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2016

document version

Publisher's PDF, also known as Version of record

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citation for published version (APA)

Slout, L. H. (2016). *Advanced technologies to assess motor dysfunction in children with cerebral palsy*.

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Summary

Walking is often a challenging or even impossible activity for individuals with cerebral palsy (CP). Limitations in walking can have a major impact on a person's daily life and therefore rehabilitation medicine aims to preserve or restore walking capacity. Several treatments are available that target the underlying impairments which hamper movement. Unfortunately, the selection of an optimal treatment for a specific patient is challenging, because of the heterogeneity of the CP population, the wide variety of (co-existing) impairments, the complex relation between impairment and gait limitations as well as compensation strategies that obscure these gait limitations (**chapter 1**). Therefore, measurements are necessary that allow for identification of impairments, in order to aid subject-specific treatment selection.

In current clinical practice, manual physical examination and gait analysis are used in combination to identify underlying impairments and assess their actual influence on gait. However, the manual tests are subjective, not suitable to quantify the contribution of different impairments and only performed during passive conditions. Current gait analysis on the other hand is not well able to discern compensation strategies, or decipher the precise cause of gait limitations. Specialized technologies could be used to improve the identification of impairments and their effect on gait. The aim of this thesis was to evaluate the feasibility and validity of advanced technologies, i.e. the motorized hyper-resistance test and interactive gait lab, to clinically assess motor (dys)function in children with CP.

Alternatively to the passive manual physical examination tests, motorized instrumented assessment allows for standardization of the imposed movement and quantification of the body's response. The motorized hyper-resistance test introduced in **chapter 2** aims to quantify the contribution of neural (reflex and background muscle activity) and tissue (stiffness) related resistance to exerted rotations around the ankle joint using a non-linear neuromuscular model. Rotations were applied at two different speeds and two different knee angles to discriminate between the characteristics of the soleus and gastrocnemius muscle. In order to validate the outcomes of this test, 38 children with spastic CP and 35 typically developing children were measured. Performing the motorized test was feasible in both non-severe patients and control children older than five years. The neuromuscular model fitted well to the measured data and the neural and tissue parameters could be estimated repeatedly between measurements. The differences in parameters between children with CP and controls were according to current knowledge of CP physiology. Background muscle activation was related to graded spasticity severity, but reflex activity was not. Four pre-post treatment comparisons gave a first indication that reflex activity was reduced after spasticity treatment. Together, these results suggest that the motorized hyper-resistance test can be used to differentiate between neural and tissue impairments in children with CP and thus is a promising alternative to current manual clinical tests.

A factor that could potentially affect the comparison between the manual and motorized tests, and thus explain the lack of correlation between spasticity severity and reflex activity, is the imposed movement profile. Therefore, both manual and motorized instrumented tests were performed in ten children with CP, with similar maximum velocity reached during both tests (**chapter 3**). The imposed movement profile as well as the evoked muscle response differed between methods, indicating that next to maximum velocity, acceleration and muscle length should be taken into account as a factor when assessing stretch reflexes. The bell-shaped manual profile matched more closely with the typical profile measured during gait, emphasizing the need for implementation of functional motorized profiles. These results implicate that the motorized hyper-resistance test cannot be used interchangeably with the current clinical or instrumented manual tests.

Interactive gait labs and instrumented treadmills are becoming more common in gait analysis. Features such as instantaneous belt speed adjustments to the subject's walking speed (self-paced speed) and a virtual reality (VR) environment together could improve the imitation of overground walking compared with conventional treadmill walking. Therefore, it is important to assess the suitability of these labs and features to perform clinical gait analysis.

To validate the use of an instrumented treadmill for gait analysis, the technical prerequisites were first examined in two treadmills. A protocol is presented in **chapter 4** to examine potential error sources in force and center of pressure data measured with instrumented treadmills. It includes an assessment of the accuracy of forces and

center of pressure, resonance of the structure, belt speed variability, and data variability over time. The protocol was able to characterize strong and weak characteristics of the treadmills and thus allowed for evaluation of their suitability for different applications in the domain of gait analysis. To improve force data accuracy, different calibration procedures using an instrumented pole were examined in **chapter 5**. The accuracy increased with addition of extra measurement locations on the treadmill belt. Correction for an inhomogeneous distribution of the center of pressure error across the belt surface resulted in the best improvement of the accuracy, either by calibration only within the walking area or by correcting for the inhomogeneous distribution over the belt's surface.

