Neurocontrol of locomotion in progressive neuromuscular diseases

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Neuromuscular disorders

- Neuromuscular disorders (NMD) are a heterogeneous group of diseases of motor unit.

- The predominant clinical sign in NMD is muscle weakness.

Gait in patients with NMD

- Difficulties in gait are
  - often presenting sign
  - one of the most frequent complaint and
  - main contributor to disability.

Control systems of posture and gait

- Standing, reaching out and walking is something we do all the time and do not thing about it.
- Yet the physiology is complex.
- It is even more complicated to understand and differentiate the causes and the consequences in a patient with gait disorder.

- Grillner et al., 1998
  - The motor system
  - Postural system
  - Goal-directed system

Motor system

Propulsive movement is generated at the :

- Spinal level – central spinal pattern generator
- Brain stem:
  - Decorticate cat (animal runs and walks without assistance)
  - Premamillary preparation (walks on the moving treadmill)
  - Postmamillary preparation (needs electrical or chemical stimulation of MLR to generate stepping)
  - Decerebrate preparation (rigidity - no walking)
- Cerebellum modulates adjustment and timing of movement
- Cortex and subcortical nuclei

Postural system

Maintains appropriate body orientation during ongoing locomotion:

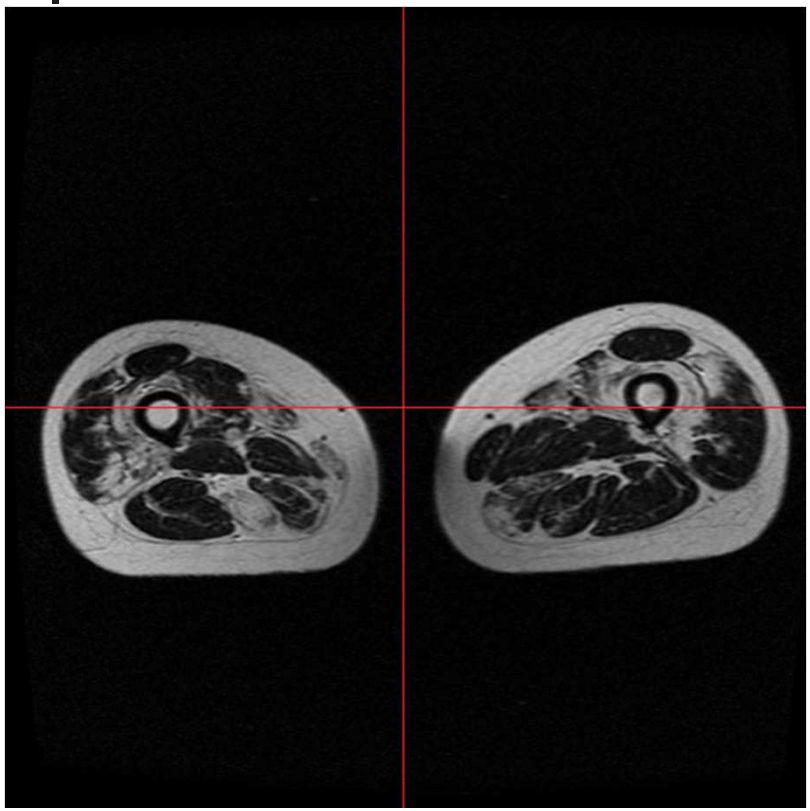
- Input:
  - Vision
  - Vestibular
  - Somatosensory
- Output:
  - Spinal cord reflexes
  - Brain stem reflexes
  - Voluntary response

