“Corticospinal System Development Depends on Motor Experience”

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Overview

- Brief background- corticospinal system
- Introduction/hypothesis
- Materials and methods
- Results/discussion

Corticospinal System

- Originates in the primary motor cortex, specifically the precentral gyrus
- Project to specific regions of the spinal cord,
- Cervical enlargement- brachial plexus nerves, responsible for innervating upper limb
  - Roughly C4-T1
- Last motor system to develop

Introduction

- Hypothesis- how motor experience shapes motor system development
- Isolate particular motor pathway and motor behavior controlled by that pathway
- Limb movements expressed soon after birth, how does preventing these movements affect normal development of corticospinal tract?

Materials and Methods

- Use Botulinum toxin injections in one limb of cats during weeks 3-7 (CS axon termination refinement period)
- CS axon terminals evaluated by anterograde tracer at the end of week 8 or in maturity
- Efficacy of injections evaluated by behavioral tasks testing limb movements
- Reinjected at weekly intervals
- Behavioral testing began at 4 or 10 weeks after the last injection

Behavioral testing

- Prehension task- 1 week of training, 1 week of testing
- Evaluated task by entrance into the cylindrical target well without touching walls, and presence of forearm supination during food withdrawal
- Aiming and grasping errors characteristic of corticospinal deficiency

Surgical Procedure

- Craniotomy- lateral potion of the frontal lobe contralateral to the BTX-injected limb
  - Forelimb representation of motor cortex
  - Injected anterograde tracers into lateral portion of forelimb representation
- At 8 weeks or longer, depending on age, cats killed, brain and spinal cord removed for analysis

Morphological analyses

- Topographic analysis in gray matter of tracings- number of pixels = total length of axonal label on the section
- Measured length, number of branch points, and number of axon varicosities of CS axon terminals
- Single axon reconstruction on serial sections- sections depended on density of labeling and absence of artifacts

