Toward regenerating or repairing “cortico-spinal” nerve / neuron connections in SCI; learning how they grow initially can help us get them to re-grow

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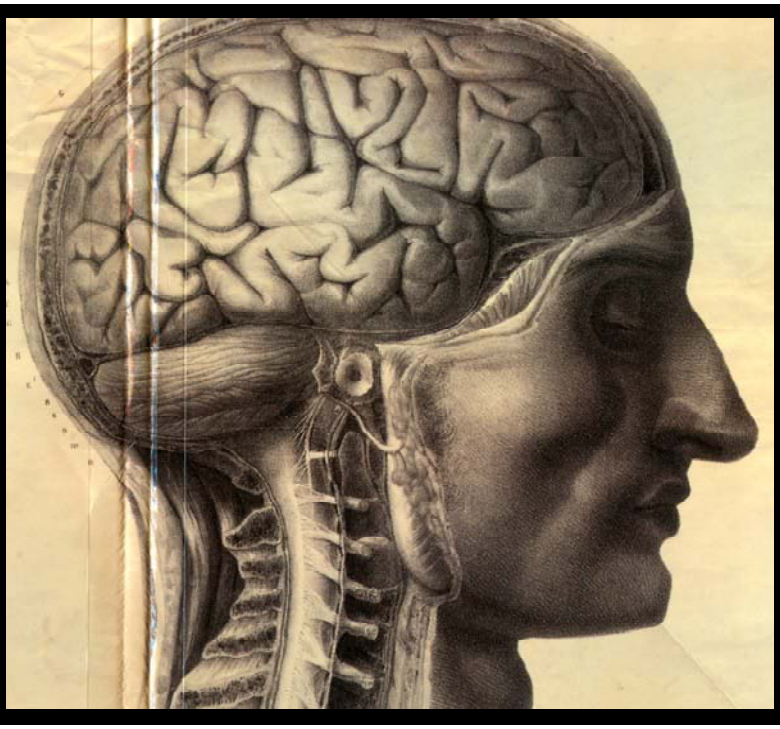
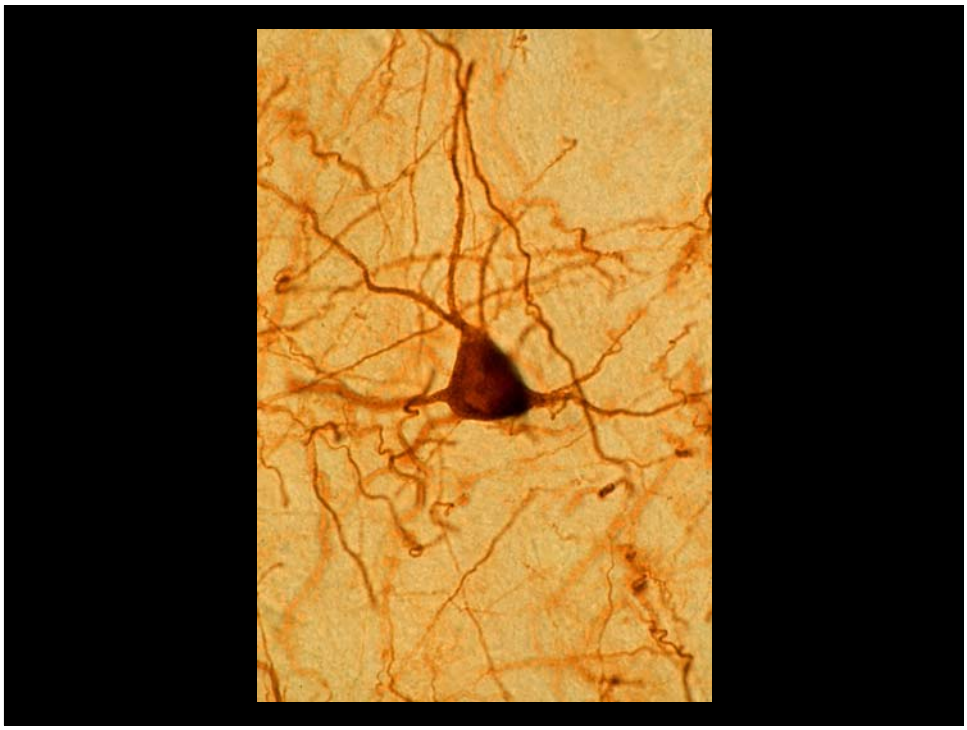
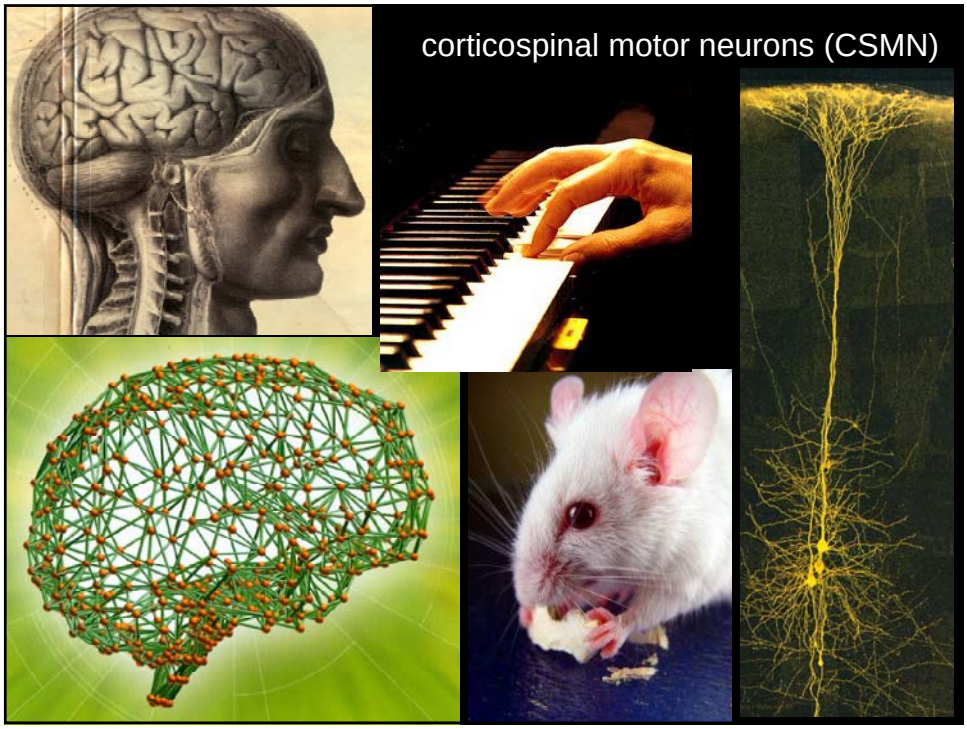
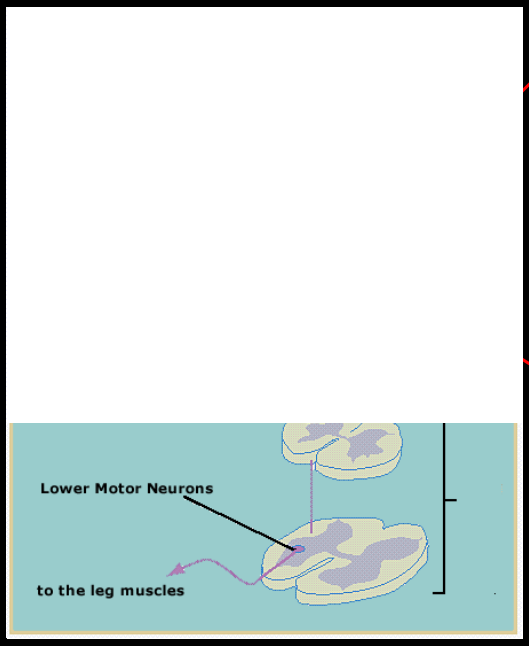
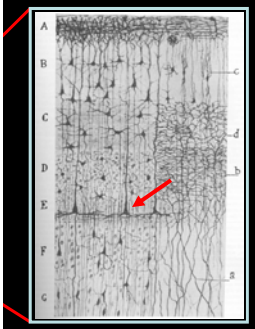