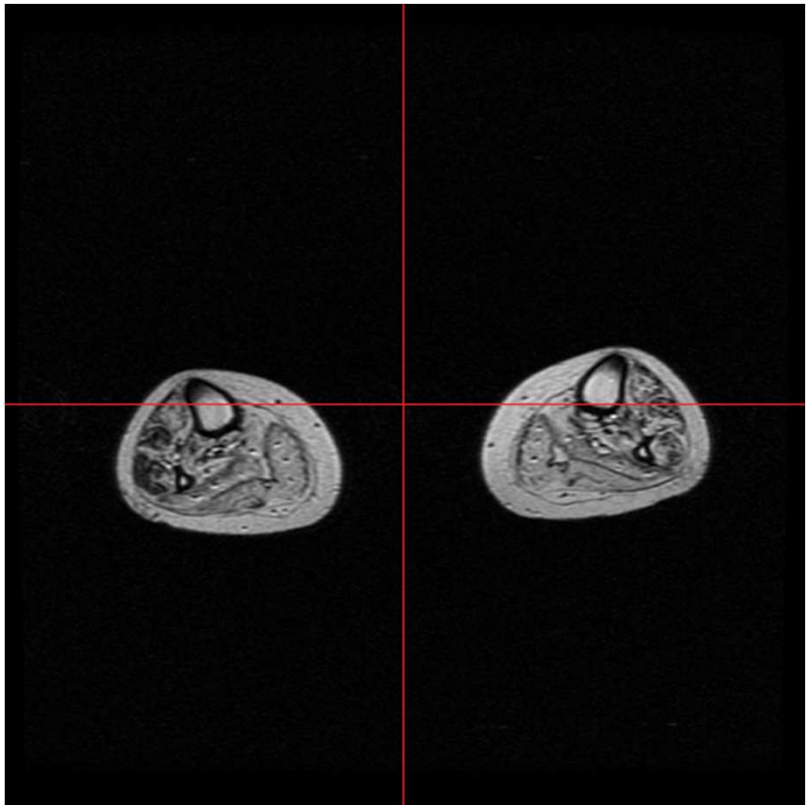
Goal-directed system

- Brings the subject to the goal of locomotor episode and avoids objects/situations that may impede locomotion.
- Specific subsets of locomotor nuclei are associated with initiation of locomotion in different behavioral circumstances:
  - *Exploratory* : basal ganglia
  - *Appetitive*: lateral hypothalamic region
  - *Defensive*: medial hypothalamus and central gray matter

