Reconsidering Spasticity

Appendix

More details for those who are interested.

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Longstanding Myths about Spasticity

1. Spasticity causes contractures.
2. All children with diplegic CP & adults with stroke & muscle stiffness have hyperexcitable tonic stretch reflexes.
3. All children with diplegic CP have static, upper motor neuron (UMN) – i.e. motor cortex – lesions.

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Longstanding Myths about Spasticity

4. Spasticity interferes with dexterity
5. Spasticity causes weakness
6. The Modified Ashworth Scale is a valid and reliable test of spasticity.
7. Research has shown that repeatedly injecting the triceps surae with a temporarily paralyzing toxin is the "best practice" to reduce "spasticity" for children with diplegia.

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On Hyperreflexia & Contracture

24 patients ≤13 mos post stroke, randomly selected

Assessments targeted the affected biceps muscle:

- Hyperreflexia (EMG) during passive stretch applied at selected velocities & elbow joint angles
- Resistance to stretch (tissue stiffness) (gauge)
- Contracture (resting muscle length deficit)
- Strength (dynamometer)
- Dexterity (elbow actions & performance scale).

(O'Dwyer NJ, Ada L, Neilsen PD. Spasticity and muscle contracture following stroke. Brain. 1996. 119, 1737)

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On Hyperreflexia & Contracture

- 5 (of 24) subjects exhibited tonic stretch reflexes at a flexion angle of ~20°; only 1 exhibited reflexes in all 3 stretching conditions.
- The biceps **with both** contracture & reflex hyper-excitability were **no more stiff** than those with contracture alone.
- Spasticity does not appear to be related to weakness or loss of dexterity following stroke.
- Spasticity does not seem cause the problem of muscle contracture.
- In fact, **contracture may potentiate** the stretch reflex, at least in some patients.

(*O'Dwyer NJ, Ada L et al 1996)*

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The Modified Ashworth Scale

1 Slight increase in muscle tone, manifested by a catch & release, or by minimal resistance at the end of the ROM when the affected part(s) is (are) moved in flexion or extension

1+ Slight increase in muscle tone, manifested by a catch, followed by a minimal resistance throughout the remainder (< half) of the ROM

2 More marked increase in muscle tone through most of the ROM, but affected part(s) is (are) easily moved

3 Considerable increase in muscle tone, passive movement is difficult

4 Affected part(s) rigid in flexion or extension.

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AS Spasticity Validity Study

- *Damiano et al (2002) sought to determine which components of passive resistance (magnitude, rate of change, onset angle of stretch, or velocity dependence) were most related to Ashworth scores and which were related to motor function in cerebral palsy (CP).*
- *They added EMG to the testing procedure.*

Damiano DL, Quinlivan JM et al 2002

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Original Ashworth scores

0 No increase in tone
1 Slight increase in tone giving a catch when the limb is moved in flexion or extension
2 More marked increase in tone but limb easily flexed
3 Considerable increase in tone, passive movement difficult
4 Limb rigid in flexion or extension

EMG data were used to identify the state of muscle activation during the passive trials, i.e. whether the muscles were quiescent or whether a stretch response was consistently evident in the antagonist.

Ashworth scores were correlated with instrumented torque measures, particularly for the quadriceps, with higher correlations to the rate of change in resistance (stiffness) and onset angle of stretch than to peak resistance torque.

Damiano DL, Quinlivan JM et al 2002

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Incidence of EMG stretch responses with AS testing:

Of the 22 children with CP:

14 showed stretch responses in the hamstrings

10 showed stretch responses in the quadriceps

7 had them in both muscles

5 had none.

Of the 9 TD peers, 0 showed stretch responses.

Damiano DL, Quinlivan JM et al 2002

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The Ashworth & Modified Ashworth Scales

- Have shown moderate to poor reliability under these investigations:

Sehgal N et al 1998; Morris S 2002; Pandyan AD et al 1999; Fosang AL et al 2003; Mehrholz J et al 2005; Yam WK et al 2006; Mutlu A et al 2008; Alhusaini AA et al 2010; Fleuren JF et al 2010.

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MAS Confusion **à** Wrong Conclusions

In Toronto, 51 adults with stroke & MAS scores of 1-4 participated in a study of the relationship between brain lesion location & volume (imaging) & upper limb "spasticity" (i.e. stiffness).

Authors identified the putamen as the area most frequently lesioned. More severe "spasticity" was associated with a higher lesion volume.

