Giant axonal neuropathy: Cross sectional analysis of a large natural history cohort

Supplementary Materials

Supplementary Methods

Description of Motor Assessments

Motor strength was quantitatively measured using a handheld dynamometer (MicroFET®2 [hogganhealth.net]) for knee flexion and extension, hip abduction, and elbow flexion and extension strength, with distal strength measured using grip and pinch dynamometers (MyoGrip and MyoPinch [Ateliers Laumonier, France,]). Handheld dynamometry results were expressed as the percentage of the highest value compared to age/weight/sex-based norms,[45] and distal strength results were expressed as the percentage of the highest value compared to age-based norms.[46] The following timed functional testing were administered when applicable: time to arise from lying supine on floor to standing; time to run 10 meters and time to ascend and descend four steps. Tasks were reported and analysed based on time for completion.

Description of Autonomic Testing Methods

The Q-Sweat was performed on the Q-Sweat Device (WR Medical Electronics Co., Maplewood, MN) using standard iontophoresis methodology and 10% acetylcholine. Iontophoresis chambers were placed on the forearm and medial ankle and sweat volume was recorded ($\mu l/mm^2$). Tilt table and HRDB were performed using beat-to-beat blood pressure and heart rate monitoring (WR Medical Electronics, Inc, Maplewood, MN). Tilt table testing was performed only in ambulatory individuals, with a head-up tilt of 70 degrees for 10 minutes after at least 20 minutes in the supine position. Changes in heart rate and BP are continuously recorded during head up tilt and after return to supine position. HRDB was performed by having the subject take 6-8 slow deep breaths with 10 seconds per respiratory cycle. Results are recorded as the average difference between the inspiratory and expiratory heart rates and are age dependent. Basal lacrimal secretion was evaluated (Schirmer I with topical anaesthesia)

using strips of blotting paper placed into the lower conjunctival fornix of the patient for 5 minutes and then measuring the extent of lacrimal secretion, reported here in millimetres (mm) from the right eye (OD).[34,47] Severity of the reduction of lacrimation (unilateral) was defined as: Severe < 5 mm, Moderate 5-9 mm, Mild 10-14 mm, and Normal > 15 mm. Patients on medications that may affect lacrimation or cholinergic function were excluded in the final analysis.

Supplementary Table 1: Cohort genotype, phenotype, and functional data

Patient	Clinical Description/ Severity Score					Genetics						Phenotype	Ambulatory Status	
	Age (Yr)	MFM32 %	FARS FXN (Item 1)[a]	Age First Concern	Early Clinical Concern								Ambulant	Age Loss Independent Ambulation
1	8	100	0.5	8 yr	High Arch, Curly Hair, Affected sibling	exon 11	c.1720C>T	p.R574C	exon 4	c.837_839delTGG	p.G280del	*axonal CMT (plus)*	Amb	
39	14	98.9	0.5	5 yr	Tripping	exon 5	c.944C>T	p.P315L	whole gene deletion			*axonal CMT (plus)*	Amb	
2	13	94.8	0.5	5 yr	Abnormal gait; Fine motor difficulty	exon 11	c.1720C>T	p.R574C	exon 4	c.837_839delTGG	p.G280del	*axonal CMT (plus)*	Amb	
37	5	90*	1.5	1 yr	Abnormal gait	exon 6	c.994G>A	p.G332R	exon 6	c.994G>A	p.G332R	Classic	Amb	
11	5	90*	2.5	3 yr	Feeding difficulty, weak grip	exon 3	c.535_537delAAA	p.K179del	exon 3	c.316_318delGTT	p.V106del	Classic	Amb	
12	5	88.3*	1.5	3 yr	Abnormal gait, frequent falls	exon 3	c.601C>T	p.R201*	exon 3	c.601C>T	p.R201*	Classic	Amb	
36	8	87.5	1	3 yr	Abnormal gait	exon 9	c.1391G>A	p.C464Y	exon 9	c.1477G>A	p.E493K	*axonal CMT (plus)*	Amb	
19	10	87.5	2	5 yr	Flat feet, Abnormal gait	intron 3	c.633+2T>C		exon 8	c.1241G>A	p.G414D	*axonal CMT (plus)*	Amb	
42	18	84.4	2	8 yr	Abnormal gait	exon 10	c.1506G>T	p.W502C	exon 5	c.944C>T	p.P315L	*axonal CMT (plus)*	Amb	
3	6	83.3	2	3 yr	Frequent falls, foot drop	exon 4	c.805C>T	p.R269W	exon 4	c.732delT	p.I244Mfs*33	Classic	Amb	
30	8	82.3	1.5	2 yr	Abnormal gait; frequent falls	Intron 2	c.283-1G>A		exon 3	c.306C>G	p.I102M	*axonal CMT (plus)*	Amb	
44	8	80.2	2	2 yr	Frequent falls	exon 3	c.545T>A	p.I182N	exon 11	c.1729A>T	p.N577Y	*axonal CMT (plus)*	Amb	
41	6	79.17	2	3 yr	Abnormal gait, frequent falls	exon 3	c.374T>C	p.L125S	exon 3	c.374T>C	p.L125S	Classic	Amb	
45	3	75*	2	1 yr	Delayed walking	exon 6	c.997G>A	p.G333S	exon 6	c.997G>A	p.G333S	Classic	Amb	