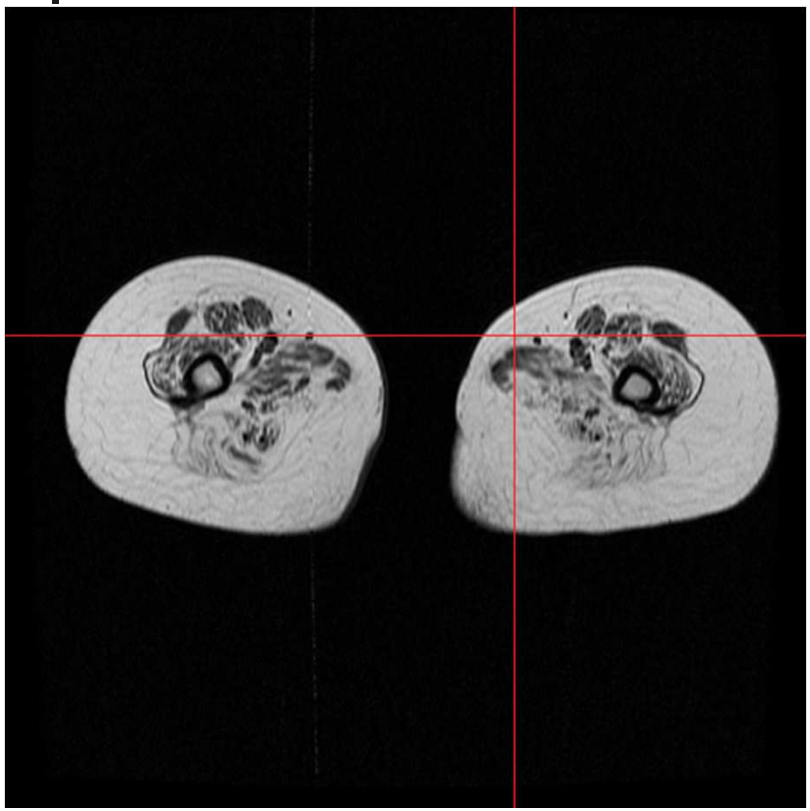
Sinnamon, 1993

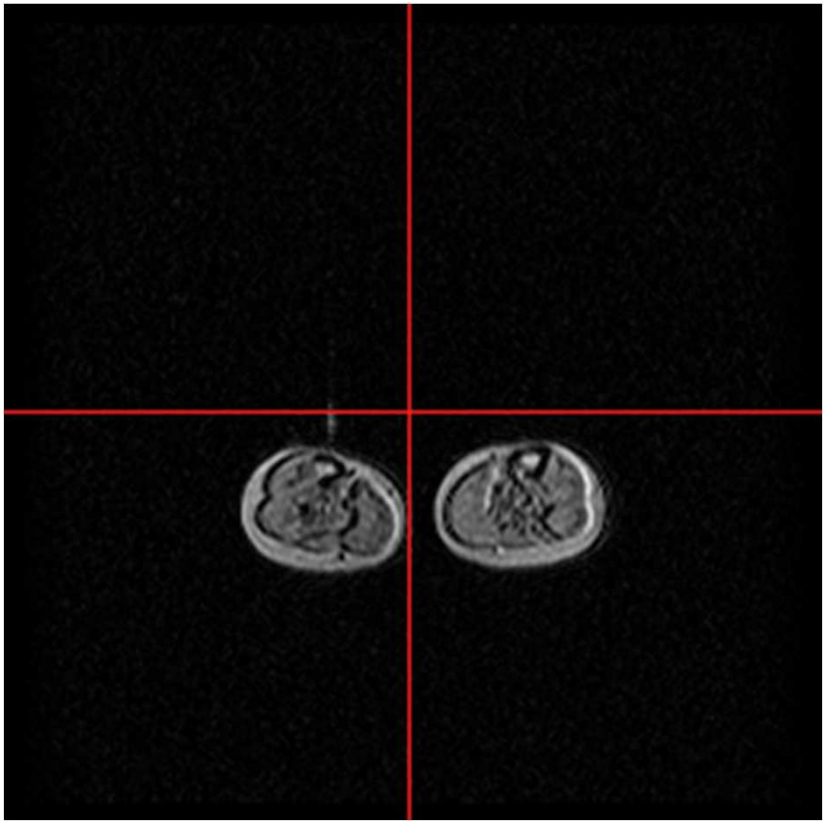
MRI - muscles (DM1)



