic neuropathy) given in % by the sudoscan device. The DAT-scan findings were categorized by a semiquantitative scale as follows: 0, normal; 1, mild; 2, moderate; 3, marked; and 4, absent uptake for each of the caudate heads and putamina separately. (ex. B, PL4, PL1, NCL2 = bilateral putaminal dopamine depletion, severe at left, mild at right, caudate heads dopamine depletion moderate at left, normal at right.

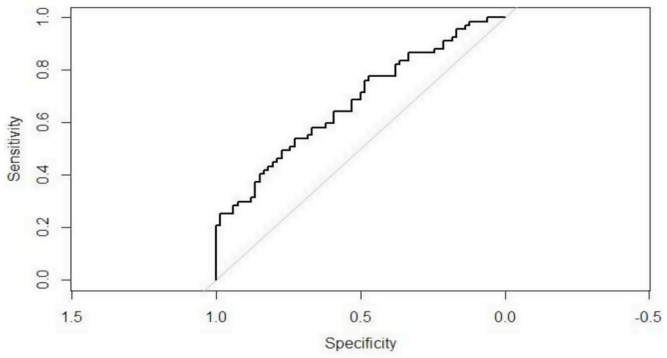

Fig. 1. Risk of neuropathy of ESC_H and ESC_F by receiver-operator characteristic curve (ROC).

Author contributions

The author conceived and designed the study, examined the patients, performed the sudoscan experiments, analyzed the data and wrote the manuscript.

Conflicts of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could represent a potential conflict of interest.

Financial disclosure statement

The author report no disclosure relevant to the manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2019.07.034.

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