THE PUTAMEN IS ONE OF THE STRUCTURES OF THE BASAL GANGLIA WHERE AFTER STROKE INJURY, THE MUSCLES BECOME STIFF AND RIGID. *DYSTONIA – INVOLUNTARY MUSCLE ACTION* IS NOT STRETCH HYPERREFLEXIA.

(Cheung DK, Climans SA et al 2016)

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More features of transformed muscles & fascia after tonic chronic use in shortened state:

- Marked decrease in collagen turnover in both tendon & muscle
- Stiffening of titin filaments within & of epimuscular CT connections between muscles.
- The sliding behavior of the deep fascial packages & the underlying muscle is compromised.
- Adhesions to nerves **à** loss of nerve mobility (glide) & extensibility

(Stecco C et al 2011, Foran JR et al 2005, Huijing PA 2007, Kjær M 2004, Butler DS 1991)

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Chronic E-Stim Effects on Muscle Structure Resemble Use History in CP & Stroke

Features of altered muscle structure in children with CP & in adults with UMN lesions are consistent with experimental studies showing that chronic, tonic electrical stimulation of muscles at low frequencies **à** transformation toward type I muscle fibers.

(Foran JR, Steinman S, Barash I et al 2005; Salmons S, Henriksson J 1981; Eerbeek O, Kernell D et al 1984; Donselaar Y, Eerbeek O, et al 1987; Rose J et al 1998)

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Eventually, with chronic E-stim:

- The fiber size decreases
- The amount & activity of the calcium transport proteins decrease **à**
- Prolonged time to reach peak tension, prolonged relaxation time, & decreased ability to relax.
- The muscle behaves like one that is predominantly made of Type I (tonic) fibers.

(Foran JR, Steinman S, Barash I et al 2005; Salmons S, Henriksson J 1981; Kernell D, Eerbeek O, et al 1987; Donselaar Y, Eerbeek O, et al 1987; Rose J et al 1998)

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Fascial Aptitude for Inter-Structural Sliding

A layer of loose CT resides between deep fascia & the epimysia of skeletal muscles & motor units. This CT is rich in hyaluronic acid which, along with water, may create the gel-like substance that provides for smooth gliding between the surfaces.

Any alteration of the hyaluronic acid can theoretically change the properties of the ECM, affecting sliding, & perhaps restrict sliding & modify the receptors within fascia.

(Stucco C, Stern R, Porzionato A et al 2011)

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Hallmarks of the myofibroblast in wound-healing mode:

- Secretes an ECM substrate (scar)
- Produces adhesion structures with ECM substrate that allow force transmission to occur between MFBs & the surrounding CT.
- Forms contractile bundles composed of *a*-smooth muscle actin.
- Can maintain contractile force over long durations with little energy cost.

(Hinz B, Phan SH, et al 2012, Hinz B 2010)

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Myofibroblasts:

Myofibroblasts develop their highly contractile cytoskeletal apparatus only above a certain ECM stiffness threshold.

(Hinz B, Phan SH, et al 2012, Hinz B 2010, Wells RG 2008)

An increased presence of MFBs is a driving factor behind chronic fascial contractures such as those in Dupuytren's, plantar fibromatosis, excessive scar formation, & frozen shoulder.

(Hinz B 2006, Gabbiani G 1998)

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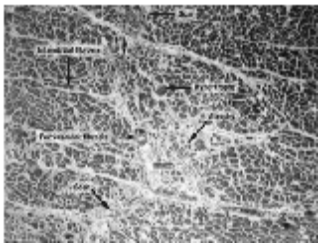
Example of Myofibroblast Activity

Tissue sample, post mortem shows myofibrobast-mediated structural remodeling of myocardium in hypertensive heart disease.



(Weber KT et al 2012)

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Fascial Stiffness Regulation

"Imbalance of this regulatory mechanism results in increased or decreased myofascial tonus, or diminished neuromuscular coordination, which are key contributors to the pathomechanisms of several musculoskeletal pathologies and pain syndromes."

(Klingler W, Velders M et al 2014, p. 439)

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Muscle Length Adaptation is Myogenic vs. Neurogenic

Small animal studies investigated the effects of either allowing the targeted tissues to shorten or maintaining their length (in a cast or on a mounting apparatus in the lab) while stimulating the muscle with electricity or with tetanic toxin.

When length was maintained, there was no loss of sarcomeres. The adaptation mechanism is in the muscle.