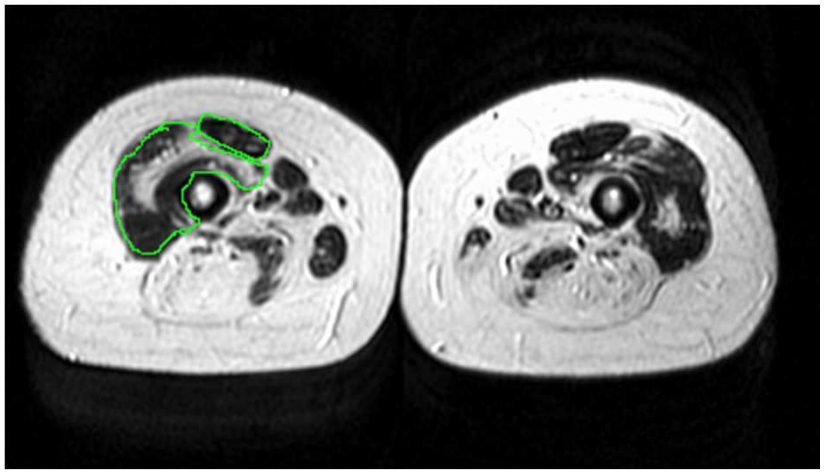


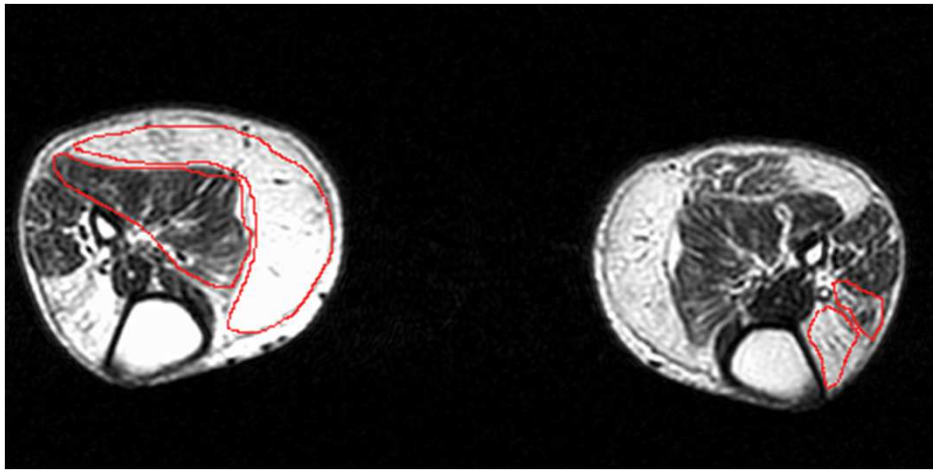
MRI - muscles (SMA III)



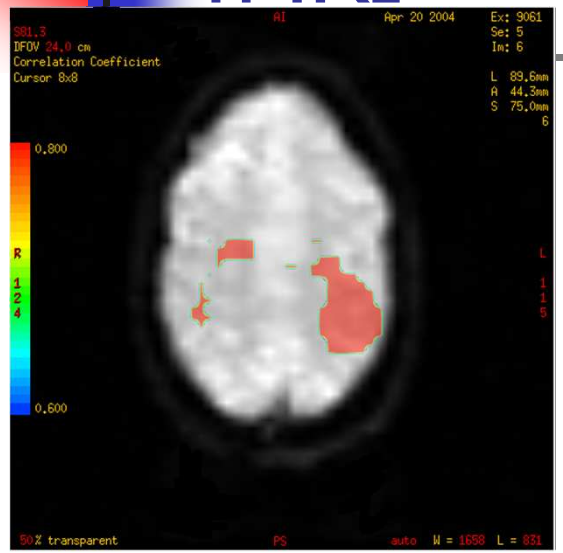


MRI muscles (FSH)

