Gait Control and Locomotor Recovery after Spinal Cord Injury

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presented by

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Summary

The gait of patients with an incomplete spinal cord injury (iSCI) has been studied previously. The most widely examined parameters to characterize iSCI gait are walking speed and time-distance measures (e.g., step length, step frequency, gait-cycle phases). In a clinical setting, the functional recovery of iSCI patients is routinely captured by specific outcome measures such as the 10-meter walk test (10mWT), the 6-minute walk test (6minWT) or the walking index for spinal cord injury (WISCI), which has been specifically established for this particular group of patients to score their walking ability. These measures are useful to monitor gross motor function and recovery during rehabilitation, but lack the ability to elucidate underlying mechanisms of gait alterations and recovery or subtle changes in locomotor pattern. In order to be able to appreciate the injury-induced deficits in locomotor control and to capture changes in motor function that may not be visible to the naked eye a sensitive and comprehensive tool is of need.

The easiest way of assessing walking capacity is to collect data of walking speed and distance. Yet, one of the most obvious gait alterations in subjects with iSCI is an impaired gait quality. In the past, gait quality has been scored by trained investigators that rate defined features of walking. However, more complex movements that require precise spatial and temporal coordination of several joints and body segments are not easy to detect by mere observation. In the first study of this thesis, we evaluated the lower-limb coordination by means of combined hip-knee angular profiles (cyclograms). Patients showed distinct types and extents of cyclogram alterations and were thereupon categorized into four groups of impairment. The cyclogram seemed to reflect the underlying deficits as it correlated well with walking performance (speed) but could not be modulated with increasing speeds in contrast to a converging normalization in all control subjects. The intralimb coordination apparently is a sensitive indicator of motor-control impairment after spinal cord injury.

We next evaluated a variety of gait-related parameters in order to find alterations of locomotor control after iSCI. With the aim of establishing a comprehensive framework to examine the organization of walking behavior in humans and how this organization gets distorted by insults to the spinal cord we
chose a data-driven holistic approach for analyzing a multivariate set of data. This approach prevents a certain investigator-induced bias that arises when more or less arbitrarily pre-selecting a specific outcome measure. Multivariate in this case means variables of different modalities, i.e., objective electrophysiological measures that represent the integrity and electrical conductivity of specific spinal fiber tracts, kinematic measures that describe the extent of movements and body-segment coordination (i.e., gait quality) as well as measures that quantify locomotor performance such as walking speed and distance. Hence, clusters of parameters were identified that were or were not altered in iSCI patients and that were distinctly modulated with respect to speed. These findings suggest that there are distinguishable domains of neural control of walking that may be differently affected in specific neurological disorders.

Consequently, the question arises as to which of these parameters change over time and what this might reveal about the mechanisms of recovery. These questions were addressed in the third study where the gait of iSCI patients was analyzed at several time points during rehabilitation in order to reveal those parameters that most strongly contribute to recovery, and also to reveal the responsiveness of the multimodal factors to an improvement in walking speed. Interestingly, the responsiveness of a single measure did not necessarily contribute to recovery, which is rather affected by the contribution of mutually interacting parameters.

It remains to be elucidated where exactly the plastic changes leading to functional recovery take place and by what mechanisms they are mediated. The great challenge of spinal cord research is the cure for paralysis, or, in other words, a way to induce functional neural repair in the growth-inhibiting environment of the central nervous system (CNS). Even though it is known that spontaneous regeneration of severed neural tissue does virtually not occur in the CNS, recovery on a functional basis does happen. In the fourth study we demonstrated that the spinal cord is capable of extensive plastic changes induced by pathological processes in the absence of motor deficits and only minor sensory impairments.
To accelerate the success of future clinical trials, the bridging from bench to bedside needs to be encouraged. Outcome measures should be standardized across species in order to appreciate differences and similarities. It could be shown that after a cervical hemisection of the spinal cord, equivalent to a the Brown-Séquard Syndrome in patients, humans and primates show superior recovery of function mediated by the corticospinal tract compared to rats. These findings support the importance of studies performed in primates to minimize the gap between preclinical and clinical outcome.
Zusammenfassung

Der Gang von inkomplett querschnittgelähmten Patienten (iSCI, engl. incomplete spinal cord injury) wird bereits seit längerem untersucht. Die am häufigsten verwendeten Größen um das iSCI Gangbild zu charakterisieren sind Gehgeschwindigkeit und Gangzyklus Parameter (z.B. Schrittlänge, Schrittfrequenz, Phasen des Ganzyklus). Im klinischen Alltag wird die funktionelle Erholung von iSCI Patienten mittels spezifischer Messgrössen bestimmt, wie z.B. der 10-Meter Gehtest (10mWT), der 6-Minuten Gehtest (6minWT) oder der walking index for spinal cord injury (WISCI), der eigens für diese spezifische Patientengruppe etabliert wurde um ihre Gehfähigkeit bewerten zu können. Diese Messgrössen eignen sich gut um die allgemeine motorische Funktion und deren Erholung während der Rehabilitation zu verfolgen, sind jedoch nicht in der Lage die zugrundeliegenden Mechanismen, die zu Gangstörungen führen sowie deren Erholung oder subtile Unterschiede des Gangmusters zu erkennen. Um die verletzungsbedingten Defizite der Lokomotionskontrolle und Veränderungen der motorischen Funktion, die sich dem blosen Auge entziehen, erfassen zu können, braucht es sensitive und umfassende Tools.

sensitiver Indikator für eine Beeinträchtigung der motorischen Kontrolle nach einer Rückenmarksverletzung.


Folglich stellt sich die Frage, welche dieser Parameter sich im Verlauf ändern und was dies bezüglich der zugrundeliegenden Mechanismen von Erholung bedeutet. Diese Fragen wurden in der dritten Studie angegangen, wo das Gangmuster von iSCI Patienten zu unterschiedlichen Zeitpunkten während ihrer Rehabilitation analysiert wurde um diejenigen Parameter zu finden, die am stärksten zur Erholung beitrugen und die am ehesten mit einer verbesserten Geschwindigkeit einhergehen. Interessanterweise waren nicht zwingend jene Parameter, die sich am meisten veränderten auch jene, die zur Erholung beitragen. Diese ist vielmehr von der Wechselwirkung unterschiedlicher Parameter abhängig.

Um den Erfolg von klinischen Studien in Zukunft zu beschleunigen muss ein Brückenschlag from bench to bedside gefördert werden. Messparameter sollten zwischen den unterschiedlichen Spezies standardisiert werden um Unterschiede und Gemeinsamkeiten feststellen zu können. Es konnte gezeigt werden, dass nach einer Hemisektion des zervikalen Rückenmarks, vergleichbar mit dem Brown-Séquard Syndrom bei Patienten, der Mensch und der Primate eine bessere Erholung der Funktionen zeigen, die durch die Kortikospinalbahn gesteuert werden, im Vergleich zu Ratten. Diese Erkenntnisse unterstützen die Wichtigkeit von Studien in Primaten, damit der Abstand zwischen präklinischem und klinischem Erfolg verringert werden kann.