(*Tabary JC, Tardieu C, et al 1981, Huet de la Tour HE, Tardieu C, 1979 & 1979a, Williams PE, Goldspink G 1976, Goldspink G, Tabary C, et al 1974)*

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5 More Kinesiological & Physiological Factors to Consider

1. The true nature of the brain "injury" in pyramidal types of CP
2. The role of deficits in trunk & hip control
3. Fascial architectural & operational features
4. Fascial behavior under prolonged stretch conditions & stress
5. The predicament of the peripheral nerves that track through transformed tissues.

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Reconsidering Signs of "Spasticity"…

- What is the influence of the added ECM on the movement & extensibility of adjacent nerves?
- Does transformed tissue dehydration cause binding of the nerves?
- Does EMG activity increase when nerves that are bound by adhesion are passively stretched at any speed?
- Is it possible that adhesions constraining nerves impair functional dexterity?

(Yucesoy et al 2007, Frascarelli M et al 2005, Castle et al 1979, Butler DS 1993)

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Ashworth Scale / EMG Agreement

Stretch responses on EMG showed **near complete agreement at extremes of the scale,** with marked inconsistencies in mid-range values.

(Damiano DL, Quinlivan JM et al 2002)

Question: *How do entrapped nerves respond to stretch? Do we know that the EMG stretch response is not a peripheral event, perhaps related to nerve entrapment in dehydrated, atrophied muscle and fascia?*

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A "Long-Term" Botox-A Follow-Up Study

After multiple BTX-A injections into gastrocs of children with CP, at **à** 3.5 years follow-up:

"…BoNT-A can be effective in reducing muscle tone [immediately] over a longer period, but <u>not in preventing development of contractures</u> in spastic [?] muscles."

(Tedroff K, Granath F, et al. 2009. Long-term effects of botulinum toxin A in children with CP. Devel Med Child Neurol. 51(2):120.)

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Serial Casting With & Without BTX-A Follow-Up Study at 12 Months

" Contrary to our hypothesis, the addition of botulinum toxin A to a serial casting regimen led to earlier recurrence of spasticity [?], contracture, and equinus during gait."

(Kay RM, Rethlefsen SA, et al 2004, p. 2377)

The use of BTX-A injections prior to below-knee serial casting has since ceased at Children's Hospital Los Angeles.

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Effect of BTX on Brain Mapping (DTI)

- 36 children w/ spastic diplegic CP, all born full term
  - Group A: BTX-A + plus PT
  - Group B: PT alone
- DTI & GMFM scores at baseline & after 6 months

At 6 months, both groups gained in sensory & motor tract formation & GMFM, but the difference between groups I & II was statistically insignificant.

Conclusion: "*the addition of BTX to physiotherapy regimen does not influence the outcome at 6 months with similar insult in children with term diplegic spastic CP." p. 647.*

(Chaturvedi SK, Rai Y, Chourasia A, et al. 2013)

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BTX-A-Induced Pathophysiology

Study of the effects of monthly injections observed at 1, 3, & 6 months - vs. none

- Rabbit quadriceps muscle strength
- Muscle mass (atrophy)
- % Contractile material in Vastus Lateralis (VL), Rectus Femoris (RF), & Vastus Medialis (VM).
- Contralateral muscles

(Fortuna R, Vaz MA, et al 2011)

Animal studies precede human trials to determine effects & toxicity. Animal responses are widely considered to be relevant to humans, particularly with regard to safe use.

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Strength losses after monthly injections, obtained at 1, 3, & 6 months respectively:

- Injected muscles, strength decreased 88%, 89%, & 95%, respectively.
- Strength in same muscle on contralateral side also decreased by increasing increments.

Injected muscles showed replacement of contractile tissue with fat, which contributed to "muscle mass" at 6 months.

(Fortuna R, Vaz MA, et al 2011)

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Implications:

- 1st BTX-A injection **à** loss of strength was mainly due to denervation effect.
- At 6 months of monthly injections, similar loss of strength was due to atrophy & loss of contractile tissue vs. denervation.
- With >3 injections, non-targeted muscles lose strength, muscle mass, & contractile tissue.

(Fortuna R, Vaz MA, et al 2011)

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Do the BTX-A-injected muscles recover?

Healthy (not transformed) rabbit muscle strength & contractile material did not fully recover within 6 months of BTX-A treatment.

(Fortuna R, Vaz MA, Sawatsky A et al 2015, *Fortuna R, Vaz MA, et al 2011)*

1 rabbit year = 9 human years. So might human tissue fail to recover in 4.5 years?

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