The effects of walking with self-paced speed and VR environment on the gait pattern were examined in 19 able-bodied adults. No clinically relevant differences were found between self-paced and fixed speed treadmill walking, although self-paced walking did result in more speed variability with fluctuations over multiple strides, as is typically seen during a long walk outside (**chapter 6**). Since self-paced walking could result in more energy exchange between treadmill and subject, this was examined in 18 able-bodied adults (**chapter 7**). The interaction only slightly increased during self-paced compared to fixed speed walking, demonstrating that the self-paced control did not result in disturbing belt accelerations. It was shown that subject-belt interactions only mildly disturbed treadmill walking, as long as there is adequate belt control. The VR environment did not affect the gait pattern to a clinically relevant extent (**chapter 8**). However, subjects perceived walking with the VR environment as more similar to normal overground walking. Thus, the lack of clinically significant differences in gait pattern suggest that walking with self-paced speed and a VR environment is a suitable alternative to conventional treadmill walking.

As walking with self-paced speed and VR might be more challenging for children with CP than for able-bodied adults, the suitability of the interactive gait lab to perform clinical gait analysis was examined in nine children with non-severe CP and eleven typically developing children. All children were able to walk with and without self-paced speed and VR. Effects of self-paced speed and VR environment were similar as for the able-bodied adults, with no clinically relevant effect on the gait pattern, increased slow fluctuations in the walking speed due to self-paced speed and a preference for walking with the VR environment (**chapter 9**). Small group interaction effects suggested that children with CP might need more time to familiarize to self-paced walking. Overall, these results indicate that walking with and without self-paced speed or VR environment can be used interchangeably for treadmill-based clinical gait analysis in children with and without CP.

The results of interactive gait analysis (with self-paced speed and a VR environment) were compared with conventional overground clinical gait analysis and natural walking in the same children with and without CP. Both groups walked slower and with shorter strides in the treadmill and overground lab compared with natural walking. Stride width was increased on the split-belt treadmill, resulting in larger maximum medio-lateral ground reaction forces. Children with CP walked with more deviation in

joint angles in the interactive gait lab, with more pelvic tilt, knee flexion at initial contact and more overall deviating knee and ankle kinematics (**chapter 10**). Both children with CP and typically developing children walked with lower ankle power generation and more absorption, as well as increased hip moments and work (**chapter 11**). This shift from ankle to hip strategy was likely due to a more backward positioning of the hip and a slightly more forward trunk lean. These differences may in part be due to increased fatigue in the interactive gait lab as a result of longer continuous walking time. The findings indicate that gait analysis performed in an interactive gait lab cannot be readily compared with a conventional overground lab when concerning children with or without CP, and that lab-specific normative data sets should be used.

The features of the interactive gait lab could also be used to perturb patients during gait to enhance identification of their impairments and gait limitations. This idea builds on the passive, controlled motorized hyper-resistance test and allows for a functional assessment of reflex activity during gait. Ten able-bodied adults were perturbed during gait by different intensities of sudden, small accelerations or deceleration of the treadmill belt during the stance phase of gait (**chapter 12**). Although the effect on the ankle angle was small, the perturbations caused clear changes in calf muscle length and stretch velocity relative to unperturbed walking. The accelerations were found to evoke stretch reflexes in the major calf muscles, while decelerations resulted in reduced feedback and muscle activation in these muscles. The application of these perturbations did not affect the overall normal gait pattern. This comprehensive study forms the basis for clinical implementation of treadmill perturbations to enable functional assessment and quantification of stretch reflexes during treadmill-based clinical gait analysis.

The feasibility and validity of the different technologies are discussed in **chapter 13**, leading to direct clinical implications and directions for further research. In addition, challenges for clinical implementation are discussed, including compromising between model complexity and clinical interpretability of outcome measures, establishing the technology's inherent value relative to current alternatives, as well as opportunities to further enhance their value for clinical decision making. Overall, it was shown in this thesis that the motorized hyper-resistance test and the interactive gait lab are promising techniques to contribute to clinical measurement of motor (dys) function in children with CP. These feasibility and validity studies set the stage for the future clinical implementation of these technologies to improve individualized decision making.