Summary

As a result of complex brain impairment, walking presents a significant challenge for many children with cerebral palsy (CP). This limited walking capacity has serious negative consequences on quality of life and active participation in society. While there is no cure for CP, rehabilitation medicine is focused on management of these limitations to maximise quality of life. In recent years, technology has developed that may be harnessed in rehabilitation medicine. For example, there has been an explosion in the use of virtual reality (VR). This allows patients to be transported out of their familiar therapeutic environment to experience challenging and stimulating surroundings. In addition, biomechanical analysis of walking can be carried out in real-time and outcomes integrated into VR. This enables the use of serious games, in which clinically relevant actions can be challenged and trained in a novel paradigm that may benefit both assessment and treatment of children with CP. The overarching aim of this thesis is to establish the extent to which children with CP can improve their gait through the novel use of biofeedback in an immersive VR environment.

In order to achieve this aim, a number of research areas were investigated. Firstly, as we are implementing an emerging real-time, biomechanical model (Human Body Model) we sought to provide a lab-specific database to further define gait in healthy children to allow fair comparison with pathological gait in children with CP. In **chapter 2**, we performed clinical gait analysis, during comfortable walking, of 90 typically developing (TD) children. Forty-nine TD children walked overground in a standard gait laboratory, while 41 walked on an instrumented treadmill, specialized for gait analysis (GRAIL). We present interesting insights into the stride-to-stride variability of gait in children and how this can often be ignored in regular clinical gait analysis. Young children show a more variable gait pattern and using only a limited number of strides in gait analysis may overemphasize impairment-based interpretation of kinematic and kinetic gait curves. Not only does the use of treadmills allow for

simplified collection of a large number of steps for gait analysis, it also opens the door for intensive repetitive functional gait training.

To further lay the foundations of the thesis, we investigated if children with CP can indeed improve walking performance with task-specific training. In **chapter 3**, we investigated the effects of gait training in children and young adults with CP in a systematic review and meta-analysis comparing its effect to standard physical therapy. Forty-one studies were identified, with 11 randomized controlled trials included. Compelling evidence was presented that functional gait training can result in clinically important benefits for children and young adults with CP, with a therapeutic goal of improved walking speed. Gait training was found to have a moderate positive effect on walking speed over standard physical therapy. Further, there is weaker yet relatively consistent evidence that functional gait training can also benefit walking endurance and gait related gross motor function. In additional exploratory analysis, estimated pooling of within-group effects suggested the added value VR and biofeedback may offer.

Developing concepts and optimisation of biofeedback, in **chapter 4** we explored the feasibility of biofeedback on gait in 16 children with CP. With visualisation of knee and hip angles in a simple bar graph, children walking in a flexed gait pattern were able to understand and adapt gait in response to challenged improvements. While hip and knee extension could be increased by clinically significant amounts, overall gait as measured by the gait profile score was not changed. The extent of adaptability was further investigated in **chapter 5**, in which biofeedback was provided on a wider range of gait parameters and visualised using an avatar to represent overall movement of the body. Twenty-five children with spastic paresis as a result of CP and related (hereditary) spastic paresis were challenged to improve step length, knee extension and ankle power at push-off. It was found that children were able to adapt their gait pattern with biofeedback, in an immediate response, reaching clinically important improvements as a result of direct biofeedback. Visualizing biofeedback with an avatar was considered subjectively preferential compared to a simplified bar presentation. Similar to the findings of **chapter 4**, no improvement in overall gait, as measured by the Gait Profile Score, was found due to exaggerated compensational movements. The individual variation and compensational movements exaggerated by the challenges of biofeedback may present a platform for advanced clinical gait analysis. In this framework, gait can be challenged in relation to clinical hypotheses and compensational movements observed may provide insight into specific gait impairment.

While we have shown that children with CP can adapt gait, is not understood how individuals achieve changes in gait at the neural level. Children with CP have impaired selective motor control (SMC) and this has been directly linked to severity of gait limitation. In **chapter 6**, we explored this concept through implementation of synergy analysis of measured muscle activity to quantify SMC during walking. While slight changes in SMC can be identified when gait is adapted with biofeedback, it is questionable is these changes are clinically relevant. In addition, high within-subject similarity of synergies to baseline walking was found. These results suggest that while gait may be adapted in an immediate response, SMC as quantified by synergy analysis is perhaps more rigidly impaired in CP. Adaptations may be limited in the short term and further investigation is essential to establish if long term training using biofeedback leads to adapted SMC.

Finally, to lay the foundation for biofeedback enhanced gait training we must show it is feasible for implementation of this tool as part of clinical practice. Clinical practice is often constrained by time and the methods implemented in **chapters 4** and **5** involve substation set up, presenting a barrier for uptake. In **chapter 7** we reported on a clinically feasible tool to provide biofeedback on gait using minimal markers and set up time. With eight makers placed on anatomical landmarks we were able to visualise movement in real-time using an avatar, in addition to calculating pelvis rotations, hip and knee flexion and spatiotemporal parameters. Piloting this application in five specialist clinical centres across the Netherlands found it to be generally feasible and showed promise for further development.

In summary, biofeedback can be used to challenge specific gait improvements in children with CP. The work presented in this thesis provides supportive evidence towards the uptake of gait training and analysis enhanced with biofeedback and virtual reality. Evidenced based intervention is essential and at present high quality randomised controlled trials are insufficient to strongly support wider uptake. Therefore, recommendations for such trials to evaluate the implementation of biofeedback as a therapeutic tool to improve walking function in children with CP are suggested.