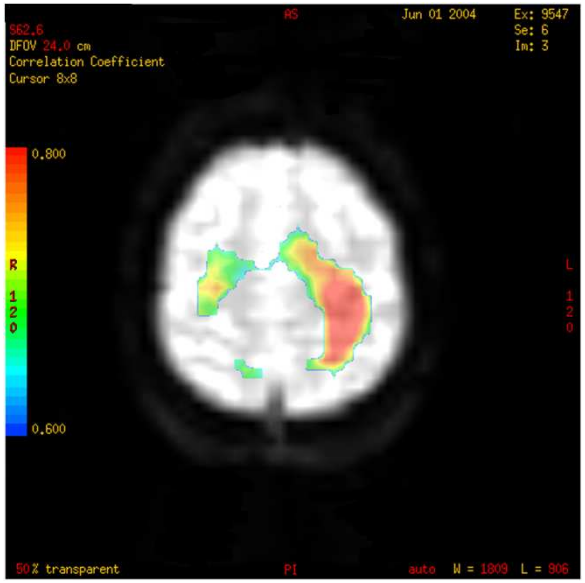




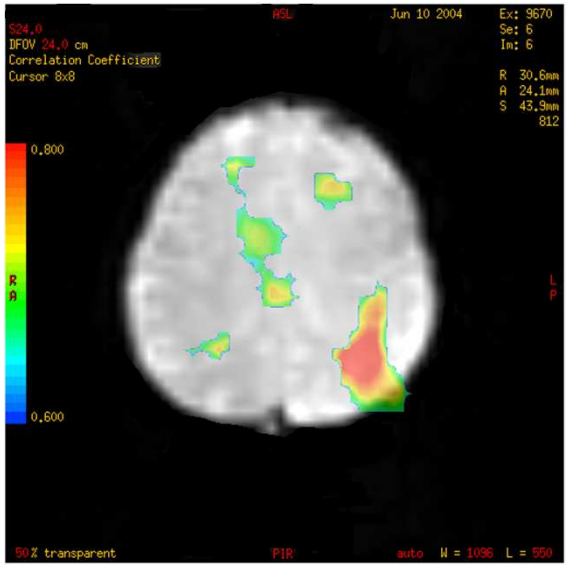
fMRI



NORMAL



FSH MD



MD1

Gait in patients with NMDs

- How to improve and to prolong it?
  - Procedures:
    - bracing
    - surgery
    - physiotherapy
    - others

Gait in patients with DMD

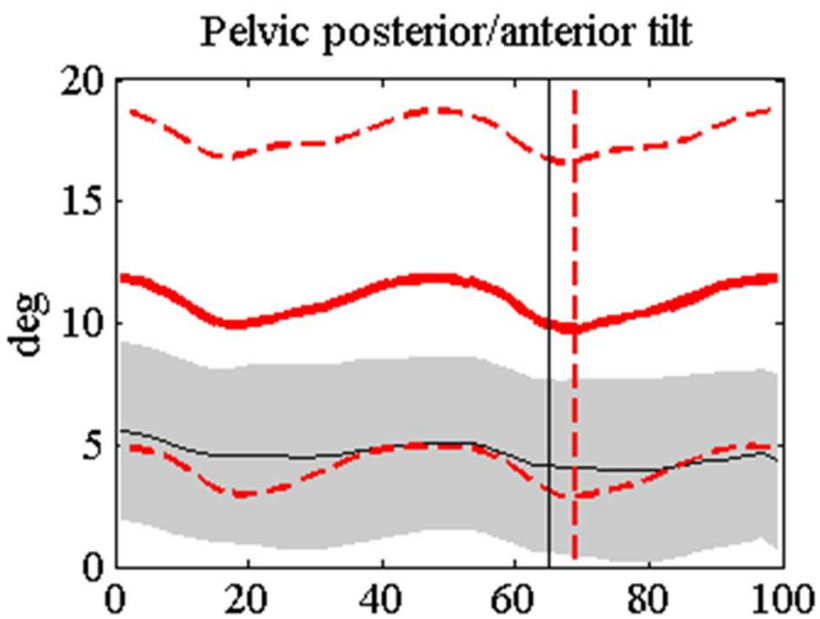
- Achille's tendon contracture:
  - weakness of quadriceps and erectors spinae ⇒ positioning of line of gravity in front of the knees for passive stabilisation
  - increased postural activity of TS (knee in hyperextension)
  - weak TA