Supplementary Table 1 (continued):

Patient	Clinical Description/ Severity Score					Genetics						Phenotype	Ambulatory Status	
	Age (Yr)	MFM32 %	FARS FXN (Item 1)[a]	Age First Concern	Early Clinical Concern								Ambulant	Age Loss Independent Ambulation
35	5	75*	2	2 yr	Abnormal gait, frequent falls	intron 4	c.851+1G>A		intron 4	c.851+1G>A		Classic	Amb	
34	16	75	2	13 yr	Nausea; falls	Exons 2-5	partial deletion		exon 5	c.944C>T	p.P315L	*axonal CMT (plus)*	Amb	
28	6	72.9	2	3 yr	Frequent falls	exon 4	c.806G>A	p.R269Q	exon 4	c.806G>A	p.R269Q	Classic	Amb	
32	10	72.9	1.5	2 yr	Abnormal gait	exon 7	c.1157delA	p.K386Rfs*3	exon 4	c.838G>A	p.G280R	Classic	Amb	
15	7	72.9	3	18 mo	Abnormal gait	exon 3	c.374T>C	p.L125S	exon 3	c.374T>C	p.L125S	Classic	Amb	
17	6	72.9	3.5	3 yr	Abnormal gait, foot abnormality	exon 2	c.266A>C	p.Y89S	exon 2	c.266A>C	p.Y89S	Classic	Amb	
21	21	71.9	3	3 yr	Abnormal gait		GAN whole gene deletion		exon 3	c.413G>T	p.R138L	*axonal CMT (plus)*	AmAs	17 yr
24	5	71.7	3.5	16 mo	Abnormal gait	exon 1	c.91G>C	p.D31H	Intron 4	c.852-13T>G		Classic	Amb	5 yr
43	5	71.7	2.5	6 mo	Foot abnormality	exon 1	c.1-?_167+?del	p.0?	exon 5	c.973G>A	p.E325K	Classic	Amb	
22	6	69.8	2.5	4 yr	Abnormal gait, frequent falls	intron 4	c.851+1G>A		intron 4	c.851+1G>A		Classic	Amb	
14	7	68.8	3	18 mo	Abnormal gait	exon 3	c.374T>C	p.L125S	exon 3	c.374T>C	p.L125S	Classic	Amb	
25	8	66.7	4	3 yr	Frequent falls	exon 1	c.143T>C	p.L48P	exon 1	c.143T>C	p.L48P	Classic	AmAs	5 yr
23	7	64.6	2	4 yr	Abnormal gait	intron 4	c.851+1G>A		intron 4	c.851+1G>A		Classic	Amb	
29	7	61.5	3.5	2 yr	Frequent falls	exon 3	c.545T>A	p.I182N	exon 3	c.545T>A	p.I182N	Classic	AmAs	6 yr
4	9	60.4	4.5	3 yr	Abnormal gait; foot abnormality	exon 10-11	c.1647-8680_*258del		exon 10-11	c.1647-8680_*258del		Classic	AmAs	7 yr

