

Supplementary Materials: Reduced Cross-Sectional Muscle Growth Six Months after Botulinum Toxin Type-A Injection in Children with Spastic Cerebral Palsy

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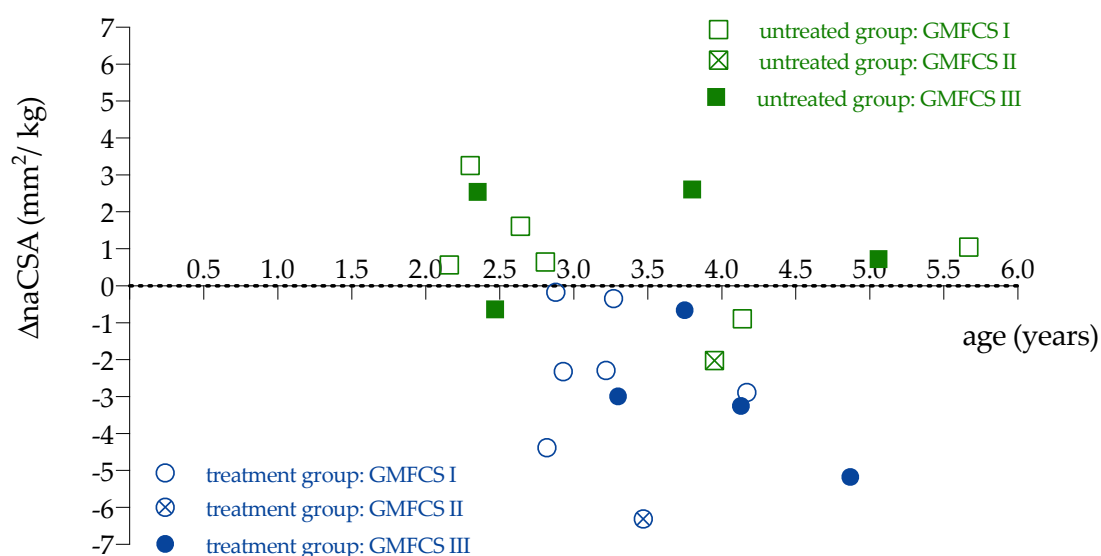


Figure S1. Individual data of the change in normalized anatomical cross-sectional area per age in the botulinum neurotoxin type-A naive treatment and untreated group, visualized per GMFCS level. *naCSA*, normalized anatomical cross-sectional area; *mm*, millimeter; *kg*, kilogram; *GMFCS*, gross motor function classification scale

Table S1. Usual care, functional mobility and clinical examination of the ankle joint for the *BoNT-A naive treatment*, *BoNT-A naive untreated* and *BoNT-A not-naive treatment* group at the time of the baseline assessment.

	BoNT-A naive treatment group	BoNT-A naive untreated group	BoNT-A not-naive treatment group
Participants (n)	11	11	15
Use of orthoses during the day	Frequently used, <i>n</i> = 10 Not frequently used, <i>n</i> = 1 Not used, <i>n</i> = 0	Frequently used, <i>n</i> = 9 Not frequently used, <i>n</i> = 2 Not used, <i>n</i> = 0	Frequently used, <i>n</i> = 13 Not frequently used, <i>n</i> = 1 Not used, <i>n</i> = 1
Use of orthoses during the night	Frequently used, <i>n</i> = 0 Not frequently used, <i>n</i> = 4 Not used, <i>n</i> = 7	Frequently used, <i>n</i> = 0 Not frequently used, <i>n</i> = 3 Not used, <i>n</i> = 8	Frequently used, <i>n</i> = 2 Not frequently used, <i>n</i> = 4 Not used, <i>n</i> = 9
Physiotherapy, min per week	120 (60 to 230)	90 (60 to 270)	120 (60 tot 240)
Oral medication	Tone reduction, <i>n</i> = 2 Anti-epileptics, <i>n</i> = 1 Others, <i>n</i> = 1 Not used, <i>n</i> = 8	Tone reduction, <i>n</i> = 1 Anti-epileptics, <i>n</i> = 2 Others, <i>n</i> = 4 Not used, <i>n</i> = 3	Tone reduction, <i>n</i> = 4 Anti-epileptics, <i>n</i> = 0 Others, <i>n</i> = 0 Not used, <i>n</i> = 11
Functional mobility scale	5m: 5 (1-6); 50m: 5 (1-6); 500m: 5 (1-6)	5m: 5 (1-6); 50m: 5 (1-6); 500m: 5 (1-6)	5m: 6 (5-6); 50m: 5 (2-6); 500m: 5 (1-6)
Ankle joint mobility	Normal, <i>n</i> = 8 Mild limitation, <i>n</i> = 3 Contracture, <i>n</i> = 0	Normal, <i>n</i> = 6 Mild limitation, <i>n</i> = 5 Contracture, <i>n</i> = 0	Normal, <i>n</i> = 5 Mild limitation, <i>n</i> = 7 Contracture, <i>n</i> = 3
Plantar flexor muscle spasticity	Normal to mild, <i>n</i> = 1 Moderate, <i>n</i> = 6 Severe, <i>n</i> = 4	Normal to mild, <i>n</i> = 4 Moderate, <i>n</i> = 6 Severe, <i>n</i> = 1	Normal to mild, <i>n</i> = 1 Moderate, <i>n</i> = 11 Severe, <i>n</i> = 3