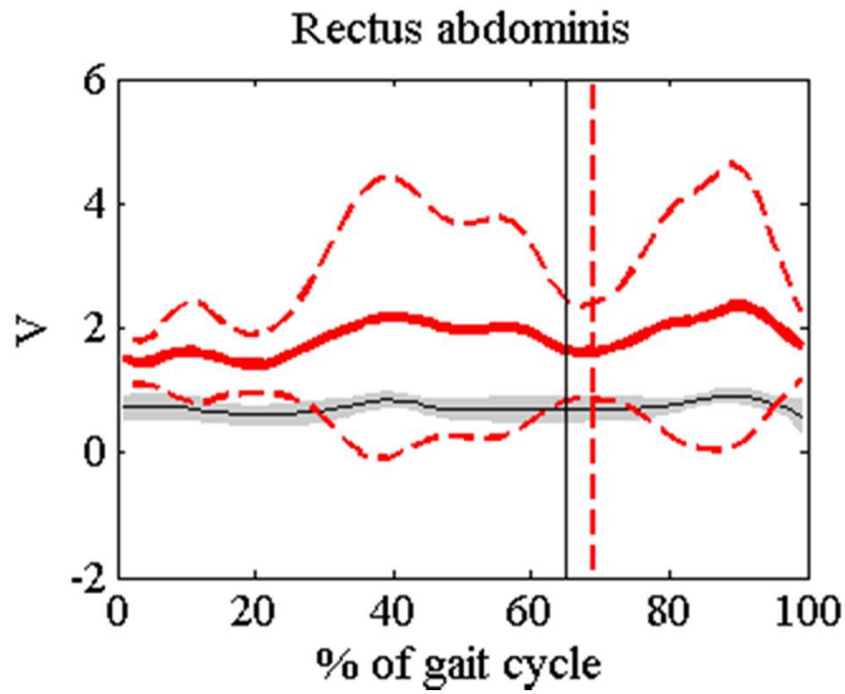
⇒ shortening of tendon, equinus formation

- first compensatory, than contributor to disturbed gait

Sutherland D et al. The pathomechanics of gait in Duchenne muscular dystrophy, 1981.

Pelvic tilt / lordosis in SMA and DMD





The **diminished strength of abdominal muscles in SMA**, type III, necessitates anterior pelvic tilt and lumbar lordosis to relieve load on the abdominal musculature. Similar posture is also required in **DMD but due to weakness of hip extensors**.

Compensatory strategies to negotiate gait problems in patients with DMD

A) *To lower the demand* (to reduce mechanical output requirements of weakened muscles) and *preserve symmetry*

- Gait velocity
- Step length
- Swing time

Temporal gait characteristics in a group of patients with SMA III

	CONTROL (n=9)	SMA (n=7)	p-value (t-test)
Cadence (steps/min)	107,61 (8,06)	94,13 (9,54)	0,815
Gait Velocity (m/s)	1,22 (0,18)	0,84 (0,10)	0,146
Stride Length (m)	1,37 (0,14)	1,08 (0,16)	0,389