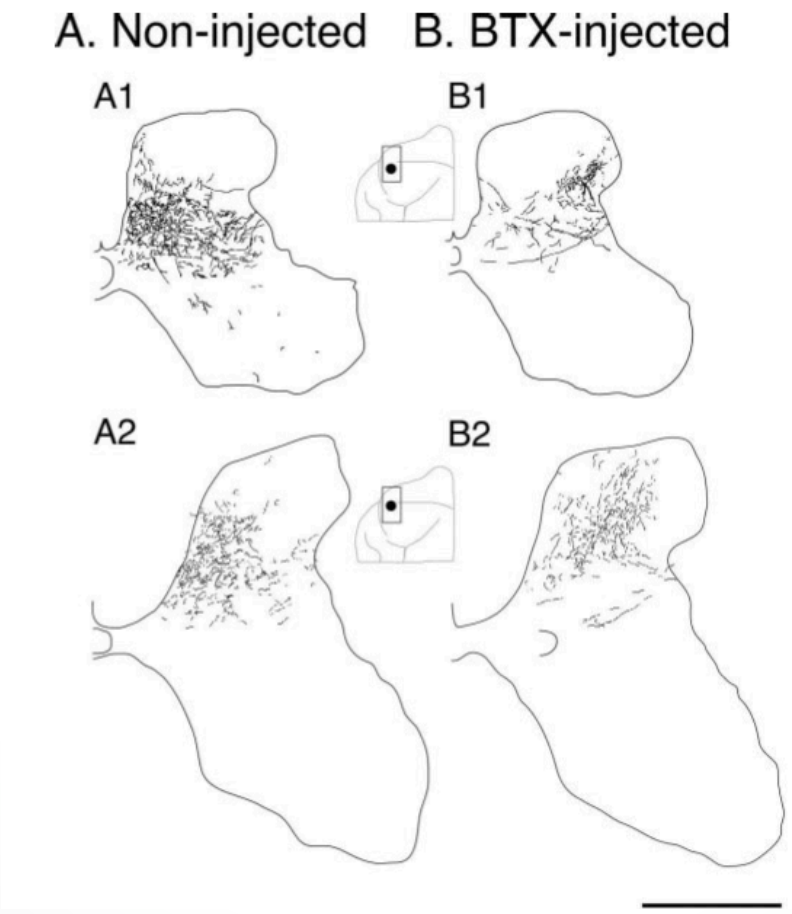
Results

- Preventing limb use between weeks 3 and 7 impairs prehension later in development and in maturity- permanent impairment in capacity to coordinate supination with shoulder retraction
  - No preferences for injected/control limb
  - No differences in trajectory error (no contact made with tube)
  - Impairment in withdrawal phase
    - Supination absent
    - 2 animals tested 4-6 weeks after, reaches made by non-injected limb- supinated 62% more often
    - 3 anmials tested 10-14 weeks after, 57% difference

Results

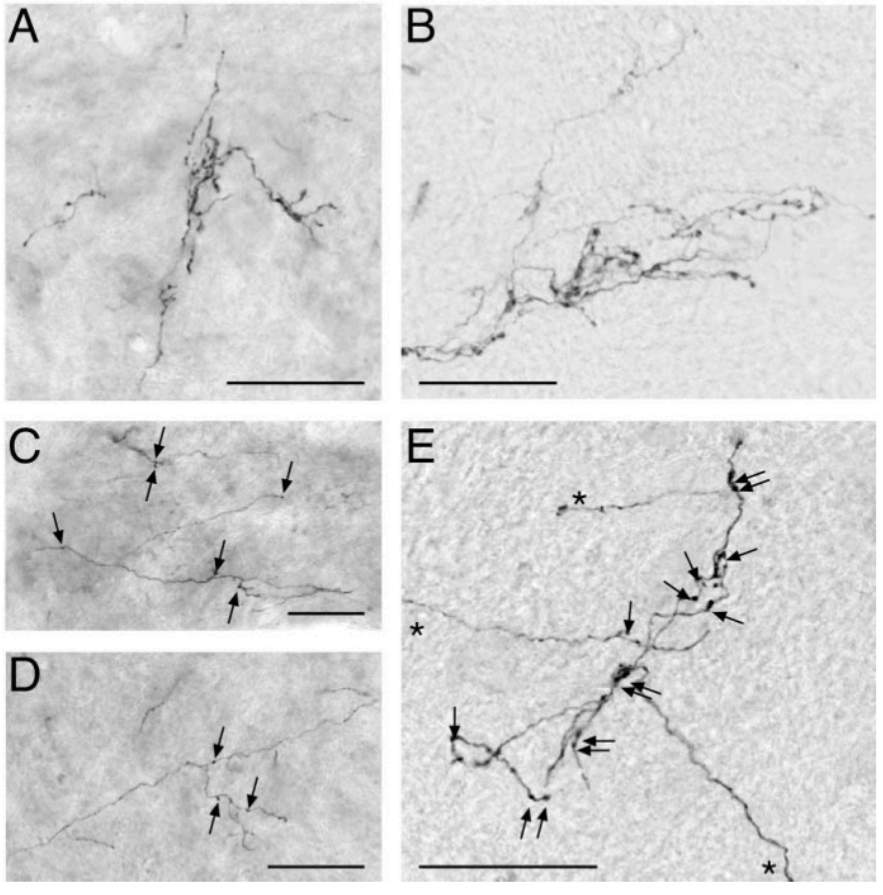
- Preventing limb use between weeks 3-7 disrupts development of the topography of the CS projection
- Paired animals for comparisons by similar motor cortex injections to ensure differences not caused by injection site of tracer
- Pooled data from animals with different cortex injection sites, but within age-matched groups
- Analysis of CS axon terminals at C8