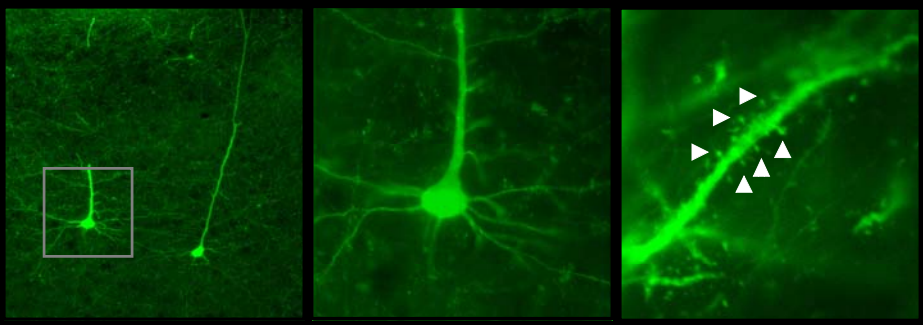
Corticospinal neuron axon damage in SCI; lost motor function





S. Ramon y Cajal

Long-distance connections matter:
A human neuron the size of your fist might send its axon a distance of several miles (!) in the spinal cord, and connect with a target area the size of the projection screen (!)



"Edwin Smith" Eqyption papyrus c. 1,700-3,000 B.C.E.

...But the functional specialization of the brain imposed on the neurones two great lacunae; proliferative inability and irreversibility of intraprotoplasmic differentiation. It is for this reason that, once the development was ended, the founts of growth and regeneration of the axons and dendrites dried up irrevocably. In adult centres the nerve paths are something fixed, ended, immutable. Everything may die, nothing may be regenerated.

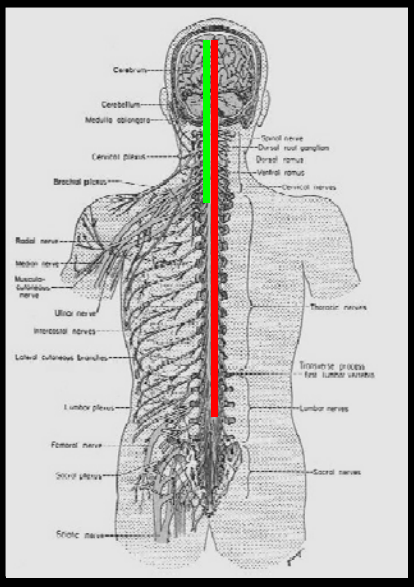
It is for the science of the future to change, if possible, this harsh decree. Inspired with high ideals, it must work to impede or moderate the gradual decay of the neurones, to overcome the almost invincible rigidity of their connections, and to re-establish normal nerve paths, when disease has severed centres that were intimately associated.

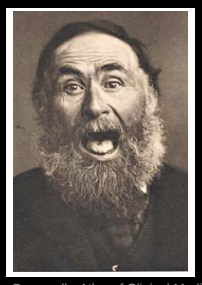
It would be ingenuous to pretend to go farther in the solution of a problem so full of difficulties. We must recognize that, in the matter of neurogenesis and nervous regeneration, we are still in the phase of collection of materials. As a consequence our hypotheses are premature, and they can aspire neither to perfection nor to permanence. They are conceptions to point the way, conjectures thrown out to excite and keep up investigation...

Santiago Ramon y Cajal

Degeneration and Regeneration of the Nervous System, 1913.

