PRELIMINARY ANALYSIS OF PERFORMANCE OUTCOMES AND GAIT CHARACTERISTICS OF PATIENTS FROM THE IAXON-BRAZIL HSP NETWORK

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BACKGROUND

Hereditary spastic paraplegia (HSP) comprises a group of neurodegenerative genetic disorders, with more than 87 associated genes already described. These disorders are characterized by axonal degeneration of the corticospinal tracts and dorsal columns in their most distal portions, resulting in spasticity, hypertonia, muscle weakness, and impaired vibratory sensation. Such manifestations lead to a progressive reduction in walking ability, for which no disease-modifying treatments are currently available.

One of the priorities of the IXON-BRAZIL HSP network is to identify sensitive biomarkers capable of detecting subtle changes in patients' movement through performance tests and gait biomechanics analysis, which may serve as reference measures for assessing the effect of future treatments, as well as to characterize the gait pattern of each disease subtype.The aim of this study was to present the preliminary results of performance outcomes and spatiotemporal gait parameters obtained in the first and largest sample of patients with the disease.

METHODS

A cross-sectionalv case-control study

58 patients with molecular or clinical diagnosis of HSP
(13-SPG4, 8-SPG7, 8-SPG76, 2-SPG10, 1-SPG3, 1-SPG5, 1-SPG5A, 1-SPG15, 1-SPG30, 1-SPG31, 1-SPG34, 1 CXT, 19- no clear diagnosis of the subtype)

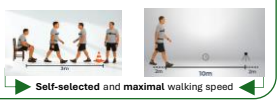
25 participants for control group
From June 2024 to June 2025.

CLINICAL OUTCOME ASSESSMENTS (COA):

Clinician-Reported Outcome (ClinRO)
1. mSPRS modified Spastic Paraplgia Rating Scale.
2. FARS-Staging Diseage Stage

Patient-Reported Outcome (PRO):
1. FARS-ADL Activities of Daily living

Performance Outcome (PerFO):
1. TUG: Timed Up and Go
2. 10MWT Ten-meter Walking Test



Self-selected and **maximal** walking speed

DIGITAL HEALTH TECNOLOGY (DHT):

Patients who did not use a walking aid were assessed with:

Inertial Sensors System, 6 IMUs:

1.Basic TUG Skills:
Sit to stand
Stand to sit
Turn duration

2. Spatiotemporal Gait Parameters:
Gait Speed, Stride duration, Stride lenght, Cadence , Foot strike angle, toe off angle, Elevation at midswing, Lateral step variability and Pelve transverse ROM.

RESULTS AND DISCUSSION

Table 1. Demographics characteristics in total HSP group

	PerFO	variables from inertial sensors	Control Group
Sample size	58	25	25
Age (years)	44.3 ± 15.1	41.2 ± 16.9	38.1 ± 15.6
FARS-staging	**1**: 5 pt	**1**: 4 pt	-
	1.5: 1 pt	**1.5** : 1 pt	-
	2:15 pt	**2** :11pt	-
	2.5: 2 pt	**2.5** : 2 pt	-
	3:12 pt	**3** : 7 pt	-
	4 : 21pt	-	-
	4.5: 2 pt	-	-
FARS-ADL	9.8 ± 4.9	6.2 ± 4.9	-
SPRS	19.4 ± 7.9	13 ± 5.7	-
Disease duration (years)	20.3 ± 12.6	14.9 ± 11.3	-
Age of onset of disease	25.1 ± 18.1	26.2 ± 20.9	-
Walking-aid assistance	27/58 (47%)	No use walking aid	

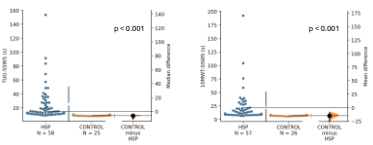


Figure 1. PerFO outcomes at SSWS in the HSP group compared with the control group.
Note: A larger difference was observed at MWS

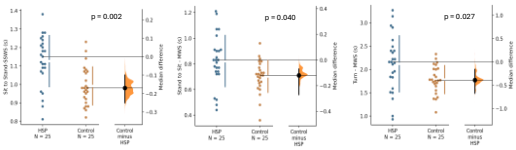


Figure 2. Basic TUG skills in the HSP group compared with the control group.
Note: Variables that presented a statistically significant difference.

Table 2. Spatiotemporal gait parameters in the HSP group compared with the control group.

Spatiotemporal gait parameters	HSP-SSWS	CONTROL-SSWS	p-value	HSP-MWS	CONTROL-MWS	p-value
Cadence (steps/min)	114 (20)	121 (9.39)	0.002	122 (42)	137 (14.5)	0.002
Gait speed (m/s)	0.95 (0.20)	1.34 (0.23)	< 0.001	1.1 (1.33)	1.77 (0.22)	< 0.001
Stride duration (s)	1.04 (0.18)	0.98 (0.8)	0.030	1.01 (0.50)	0.88 (0.10)	0.001
stride length (m)	1.08 (0.25)	1.35 (0.20)	< 0.001	1.08 (1.27)	1.5 (0.17)	< 0.001
foot strike angle (°)	11.9 (11.4)	27.5 (4.26)	< 0.001	10.5 (15.4)	29.5 (3.86)	< 0.001
Toe Off Angle (°)	32.1 (8.96)	40.4 (4.33)	< 0.001	31.3 (24)	41.7 (5.04)	< 0.001

Note: 0.95 m/s = 3.4 km/h; 1.3 m/s = 4,6, 1,1= 3,9 km/h; 1.7 m/s = 6.1 km/h

Table 3. Correlation between TUG test and ClinRO

ClinRO		TUG-SSWS	TUG-MWS	Stand to Sit-MWS
SPRS	rho	,763**	,738**	-
FARS-Staging	rho	,811**	,799**	,518*
FARS-ADL	rho	,479**	,532**	-
Duration Disease	rho	,334*	,362**	-

Table 4. Correlation between 10MWT and ClinRO

ClinRO		10MWS-SSWS	10MWS-MWS	SSWS-Cadence	SSWS-Stride Duration	SSWS-Gait Speed	SSWS-Lateral Step Variability	SSWS-Foot Strike	SSWS-Stride Length	SSWS-Lumbar Transverse RoM	SSWS-Trunk-Transverse RoM
SPRS	rho	,739**	,744**	-,445*	,491*	-,676**	,518*	-,623*	-,640*	-	,447*
FARS-Staging	rho	,780**	,800**	-	-	-,554**	,694**	-,492*	-,498*	-	,464*
FARS-ADL	rho	,411**	,477**	-	-	-	,549**	-	-	-	-
Duration Disease	rho	,282*	,328*	-	-	-	-	-	-	,441*	-

Note: *. A correlação é significativa no nível 0,05 (2 extremidades); **. A correlação é significativa no nível 0,01 (2 extremidades).

CONCLUSION

The patients showed worse gait performance compared to the control group, being 3 to 4 times slower in completing the tests. On the other hand, six of the eleven spatiotemporal gait parameters initially analyzed showed statistically significant differences compared with the control group. In addition, maximum speed during the performance tests affected the basic motor abilities assessed by the TUG and the spatiotemporal gait parameters, possibly due to increased spasticity.

The IAXON-BRAZIL HSP Network remains committed to increasing the sample size in order to determine which among the more than 17 biomechanical gait variables acquired through the inertial sensor system are the most sensitive to detect the minimal clinically significant difference to be applied in future clinical trials. In addition, the network aims to enable the identification of gait patterns by subtype, given that the current sample size is still insufficient for this type of analysis. Finally, the network is working on the characterization of reference values by assessing the control group with the same technology.

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