Supplementary Table 1 (continued):

Patient	Clinical Description/ Severity Score											Phenotype	Ambulatory Status	
	Age (Yr)	MFM32 %	FARS FXN (Item 1)[a]	Age First Concern	Early Clinical Concern	Genetics							Ambulant	Age Loss Independent Ambulation
13	9	59.4	4	2 yr	Abnormal gait	exon 3	c.374T>C	p.L125S	exon 3	c.374T>C	p.L125S	Classic	AmAs	7 yr
5	11	55.2	4.5	5 yr	Frequent falls, turning of feet	intron 4	c.851+5G>A		exon 7	c.1236+1G>A		Classic	AmAs	10 yr
7	12	55.2	5.5	1 yr	Delayd milestones	exon 9	c.1456G>A	p. E486K	1st intron - 3rd exon deletion	57–131 kb microdeletion		Classic	NAmb	8 yr
16	10	53.1	3.5	2 yr	Abnormal gait, frequent falls	exon 1	c.1-?_167+?del	p.0?	exon 1	c.1-?_167+?del	p.0?	Classic	AmAs	9 yr
26	11	53.1	5	3 yr	Frequent falls	exon 2	c.213T>A	p.Y71*	exon 10	c.1539_1540delinsT	p.A514Pfs*12	Classic	AmAs	5 yr
27	12	52.1	4.5	3 yr	Abnormal gait, frequent falls	intron 4	c.851+1G>A		intron 4	c.851+1G>A		Classic	AmAs	9 yr
40	8	50	4.5	3 yr	Frequent falls	intron 4	c.851+1G>A		intron 4	c.851+1G>A		Classic	NAmb	7 yr
6	9	49	5	2 yr	Frequent falls	exon 4	c.805C>T	p.R269W	exon 4	c.732delT	p.I244Mfs*33	Classic	NAmb	8 yr
31	6	46	4.5	3 yr	Frequent falls	exon 3	c.484C>T	p.R162*	exon 3	c.484C>T	p.R162*	Classic	AmAs	5
18	11	44.8	5	15 mo	Delayed walking/ abnormal gait	exon 4	c.724C>T	p.R242*	exon 4	c.724C>T	p.R242*	Classic	NAmb	10 yr
33	10	41.7	5	3 yr	Frequent falls	exon 9	c.1382C>T	p.A461V	exon 9	c.1382C>T	p.A461V	Classic	NAmb	5 yr
9	11	38.5	6	12 mo	Frequent falls, Delayed walking	genomic locations: 81,396,399 in intron 6 and 81,399,587 in intron 9	3.2kb deletion encompassing exon 7 to exon 9		exon 9	c.1456 G>A	p.E486K	Classic	NAmb	9 yr
38	5	34*	5	9 mo	Difficulty sitting	Exon 2	c.266A>C	p.Y89S	Exon 2	c.266A>C	p.Y89S	Classic	NAmb	0
8	10	30.2	6.0	18 mo	Delayed walking	exon 1	c.146C>A	p.A49E	exon 1	c.146C>A	p.A49E	Classic	NAmb	8 yr
10	15	30.2	5.5	3 yr	Abnormal gait	exon 6	c.994G>A	p.G332R	exon 6	c.994G>A	p.G332R	Classic	NAmb	12 yr
20	18	20.8	6	15 mo	Abnormal gait, frequent falls	exon 1	c.1-?_167+?del	p.0?	exon 1	c.1-?_167+?del	p.0?	Classic	NAmb	8 yr