There is a range of different corticospinal connections we would like to regenerate to help in SCI





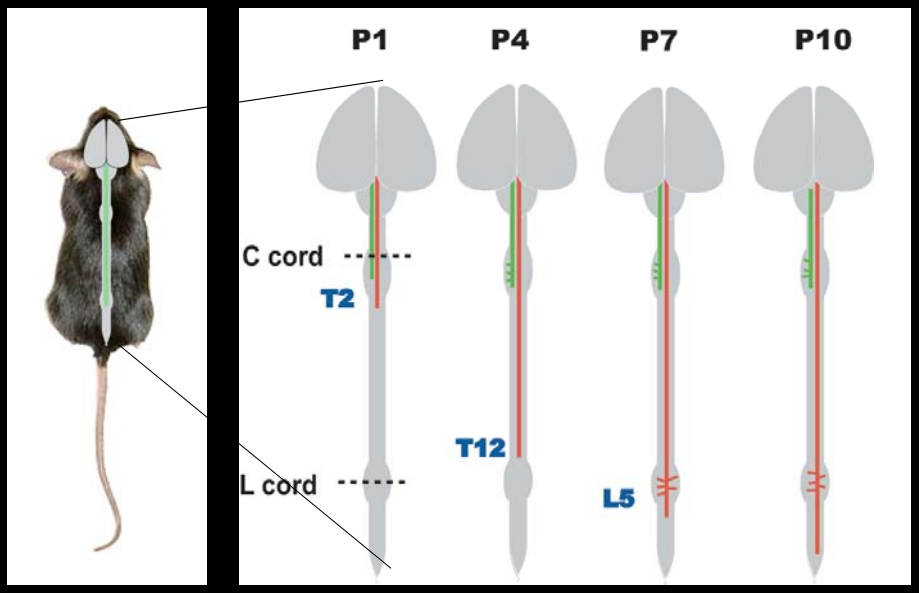
Bramwell, *Atlas of Clinical Medicine*, 1892

Cervical

Strumpell, *Arch Psy Nerv*, 1880

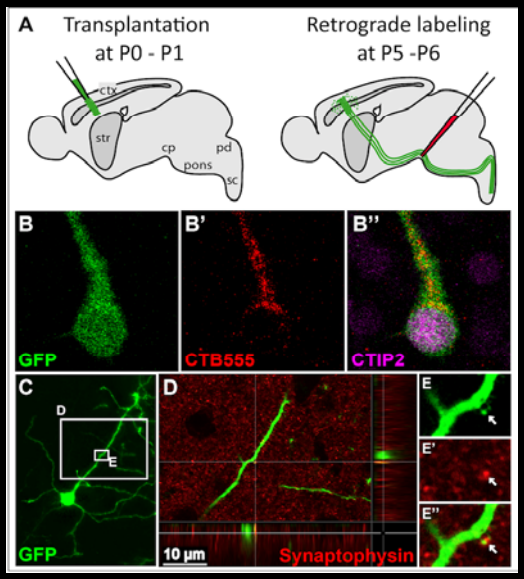
Lumbar and sacral

Development and approaches to regeneration of the corticospinal tract in mice helps get to human therapy

