Restoration of locomotion in posttraumatic paraplegics: the multidisciplinary approach and unexpected plasticity of single neurons – facts and fantasy

K. R. H. von Wild1, G. Brunelli2

1 Medical Faculty of the Westphälische Wilhelms-University Münster, Münster, Germany
2 Foundation for Research on Spinal Cord Lesions, Brescia, Italy

Summary

In Europe there are about 300,000 paraplegics and in every country approximately 1000 new cases per year. Treatment requires a multidisciplinary approach with scientific cooperation targeted to exchange personal knowledge and expertise. At present a completely disrupted spinal cord cannot heal for recovery of motor and/or sensory functioning, although some promising treatment modalities in laboratory animal experiments have been reported. No interventional stem cell procedure so far has shown evidence to restore impaired functioning in human paraplegics. However, functional electrical stimulation (FES) via an implanted neuroprosthesis (SUAW concept) and central nervous system-peripheral nervous system (CNS-PNS) connection have successfully been used for alternative compensatory strategies for voluntary locomotion. This report is to analyse the authors’ experience from two European projects in paraplegic. Factors will be identified that might have caused the one or other pitfall since so far both surgical reconstructive procedures have not been adopted by rehabilitation physicians and/or restorative (neuro-)surgeons despite the promising functional results we have achieved. Unexpected plasticity of single neurons following CNS-PNS by-pass procedures is discussed. Future interventions, for example the present phase I prospective multiple centre study on the side effects, effectiveness, and reliability of intrathecal treatment of anti-Nogo-A antibodies, are presented and the Chinese stem cell implantation is critically reviewed.

Keywords: Posttraumatic paraplegia; reconstructive surgery in complete SCI; restoration of locomotion in paraplegia; functional electrical stimulation (FES) in SCI; current concepts to improve complete SCI; network of functional neurorehabilitation.

Introduction

Experimental and clinical research in neurotraumatology demands a faithful multidisciplinary approach. This is especially true for the scientific cooperation targeted to exchange the scientist’s knowledge within a very important but sensible field of restoration of voluntary locomotion in posttraumatic paraplegics [3, 7, 9–12]. This report is to analyse the authors’ personal experience from two European projects to identify factors that might have caused the one or other pitfall since both surgical concepts have not yet been accepted in routine clinical or even experimental re-engineering despite evidentiary clinical results that were later on explained by a series of sophisticated analyses (electroneurophysiologically and gene-bio-technologically) [13, 14]. Unexpected motor cortical brain plasticity [9, 10, 12] by single neurons in the human being with reference to the proven fact that supraspinal neurons can target skeletal muscles retaining the plasticity of generated functional glutamatergic neuromuscular junction in rats following surgical connection of the corticospinal tract with peripheral nerves of the hip mussels is a matter of intensive scientific debate and a mystery to SCI experts. In this context, also future interventions will be mentioned, for example the ongoing phase I prospective multiple centre study on the side effects, effectiveness, and reliability of intrathecal treatment of anti-Nogo-A antibodies, just as the Chinese stem cell implantation which is critically reviewed [7, 8, 15].

Methods

Review of the authors’ approach by participating in two international experimental clinical projects to establish an international scientific
network for functional rehabilitation of paraplegics and restoration of voluntary locomotion following complete SCI.

1. Biomed 2 (1997) became known as the SUAW (stand up and walk) project, a European Community scientific research project that followed the first CALIES grant (Computer Aided Locomotion by Implanted Electrical Stimulation in paralysed persons). Directors were Prof. J. Edwards and the late Prof. K. R. Krishnan, University of Salford, Manchester; project management co-ordinator P. Rabischong, Montpellier/France (Fig. 1), with participation of industrials and researchers from Finland, Italy, The Netherlands, Ireland, Great Britain, and Germany. Along with the European CALIES association 9 of 14 technicians were from France. Bernard Denis (Neuromedics) was responsible for industrial partners, assisted by Pierre Coudere (Neuromedics implant). Others were from IBM France and Thomson CSF, Paris, Het Roessingh, R. & DFD, Enschede/Netherlands, and the Fraunhofer Institut St Ingbert/Germany. The surgical procedure consisted of implantation of neuroprosthesis connected with epimysial and perineural electrodes for FES of the selected hip muscles for locomotion (Fig. 2a–d).

2. CNS – PNS Connection (Brunelli’s Paradigm) (Fig. 3): In prone position connection of the intact ventrolateral corticospinal tract (first motor neuron) above the complete cord lesion via three fascicles of autologous sural nerve grafts on both sides to the receiving stumps of peripheral muscle nerves as they were (from dorsal) the gluteus maximus (hip extension), gluteus medius (abduction and stabilisation of the pelvis), and — after the patient is turned on his back (ventral incision) — the quadriceps muscle (for hip flexion while standing and knee extension).

3. Learning by doing: SUAW matched perfectly the authors’ interest in functional neurorehabilitation and re-engineering of spinal cord lesions. Following the project from 1997 to 2002 the authors met during the SUAW cadaver (Fig. 1) and technical workshops when Giorgio Brunelli (GB) raised interest in his CNS-PNS (central nervous system-peripheral

![Fig. 1. SUAW cadaver workshop Clermont Ferrand, France, March 26–27 1999. From left to right: M. Benichou, P. Rabischong, B. Soni, G. Brunelli, the late K. Krishnan, and KvW](image1)

![Fig. 2. SUAW concept of implanted FES; (a) Sketch, (c) M.M. two weeks after implantation. (b) FES-neuroprosthesis with cables before and (d) after implantation (X-ray)](image2)