Supplementary Table 1: Legend

Entire cohort ranked in order by their motor function measure (MFM-32) total percent score. Ambulatory status is listed and appears to correspond to the MFM-32 total percent score. If ambulation has been lost, the age at loss of independent ambulation is listed in parentheses (in years). Genetic variants are listed, and segregation confirmed in 40/ 45 patients (the remaining patients were clinically confirmed by distinct clinical phenotype or nerve pathology findings performed prior to referral to the study). The clinical phenotype defined as classic GAN or axonal CMT (plus) is noted for each patient.

a) Friedreich Ataxia Rating Scale (FARS) – Item 1 – Rating of Functional Impact of Ataxia (scores ranging from 0= 'normal' to 6.0 = 'confined to wheelchair or bed with total dependency for all ADL'.

Abbreviations in table are as follows: Amb = ambulatory, AmAs = requires assistance for ambulation, mo = month, NAmb = not able to ambulate without an assistive device, yr = year

Supplementary Table 2: Clinical cohort characteristics

Patient	Progression of Primary GAN Related Signs and Symptoms												Pulmonary		Additional GAN Signs and Symptoms								GAN Imaging		
	History of Unsteady/ Abnormal Gait	Contrac-tures	Spasticity	Patellar tendon DTR [a]	Babinski [b]	Scoliosis (Age of surgery)[c]	Decreased visual acuity	Nystag-mus	Dysarthria	Dysphagia (Age Onset)[c]	NG or G-tube	Urinary[d]	Sleep Apnea	FVC	Seizures (Age Onset)[c]	Vertigo	Learning Difficulties	Macro-cephaly	Hypo-thermia	Precocious Puberty	Menstrual Irregularities	Lactose Intolerant	MRI brain (CWM)	MRI brain (CerWM)	Spine MRI Thinning
1	N	N	**Y**	+++	F	N	N	N	N	N	N	N	N	ND	N	N	N	**Y**	N	N	N	N	0	0	0
39	**Y**	**Y**	**Y**	+++	**E**	N	N	N	N	N	N	N	N	115	N	N	**Y**	**Y**	N	N	N	N	0	0	0
2	**Y**	**Y**	**Y**	+++	F	N	N	N	N	N	N	N	N	ND	N	N	N	N	N	N	NA	N	0	0	0
37	**Y**	**Y**	N	-	F	N	N	**Y**	N	**Y (birth)**	N	N	N	93	N	N	N	**Y**	N	N	NA	**Y**	0	**I**	0
11	**Y**	N	N	-	F	N	N	N	N	N	N	N	N	ND	N	**Y**	**Y**	N	N	N	NA	**Y**	ND	ND	ND
12	**Y**	N	N	-	F	N	N	N	N	N	N	N	N	ND	N	N	N	N	N	N	NA	**Y**	0	**I**	0
36	**Y**	**Y**	**Y**	-	M	N	N	N	N	N	N	**Y**	N	113	N	N	N	**Y**	N	N	NA	N	0	0	0
19	**Y**	**Y**	N	-	F	N	N	N	N	N	N	N	N	110	N	N	N	**Y**	**Y**	N	N	N	0	**I**	0
42	**Y**	**Y**	N	-	F	N	N	N	N	N	N	N	N	94	N	N	N	**Y**	N	N	NA	**Y**	0	0	0
3	**Y**	N	N	-	M	N	N	N	N	N	N	N	N	84	N	N	N	N	N	N	NA	N	0	**I**	0
30	**Y**	**Y**	N	-	M	N	N	N	N	N	N	N	**Y**	103	N	**Y**	N	**Y**	N	N	N	N	0	0	0
44	**Y**	**Y**	N	-	M	N	N	N	N	N	N	**Y**	N	106	N	N	N	N	N	N	NA	N	0	0	0
41	**Y**	**Y**	**Y**	-	**E**	**Y**	N	N	N	N	N	N	N	79	N	N	N	N	N	N	NA	N	0	**I**	0
45	**Y**	N	**Y**	-	**E**	N	N	N	N	N	N	N	N	ND	N	N	N	N	N	N	NA	**Y**	ND	ND	ND

