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Curriculum vitae

Born on 21st November 1976 in Lokeren, Belgium, I graduated in Medicine CUM LAUDE in 2002, specialized in Sports Medicine CUM LAUDE in 2004, in Physical Medicine and Rehabilitation in 2007, and in Locomotor Rehabilitation in 2007. I became head of the Child Rehabilitation Center, Ghent University Hospital, in 2011.

Professionally, I would describe myself as a passionate and experienced Child Rehabilitation specialist, who loves to teach about my special interests in developmental neuroplasticity, neonatal brachial plexus injuries, paediatric electrodiagnostics, biomechanics and technology enhancing rehabilitation care. I am dedicated to establish collaborations and advance medical research projects with clinical and societal relevance.

I am a grateful mother of 3 fantastic children. In my spare time, together with my husband, I followed the beat of my second passion: latin dance. Dance is a form of expression that brings people together, allows us to be creative and is a fantastic way to escape from stress and reload the batteries: mens sana in corpore sano (Juvenalis)!

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NEONATAL BRACHIAL PLEXUS PALSY

risk management, nerve regeneration and developing brain plasticity

Ruth Van der Looven

Thesis submitted to fulfill the requirements for the degree of 'Doctor in medical sciences' Faculty of Medicine and Health Sciences, Ghent University, Belgium

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FACULTY OF MEDICINE AND HEALTH SCIENCES

Preface

This thesis aims to yield new insights to improve therapy outcome of our children with Neonatal Brachial Plexus Palsy. Several topics were studied specifically related to risk management, nerve regeneration and developmental plasticity. The uniqueness of the thesis is the collaborative effort among the relevant specialties involved in the treatment of NBPP.

Without the extensive amount of effort by our colleagues from the Child Rehabilitation Centre of the University Hospital Ghent, and the University of Ghent, who helped with the study set up, the rigorous testing of the children and MRI scanning, this thesis would never have been realized. I extend my deepest thanks to all the children who so kindly and bravely participated. Most importantly, endless love and gratitude to my husband and children, family and friends, who supported me in so many, treasured ways.

I hope you will value the reading of the dissertation. I am certain this is only the beginning of a further research pathway.

Ruth Van der Looven

Summary

A Neonatal Brachial Plexus Palsy (NBPP) involves a closed partial or total stretch injury to the network of nerves that usually originates from spinal roots C5-T1 during complicated child delivery. Shoulder dystocia, macrosomia, maternal diabetes, instrumental delivery and breech delivery are the main risk factors for NBPP, with shoulder dystocia presenting the highest risk. Prevention remains difficult owing to the unpredictability and relatedness of these factors. Although Caesarean section appeared protective, it does not totally prevent NBPP and carries significant neonatal and maternal morbidities.

The incidence of NBPP has decreased over time, possibly as a result of increased awareness of the risk and improved obstetric strategies. In the view of its lifelong impact, the risk for NBPP, its severity, and morbidity should be further lowered. The focus needs to be on risk stratification, antenatal counselling, enhanced labour surveillance and simulation training.

The nerve damage causes a multifaceted clinical picture consisting of sensorimotor disturbances: muscle weakness or paralysis, absence of correct sensory feedback, muscle imbalance, co-contractions, inefficient substitution movements, pain and underuse of the affected arm. The natural course is diverse with a recovery depending on lesion extent and severity, but also on the child's recovery potential and the speed of nerve recovery. Preoperative investigations should provide this information accurately to select babies most likely to benefit of a microsurgical intervention. Although very few electrophysiological studies on the NBPP have been published, the most methodologically sound studies support the use of electrodiagnostic studies at standardized time-frames, as a key prognostic modality complementing clinical judgment and neuroimaging. NBPP strikes a developing nervous system at a critical moment of sensorimotor development. Apart from the direct consequences of the peripheral nerve injury, the brain has to cope with atypical and possibly erroneous in- and output signals whilst building the 'sensorimotor' programs to drive the affected limb. First, we investigated the central hand size representations. As in the adult, our study demonstrated its dual in typical developing children and young adults: a systematic misperceived implicit and an approximately veridical explicit hand representation. The subsequent study in NBPP revealed the impact of a sensorimotor lesion at birth on the development of implicit hand mapping, but not the explicit hand shape. This is an important finding as the implicit hand map is, for instance, known to mediate in tactile registration and perception. The misperception in NBPP could impact on calibrating grasp and therefore, haptic ability, dextral performance and everyday hand function. The traditional view of NBPP as a main problem of decreased 'motor output' with minimal sensory deficits is challenged by our findings.

Intriguingly, our study on morphometric analysis of the hand knob area did not reflect an effect of the unilateral upper limb sensorimotor impairment of NBPP. Overall, our studies, supported by previous literature, may point to an effect on the motor association areas involved in motor planning after a NBPP rather than an effect on the primary motor region.

Our data added another interesting insight concerning hand preferences. Assuming that most of our NBPP would have developed a right hand preference but were forced by NBPP into left hand preference, our results suggest that the implicit representation of the left hand and the primary motor areas of both hands in NBPP adapted to left hand preference.

In conclusion, as NBPP cannot be totally prevented, it is critical to optimize its recovery. Although maximization of peripheral motor and sensory nerve recovery together with mitigation of secondary complications from nerve damage remains a primary goal in NBPP children, the new insights in the innate central reorganization are vital to empower early interventional treatment designs.

Living in extraordinary times witnessing an explosion of technology, the next step is definitely implementing techniques that can be used to access particular parts of the brain that require strengthening as a response to NBPP. Neuromodulatory intervention techniques should take into account the temporal and spatial profile of critical and sensitive periods that orchestrate neuronal and network responses during development. Targeting the implicit hand presentation, virtual and augmented reality, combining environment, visual illusion and motor tasks, can be a promising rehabilitation tools for children with NBPP.

The challenge in future research is to further unravel the exact reorganizational mechanisms of the developing brain as response to a NBPP.

Above all, we stress the importance of the multidisciplinary approach in this complex, challenging and fascinating condition. I am privileged to be part of such an extraordinary team of enthusiastic experts.