Frequently used indicated $\geq 50\%$ of the day or night whereas not frequently used indicated $< 50\%$ of the day or night. The amount of physiotherapy and the sub-scores of functional mobility scale are shown as median (minimum to maximum values). Mobility was classified as no contracture (≥ 10 degrees of dorsiflexion), mild restriction in ROM (10 to 0 degrees of dorsiflexion) and contracture (< 0 degrees of dorsiflexion). Spasticity was classified as normal to mild increased tone (MAS of 0 or 1), moderate spasticity (MAS of 1+ or 2) and severe spasticity (MAS of 3). The most involved leg is reported. *BoNT-A*, *botulinum neurotoxin type A*; *n*, number.

Table S2. BoNT-A treatment doses (units/body mass) in the *BoNT-A naive treatment* and *BoNT-A not-naive treatment* group

The doses expressed as units (U) per kg body mass are shown as median (minimum to maximum values). *BoNT-A*, botulinum neurotoxin type A; *n*, number; *NA*, not applicable.

	BoNT-A naive treatment group		BoNT-A not-naive treatment group	
	Participants (n)	Dose (U/kg)	Participants (n)	Dose (U/kg)
Total	11	8.0 (4.4–10.8)	15	7.9 (4.4–10.9)
Medial gastrocnemius	11	2.7 (0.9–4.1)	15	2.7 (1.7–4.3)
Psoas	6	1.4 (0.9–1.6)	2	0.8 (0.8–0.9)
Rectus femoris	0	NA	3	1.5 (1.2–1.8)
Semitendinosus	10	2.9 (1.5–5.9)	13	1.8 (1.1–3.8)
Semimembranosus	5	1.3 (0.7–1.8)	13	1.4 (0.9–2.3)
Gracilis	6	1.9 (1.5–2.7)	11	1.5 (1.0–2.6)
Adductors	2	0.7 (0.7–0.8)	1	1.1
Soleus	1	2.2	7	1.7 (1.0–2.3)

Table S3. Comparison of median group values for anthropometric measures and normalized medial gastrocnemius muscle outcomes between the *BoNT-A treatment groups, BoNT-A naïve untreated and TD group* at the time of the baseline assessment.

Baseline	BoNT-A naïve treatment (a)	BoNT-A naïve untreated (b)	BoNT-A not-naïve treatment (c)	TD (d)	<i>p</i>	a-d, <i>p</i>	b-d, <i>p</i>	c-d, <i>p</i>
Participants (n)	11	11	15	49				
Age (y)	3.3 (1.2)	2.8 (1.8)	6.4 (2.5)	5.5 (3.7)	<0.001	0.008	0.004	0.453
Body mass (kg)	13.6 (1.3)	14.5 (4.9)	20.0 (7.5)	20.0 (6.9)	<0.001	0.000	0.004	1.000
Body length (cm)	91.0 (9.20)	97.0 (18.4)	114.0 (26.0)	112.0 (21.6)	<0.001	0.000	0.001	1.000
Leg length (cm)	44.2 (5.0)	46.0 (9.5)	55.4 (15.5)	55.0 (14.3)	<0.001	0.001	0.003	1.000
nMV (mL/(kg·m))	1.47 (0.43)	1.52 (0.45)	1.39 (0.62)	1.78 (0.40)	<0.001	0.003	0.060	0.003
nML (%)	23.6 (4.05)	23.3 (5.82)	23.4 (3.46)	26.70 (3.85)	<0.001	0.031		0.002
nMTUL (%)	45.8 (1.92)	46.7 (5.55)	45.5 (1.49)	46.88 (2.45)	0.001	0.204		0.006
aCSA _{norm} (mm ² /kg)	16.7 (6.40)	17.5 (4.15)	17.8 (5.56)	21.79 (3.82)	<0.001	0.001	0.001	0.000
EI (bit)	153.2 (12.1)	158.5 (31.5)	175.3 (22.4)	152.3 (19.9)	0.004	1.000	1.000	0.002
Growth rate (mL/mo)	0.47 (0.25)	0.51 (0.09)	0.42 (0.21)	0.58 (0.18)	<0.001	0.003	0.344	0.000

Data are presented as median (interquartile range). Muscle growth rate was calculated as ratio of muscle volume (milliliter) per age (months). Kruskal-Wallis test with pairwise post-hoc analysis and significance level of 0.01 after Bonferroni correction was used. Significant results were indicated with grey color. *BoNT-A*, botulinum neurotoxin type A; *TD*, typically developing; *n*, number; *y*, years; *kg*, kilograms; *cm*, centimeter; *nMV*, muscle volume normalized to the product of body mass and body length; *mL*, milliliter; *m*, meter; *nML*, muscle belly length normalized to leg length; *nMTUL*, muscle-tendon unit complex length normalized to leg length; *aCSA_{norm}*, anatomical cross-sectional area normalized to body mass; *EI*, echo-intensity; *mo*, month.