Supplementary Table 2 (continued):

Patient	Progression of Primary GAN Related Signs and Symptoms												Pulmonary		Additional GAN Signs and Symptoms								GAN Imaging		
	History of Unsteady/ Abnormal Gait	Contrac-tures	Spasticity	Patellar tendon DTR [a]	Babinski [b]	Scoliosis (Age of surgery)[c]	Decreased visual acuity	Nystag-mus	Dysarthria	Dysphagia (Age Onset)[c]	NG or G-tube	Urinary[d]	Sleep Apnea	FVC	Seizures (Age Onset)[c]	Vertigo	Learning Difficulties	Macro-cephaly	Hypo-thermia	Precocious Puberty	Menstrual Irregularities	Lactose Intolerant	MRI brain (CWM)	MRI brain (CerWM)	Spine MRI Thinning
35	Y	N	N	-	E	N	N	N	N	N	N	N	N	91	N	N	N	N	N	N	NA	Y	0	1	0
34	Y	Y	Y	+++	E	N	N	N	N	N	N	N	N	93	N	N	N	Y	N	N	N	N	0	0	0
28	Y	Y	N	-	M	N	N	N	N	N	N	N	N	ND	N	N	N	N	N	N	NA	N	ND	ND	ND
32	Y	Y	Y	-	M	Y	Y	Y	N	N	N	N	N	90	N	N	N	Y	N	N	NA	N	1	1	1
15	Y	Y	N	-	M	N	N	Y	N	N	N	N	N	98	N	N	N	N	N	Y	NA	Y	1	2	1
17	Y	N	N	-	ND	N	Y	Y	Y	N	N	Y	N	ND	N	N	N	Y	N	Y	NA	Y	1	2	1
21	Y	Y	Y	+++	M	Y	Y	Y	N	N	N	N	N	105	N	N	N	Y	N	N	N	N	0	0	0
24	Y	Y	N	-	E	N	N	N	N	N	N	N	N	101	N	Y	N	Y	N	N	NA	Y	0	1	0
43	Y	Y	Y	-	F	N	N	N	Y	N	N	N	Y	ND	N	N	N	Y	N	N	NA	Y	ND	ND	ND
22	Y	Y	N	-	E	N	N	Y	N	Y	N	N	Y	83	N	N	Y	Y	N	N	NA	N	2	2	1
14	Y	Y	N	-	F	N	Y	Y	Y	N	N	N	N	97	N	N	N	N	N	Y	NA	Y	1	2	1
25	Y	Y	N	-	M	Y	Y	Y	N	Y	N	N	Y	60	N	N	N	Y	N	N	NA	N	1	1	0
23	Y	N	N	-	F	N	Y	Y	N	N	N	N	N	100	N	N	Y	Y	N	N	NA	N	2	2	1
29	Y	Y	N	-	M	N	Y	Y	Y	N	N	N	N	57	N	Y	Y	Y	N	N	NA	Y	ND	ND	1
4	Y	Y	N	-	ND	Y	Y	Y	Y	Y	N	N	Y	ND	N	Y	N	Y	N	N	NA	Y	2	2	1

Supplementary Table 2 (continued):