Matjacic et al., 2008

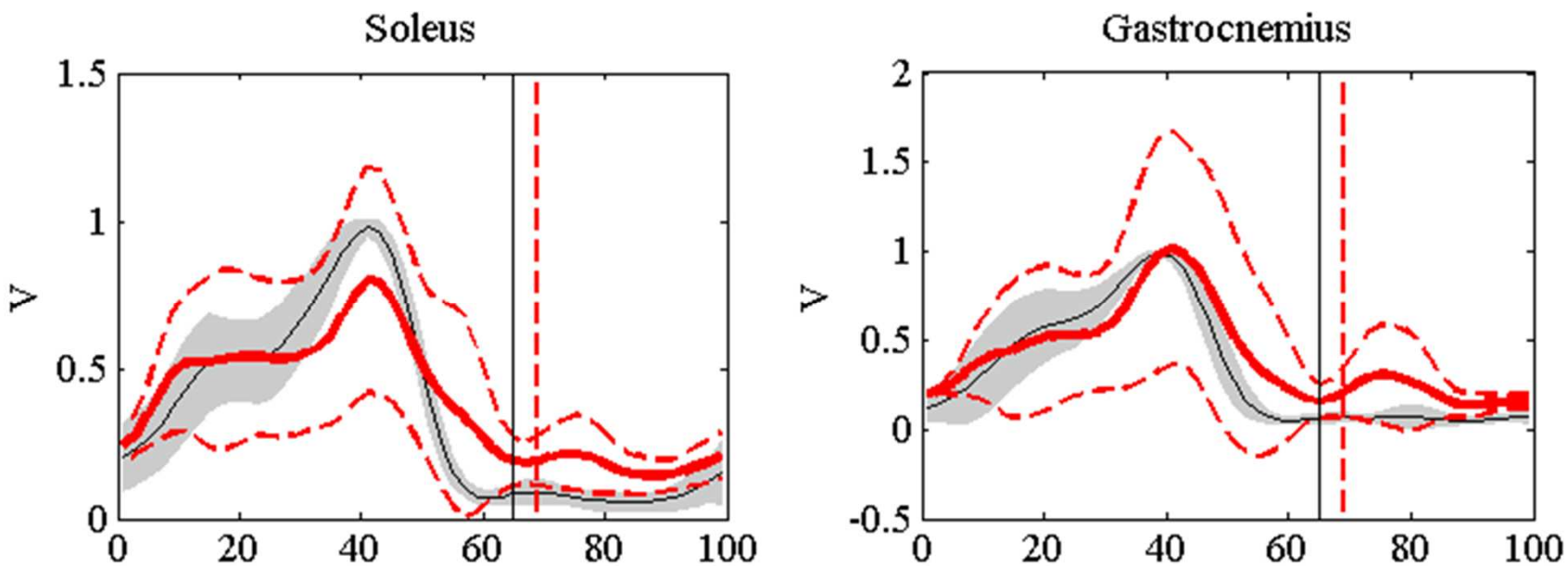
Compensatory strategies to negotiate gait problems in patients with SMA III

B) *to cope with the demand*

→ strategies that minimizes external moments produced by GRF on the knee and hip

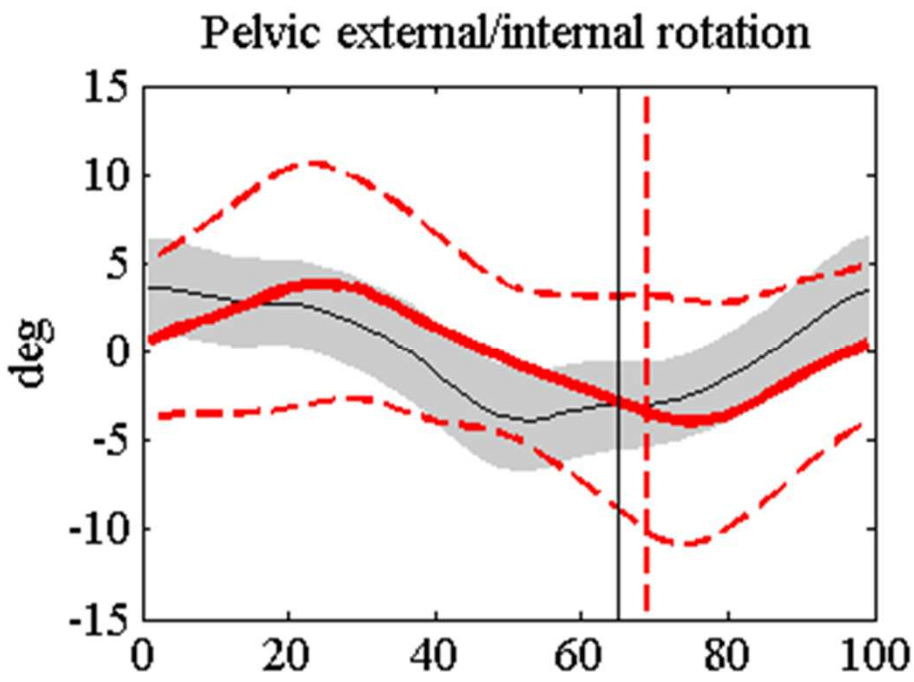
- Stronger activity of plantar flexors
- Anterior rotation of pelvis
- Prolonged activity of contralateral hip abductors