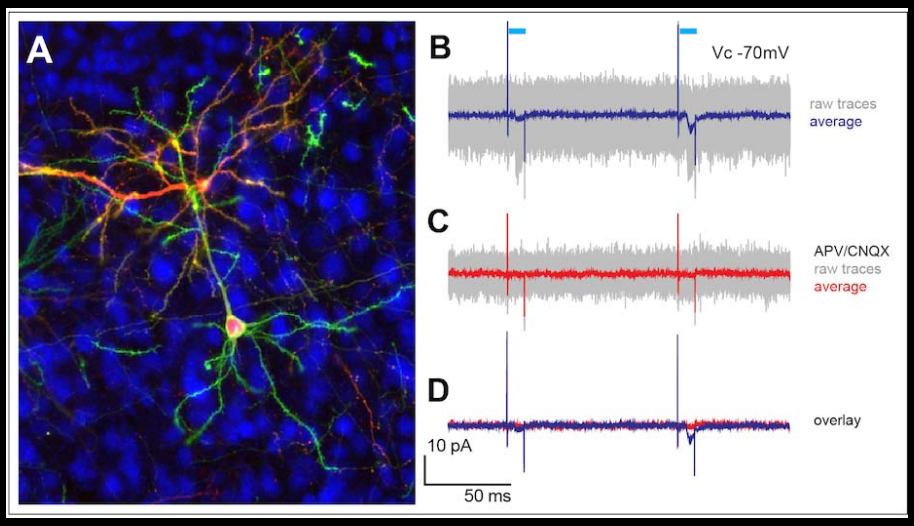


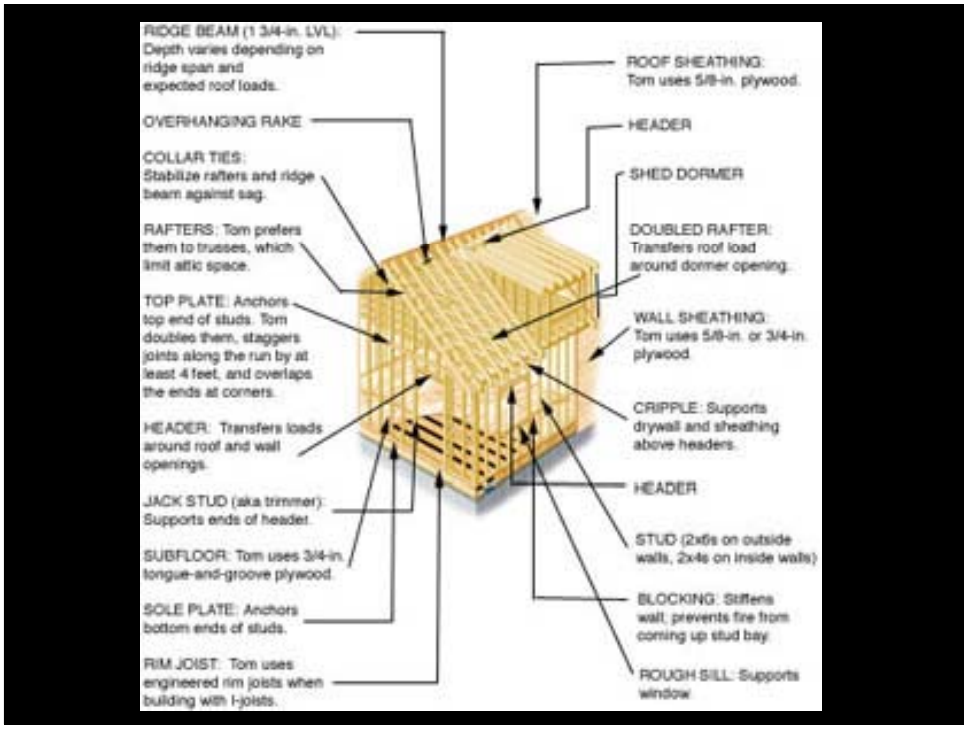
Adapted from Bareyre et al., *Nat Med*, 2005

Transplanted immature neurons maintain / acquire correct molecular identity, and establish subcerebral axon projections



New cortical projection neurons form correct long-distance functional output synaptic connections with host neurons, and receive incoming connections and synapses from distant areas




RIDGE BEAM (1 3/4-in. LVL): Depth varies depending on ridge span and expected roof loads.
OVERHANGING RAKE
COLLAR TIES: Stabilize rafters and ridge beam against sag.
RAFTERS: Tom prefers them to trusses, which limit attic space.
TOP PLATE: Anchors top end of studs. Tom doubles them, staggers joints along the run by at least 4 feet, and overlaps the ends at corners.
HEADER: Transfers loads around roof and wall openings.
JACK STUD (aka trimmer): Supports ends of header.
SUBFLOOR: Tom uses 3/4-in. tongue-and-groove plywood.
SOLE PLATE: Anchors bottom ends of studs.
RIM JOIST: Tom uses engineered rim joists when building with I-joists.
ROOF SHEATHING: Tom uses 5/8-in. plywood.
HEADER
SHED DORMER
DOUBLED RAFTER: Transfers roof load around dormer opening.
WALL SHEATHING: Tom uses 5/8-in. or 3/4-in. plywood.
CRIPPLE: Supports drywall and sheathing above headers.
HEADER
STUD (2x6s on outside walls, 2x4s on inside walls)
BLOCKING: Stiffens wall; prevents fire from coming up stud bay.
ROUGH SILL: Supports window

Brain and Spinal Cord Repair: no longer science fiction