Patient	Progression of Primary GAN Related Signs and Symptoms												Pulmonary		Additional GAN Signs and Symptoms								GAN Imaging		
	History of Unsteady/ Abnormal Gait	Contrac-tures	Spasticity	Patellar tendon DTR [a]	Babinski [b]	Scoliosis (Age of surgery) [c]	Decreased visual acuity	Nystag-mus	Dysarthria	Dysphagia (Age Onset) [c]	NG or G-tube	Urinary [d]	Sleep Apnea	FVC	Seizures (Age Onset) [c]	Vertigo	Learning Difficulties	Macro-cephaly	Hypo-thermia	Precocious Puberty	Menstrual Irregularities	Lactose Intolerant	MRI brain (CWM)	MRI brain (CerWM)	Spine MRI Thinning
13	Y	Y	N	-	M	Y	Y	Y	Y	N	N	N	Y	86	N	N	N	N	N	Y	NA	Y	1	1	1
5	Y	Y	N	-	ND	Y	Y	Y	N	Y	N	N	N	ND	N	N	N	N	N	Y	N	Y	2	2	2
7	Y	Y	N	-	ND	Y	Y	Y	Y	Y	Y	Y	N	ND	N	N	Y	Y	N	N	NA	Y	3	2	3
16	Y	Y	N	-	E	Y	N	N	Y	Y	N	Y	Y	58	N	Y	Y	Y	N	N	NA	N	2	2	2
26	Y	Y	N	-	M	Y	Y	Y	Y	Y	N	N	N	83	N	N	N	N	N	N	NA	N	2	3	2
27	Y	Y	N	-	M	Y	Y	Y	Y	N	N	Y	Y	91	N	N	N	N	N	N	NA	N	3	2	2
40	Y	Y	N	-	E	Y	Y	Y	Y	N	N	Y	Y	94	N	Y	Y	Y	Y	Y	NA	N	ND	ND	2
6	Y	Y	N	-	E	Y	Y	Y	Y	Y	N	Y	Y	ND	N	Y	N	Y	N	Y	Y	N	0	1	0
31	Y	Y	N	-	M	N	Y	Y	Y	N	N	N	N	ND	N	Y	Y	N	N	N	NA	Y	ND	ND	2
18	Y	Y	N	-	ND	Y	Y	Y	Y	Y	Y	N	N	ND	N	N	N	Y	N	N	Y	N	3	3	2
33	Y	Y	N	-	M	Y	Y	Y	Y	N	N	Y	N	57	N	N	N	Y	N	Y	Y	N	1	2	1
9	Y	Y	N	-	M	Y (11 yr)	Y	Y	Y	Y	Y	Y	Y	ND	N	Y	Y	N	Y	N	Y	N	3	3	3
38	Y	Y	N	-	E	Y	N	N	N	N	Y	Y	N	ND	N	N	N	N	N	Y	NA	Y	ND	ND	2
8	Y	Y	N	-	ND	Y	Y	Y	Y	Y	Y	N	Y	ND	N	N	Y	Y	Y	Y	NA	N	3	3	2
10	Y	Y	N	-	ND	Y (13 yr)	Y	Y	Y	Y	Y	Y	Y	ND	Y (15 yr)	Y	Y	Y	Y	N	NA	N	3	2	3
20	Y	Y	N	-	M	Y (10 yr)	Y	Y	Y	Y	N	Y	Y	44	N	N	N	Y	N	Y	NA	N	2	3	3

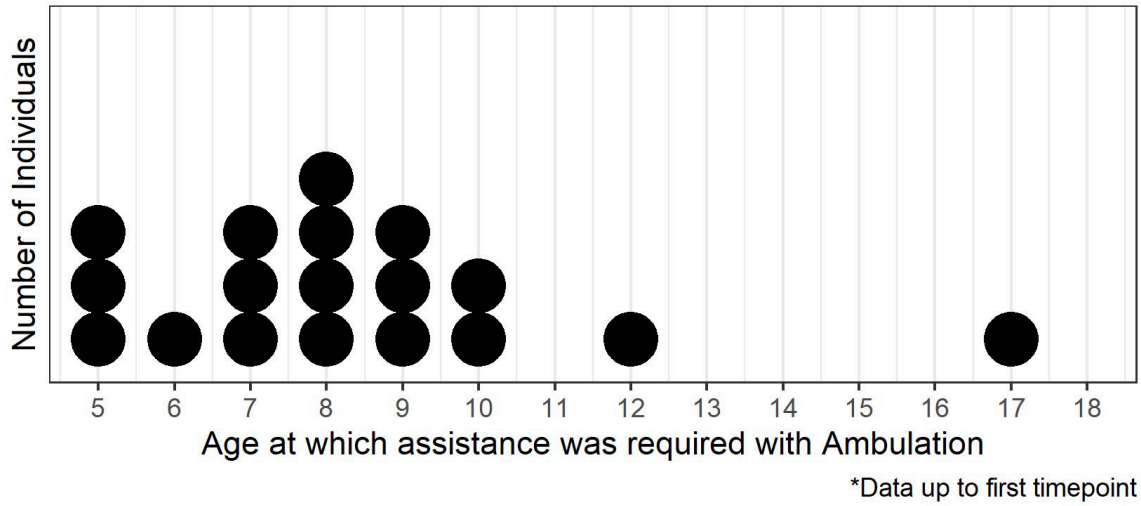
Supplementary Table 2: Legend:

This table highlights the increased prevalence of additional motor and systemic signs and symptoms occurring in individuals with giant axonal neuropathy, such as: gait impairment, dysarthria, dysphagia, spasticity, scoliosis, and urinary symptoms as the disease progresses (those individuals with lower total MFM32 score or motor functional status are listed lower in the table). The presence or absence of disease associated conditions is marked by Y (Yes) or N (No). Clinical signs of upper motor neurone involvement include: presence of spasticity, brisk or +++ deep tendon reflexes at the patellar tendon, or an extensor Babinski response. Macrocephaly is defined as head circumference > +2 standard deviations above the mean, or > 98 percentile for age. We qualitatively define the level of severity of the T2 hyperintensity in the cerebral white matter and cerebellar white matter as well as the extent of spinal cord atrophy or thinning. Rating is as follows: 0 =normal, 1 = mild, 2 = moderate, and 3 = severe. Evaluations not completed are listed as ND = Not Done.

a) Patellar tendon deep tendon reflexes: Graded as (+++) = brisk; (++) = normoactive); (+) =diminished; (-) =absent
b) Babinski response: Graded as E (extensor); F (flexor); M (mute, no movement)
c) Numbers in parentheses represent the reported age at onset; except for scoliosis, where the number represents age at time of surgical repair for scoliosis.
d) Urinary symptoms included either urinary urgency, hesitancy to initiate voiding, or urinary incontinence.

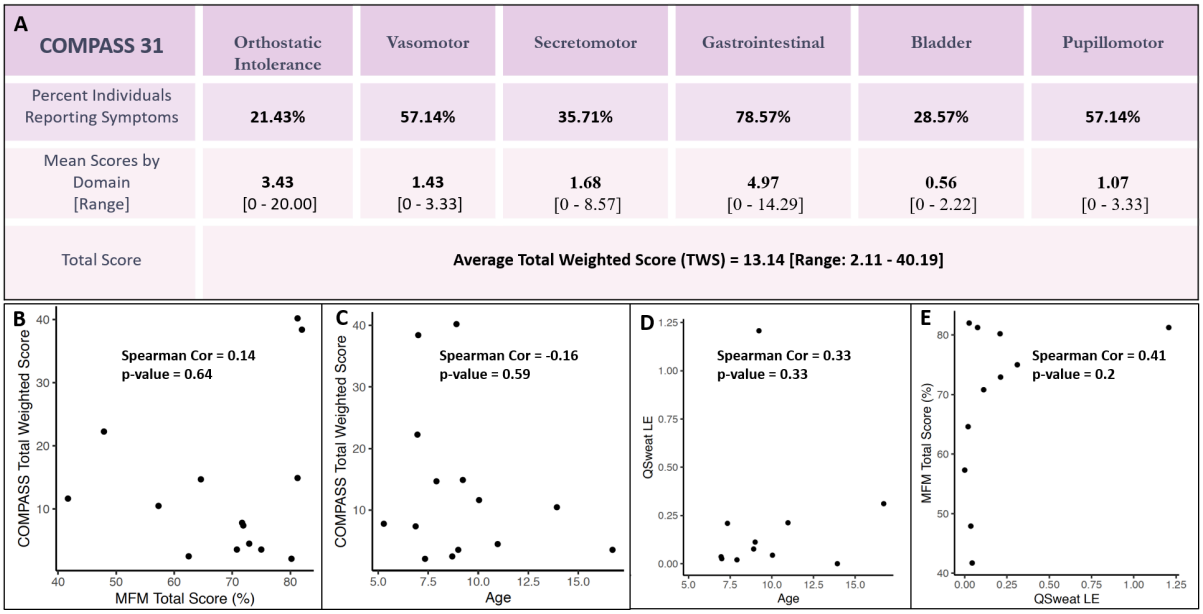
Abbreviations in table are as follows: CWM= cerebral white matter, CerWM= cerebellar white matter, E= extensor Babinski response, F= flexor Babinski response, FVC = forced vital capacity, M= mute Babinski response, N= no, NA = not applicable, ND= not done, Y=yes (to note that a sign or symptom is present), yr = year