Results



Results

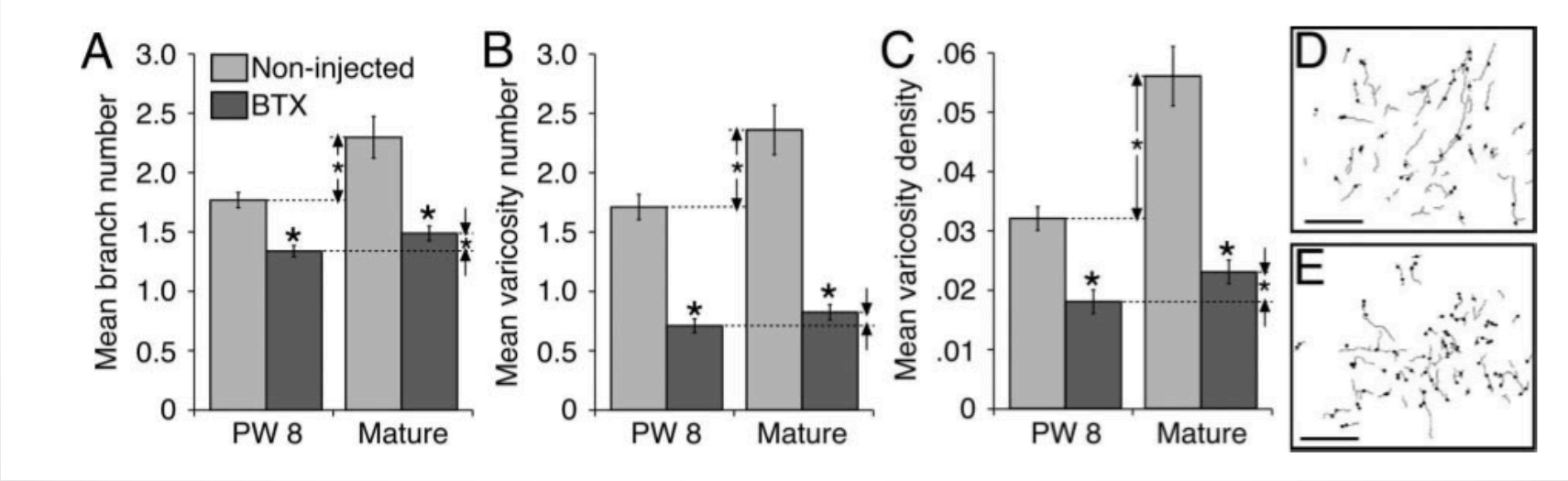
- CS axon terminal morphology is impaired after early postnatal limb disuse



Results

Morphometric analysis on terminal and preterminal CS axons at C8 within densest field of terminations

After BTX injections, the mean numbers of CS axon branches, mean number of varicosities, and mean varicosity density were all significantly reduced, both at 8 weeks and in maturity



Discussion

- Absence of limb movement reduce afferent input to cervical cord
- Preventing limb movement alters somatic sensory input, and the loss of sensory input alters motor control
- Decreased termination density in medial dorsal horn and intermediate zone may be activity dependent
- Failure to establish connections in particular regions and lack of axon branch and varicosity development caused by reduced activity-dependent growth

Discussion

- Transient CS terminations- inverted U curve
  - Sparse at first, grow as system develops, and then are eliminated
  - Eliminated of transient segmental branches least affected
  - Preventing limb use would reduce activity-dependent growth = decreased axon branching and varicosity density, mute synaptic competition==long, sparsely branched axons

Failure to regain normal function

- After limb movement returned, minimal subsequent CS axon terminal growth
- CS axons normally continue to develop between weeks 8 and 12
- Long term consequences of competitive disadvantage compared with other pathways. Become less effective in driving spinal circuits

CS control signals

- Disruption of CS projection to the cervical enlargements negatively affects cats capacity to retrieve food correctly
- less CS axon branching and fewer varicosities would decrease the potential for control signals to activate spinal interneurons strongly
- Importance of early motor experience for complex, coordinated movements