1) Stronger activity of plantarflexors



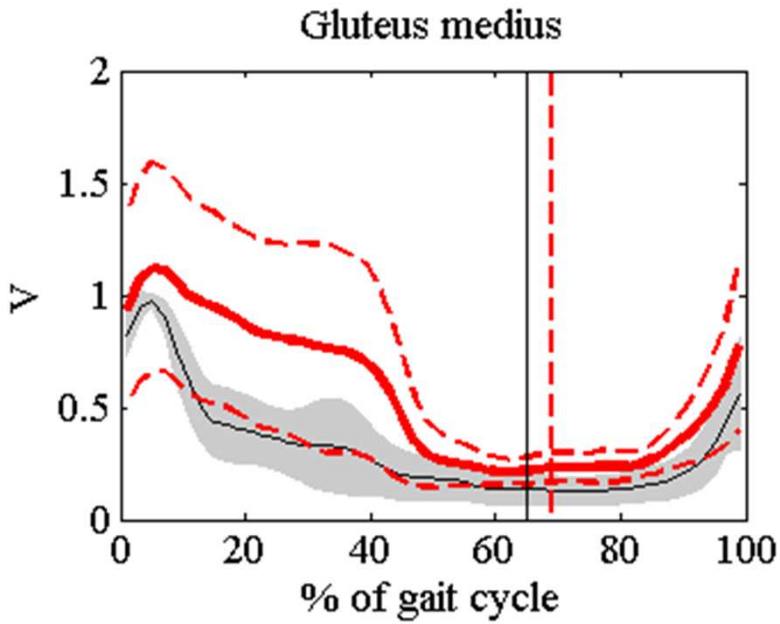
controls COP during loading response and midstance to facilitate minimization of external flexion moment acting on the knee and hip

2) Anterior rotation of pelvis in the stance



facilitates rapid hip extension to secure GRF in front of the knee and behind the hip

3) Prolonged activity of hip abductors on the contralateral side



decreases weight acceptance

Gait of patients with FSH

- Patients with FSH:
  - 92% of max. voluntary torque during dorsal flexion of foot and 30% during plantar flexion of control group.
  - the gait velocity was 68 % of the gait velocity of control group,
  - a significant correlation between peak torque of plantar flexors and MRI changes – but not foot dorsal flexors or flexors of the knee
  - a significant correlation between peak torque of plantar flexors and gait velocity
- But, all of the examined patients had hyperintense lesions in brain tissue on T2-weighted MR images of head.

Some gait and torque data - FSH

N	Limp index]	Gait velocity	max torque knee ext [Nm]	flex [Nm]	pf [Nm]	df [Nm]
1	1,03	0,82	23,70	93,30	8,40	64,00
2	1,07	0,63	74,90	31,50	4,70	1,40
3	1,02	0,47	69,02	1,01	22,80	1,80
4	1,01	1,04	86,50	26,40	21,20	89,40
5	1,03	0,84	9,50	6,80	8,50	1,20
6	1,00	0,95	138,04	33,40	35,80	13,80
7	1,02	0,96	27,30	16,50	34,60	11,40
8	1,01	0,75	87,50	27,30	16,70	3,90
9	1,00	0,97	133,20	72,80	64,40	22,90
mean	**1,03**	**0,82**	**72,27**	**36,11**	**24,12**	**23,31**
SD	**0,02**	**0,18**	**45,90**	**28,34**	**18,72**	**31,75**

Conclusion

- Outcome measure?
- To recognize causes and compensatory mechanisms developed by patients with NMD to negotiate the gait problems of disturbed gait is necessary to plam proper rehabilitation and/or preventive exercise programs :
  - SMA III - targeting maintenance of ankle plantarflexors strength, but also focus on maintaining ability of hip rotators and abductors.