Supplementary Figure 1: Reported age when assistance is required with ambulation in GAN



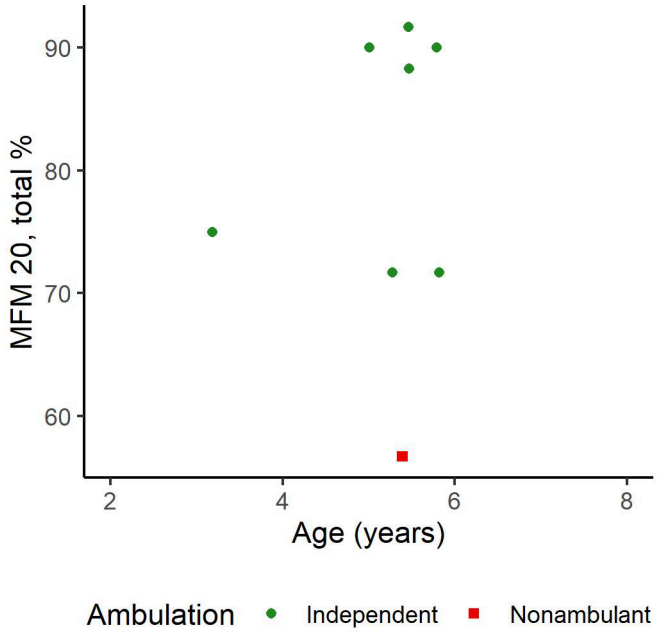
This plot highlights the progression of disease in our cohort, with each circle representing an individual patient's family-reported age at which assistance with ambulation was required. 20 of 45 individuals required assistance or fully lost ambulation by the time of their first study visit (2 had unknown age of loss). The median age was 8 years old [IQR: 7-9 years].

Supplementary Figure 2: Autonomic Impairment in GAN



Patient/ parent reported and measured assessments of autonomic impairment in individuals with GAN are shown here based upon the first recorded autonomic measures in the natural history study. **A**) Individuals with GAN report symptoms related to autonomic dysfunction based upon the COMPASS 31 self-assessment questionnaire, specifically affecting the domains of autonomic function as demonstrated within the table, with gastrointestinal, vasomotor, and pupillomotor being most frequently reported as affected. The gastrointestinal domain also had the highest mean score (corresponding to worse reported function). The plots underneath show the correlations between the COMPASS 31 total weighted score (TWS) as compared to MFM-32 total score and age (**B** and **C**) and between the QSWEAT volume as compared to age and MFM-32 score (**D** and **E**). Overall, these two markers, the COMPASS 31 TWS and QSWEAT volume are abnormal, but do not correlate significantly to age or motor function.

Supplementary Figure 3: MFM-20 Total Percent Score Compared to Age



This plot demonstrates the MFM-20 total percent score as compared to age for those participants under 6 years old. There is not any clear trend between age versus MFM-20 score; however, this may be due to the concentration of participants around the same age and the low number (n=8).