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Structural and Functional Changes in the Brain after Surgically Repaired Median Nerve Injury

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Avhandlingen kommer att försvaras på engelska.

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Abstract
Despite the best available surgical repair, traumatic median nerve injury within the forearm typically causes lifelong impairment in hand function. This stems from an inadequate reinnervation of the nerves supporting sensory functions of the thumb, index and long finger, and of nerves supplying intrinsic hand muscles. This thesis examines whether median nerve injuries can cause structural and functional changes in the brain. Understanding such changes can help the development of new treatments for improved recovery of hand function.

The first study introduces a novel apparatus and paradigm for examining tactile neural processing with fMRI under well-controlled behavioral conditions. The scientific issue challenged was whether, in healthy adults, different cortical areas could be involved in processing tactile stimuli depending on their temporal frequency content. In a threshold-tracking paradigm, the participants' task was to detect oscillatory mechanical stimulations of various frequencies delivered to the tip of either left or right middle finger. Regardless of stimulated hand, tactile detection of audible frequencies (20 and 100 Hz) engaged the left auditory cortex while detection of slow object displacements (3 Hz) engaged visual cortex. These results corroborate and advance the metamodal theory of brain function, which posits that brain areas can contribute to sensory processing by performing specific computations – those for which they are specialized – regardless of input modality.

The second and third studies concern structural and functional changes in the brain of adults with one reinnervated hand after an injury transecting the median nerve in the forearm. Healthy individuals matched for sex, handedness and age served as controls. Irrespective of side of injury (left or right), voxel-based morphometry applied on T1 MR-images revealed reductions of gray matter in the left ventral and right dorsal premotor cortex, and reductions of white matter in related commissural pathways. We interpreted these as activity-dependent structural adaptations to reduced neural processing linked to restrictions in the diversity of the natural manual dexterity repertoire caused by a disturbed innervation of the hand. Conversely, increases in gray matter were observed bilaterally in a motion-processing visual cortical area. We interpreted this as a structural manifestation of increased neural processing linked to greater dependence on vision for controlling manual dexterity due to impaired tactile innervation of the affected hand.

To reveal functional changes in tactile cortical processing after median nerve reinnervation, we recorded brain activity using fMRI when study participants performed perceptually demanding tactile threshold-tracking and oddball detection tasks with our novel apparatus. The hand representation of the contralesional primary somatosensory cortex (S1) showed greater activity compared to the controls when the reinnervated index finger was engaged in the tasks, but strikingly also when fingers of both hands innervated by uninjured nerves were engaged, i.e., little finger of the reinnervated hand and index and little finger of the other hand. The generally increased activity indicates a general disinhibition of contralateral S1, suggesting that increased functional reorganization is an ongoing process of chronic nerve injury. In addition, prefrontal areas implicated in processes that support decision-making and response selection showed increased activity, suggesting that such processes were more computationally demanding after nerve injury.

Together, these results indicate that brain areas can undergo significant changes after peripheral nerve injury, even when followed by best available surgical repair and reinnervation conditions. These changes can include activity-dependent structural adaptations consisting of either regional decreases or increases in gray matter concentration, which likely depend on an area's functional specialization and on changes in its processing load due to behavioral constraints imposed by the injury. Moreover, the results also suggest that the affected hand's primary cortical projection area is still in a state of ongoing functional reorganization despite the fact that peripheral reinnervation of the hand should have been completed long ago, which should inspire the development of new therapeutic regimens for what today is considered a chronic impairment.

Keywords
Humans, Hand, Touch, Peripheral nerve injury, Magnetic resonance imaging, Somatosensory Cortex, Cortical plasticity

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