

## INFOMOTRICE n°21

### RESEARCH PAPERS, November 2016

#### **Eight projects to make research progress**



#### **Leader**

Pr Olivier Baud, President of the Scientific Board

In 2016, La Fondation Motrice celebrated its 10 year anniversary: a key moment to reassess its commitment.

Since its beginnings, La Fondation Motrice has embodied research on Cerebral Palsy, which is the center of its work. The place it occupies in France and in Europe should favor international interactions and projects developments with institutions such as CP Alliance in Australia and CPIRF in the United States. The foundation raises awareness of this pathology during events like the World CP Day, on 5 October.

A nation-wide survey(ESPACE) was launched in summer to evaluate how care is received, what the needs are, and what priorities and improvements are expected in motor rehabilitation by people with CP. It should lead to improved practices in motor rehabilitation, in connection with the French National Authority for Health.

Eight innovative projects covering a large range of issues in connection with CP were chosen in the last call for projects at the end of a rigorous selection process, as they are each year (15% of the applicants).

The foundation will continue to finance targeted research projects of reasonable scale like these ones, but it is also exploring for the future the possibility of financing a « big project » that would bring together a few teams around an issue which is considered a priority.

All this work is done in close association with scientists, practitioners and patients. Only renewed support from our sponsors and donors makes it possible.

Many thanks to them.

**Eight prize-winners were distinguished in the call for projects 2015/2016. Their works, selected for their excellence, will be a part of the research effort expanded for 10 years.**

From 2005 to 2015, we initiated ten calls for projects {on brain damage, motricity, language, communication, cognition, dystonia, rehabilitation, quality of life, orthopedic problems, pain

70 articles were published in national and international peer-reviewed journals.

63 research projects were backed: 47 in France, 15 in Europe, 1 in the United States.

Around 3 million Euros were put directly into research.

The foundation's income mainly stems from donations: patients' families and friends, the general public who is sensitized through communication campaigns or charitable events, or philanthropic companies. Without their generosity, research couldn't progress as much.

### **5 projects supported in 2006 Focusing on rehabilitation**

**Aur lie Sarcher, Motion Analysis Laboratory, Nantes Teaching Hospital (France)**

**SHORT AND LONG-TERM EFFECTS OF CONSTRAINT-INDUCED MOVEMENT THERAPY ON THE AFFECTED ARM'S MOVEMENTS IN CHILDREN WITH SPASTIC HEMIPARESIS.**



Children with unilateral spastic CP show muscle disorders on one side of the body, which leads them to overuse their valid arm to compensate for activity limitations in the affected arm.

Constraint-induced movement therapy consists in making them use the affected arm a few hours a day during a few weeks in order to limit this asymmetry. We know that this therapy globally improves the affected arm's motor function, but the mechanisms leading to this improvement are still relatively unknown. The aim of this study is to evaluate quantitatively and objectively the effects of constraint-induced movement therapy on the affected arm's movements in children with unilateral CP with measurements made by sensors already used for gait analysis.



This project furthers preliminary works achieved in the Rehabilitation Engineering Chair Applied in Pediatrics of Montreal (Canada) and is part of an approach consisting in validating rehabilitation practices. It should allow us to develop a therapeutic decision-making tool by highlighting which muscles and which movements must be targeted for each child. We expect from it the optimization of rehabilitation efficiency, and thus an improvement of the affected arm's motricity. The next step will be to extend this evaluation to adults, and to adjust it for other kinds of therapies (mirror therapy, botulinum toxin...).

### ***With the support of Envoludia***

*We are a founder member of La Fondation Motrice – Foundation for Cerebral Palsy (following APETREIMC) and support for Cerebral Palsy is one of the pillars of our community project. What motivates us is the hope to improve the quality of care for our children.*

*The project of Aurélie Sarcher meets this goal. By allowing a better understanding of the mechanisms implemented in constraint-induced movement therapy, and of the evolution of muscle disorders, it should give leads to improve this therapy.*

*As in 2015, we thus mobilized families and professionals to run the Heroes Race and to collect funds allowing us to bring the foundation the necessary amount to fund this study. This Envoludia-Fondation Motrice research grant shows our commitment.*

### **Inge Franki, Louvain Teaching Hospital (Belgium)**

#### **EVALUATION OF THE EFFECTS OF USING A PLATFORM OF SPECIFIC REHABILITATION GAMES SOFTWARE DURING PHYSIOTHERAPY SESSIONS IN CHILDREN WITH SPASTIC CEREBRAL PALSY.**



This study originated from the observation that we need motivational tools in standard physiotherapy sessions to help children reach personalized rehabilitation goals.

One difficulty was that children with CP are often excluded from interactive games requiring rapid movements. But by using adapted games, these can be integrated into rehabilitation.

A gaming software compatible with games consoles available in stores was specifically designed for children with CP; it contains games that can be personalized in terms of speed, sensibility and variability of the game control by different limbs.

A case-control study with 30 children will compare the effects of physiotherapy sessions with and without the integration of 15 to 20 minutes of rehabilitation games. We will measure the reach of individual goals, the range of joint movements as well as muscle tone, strength, equilibrium, motor function and motivation.

These results will allow us to better understand the possibilities of this group of children in terms of participation (in the games) and rehabilitation (through the games).

**Astrid Balemans, Utrecht Teaching Hospital (Netherlands)**

**INDIVIDUALIZATION OF ACTIVITIES ADVISEMENTS AND CEREBRAL PALSY: DEVELOPMENT OF A TREATMENT ALGORITHM.**



Walking requires an important effort for people with CP: they become tired, which leads them to limit their physical activities, which has repercussions on their health. A better understanding of these obstacles to physical activity would allow us to better intervene at the individual level, with long-term benefits on these persons' health.

Indeed, to be efficient, therapies should be as personalized as possible. This study thus aims to reorient rehabilitation from individual evaluations.

In 30 adults and teenagers with CP, we will measure the level of tiredness, physical effort in walking, maximal aerobic capacity and the repartition of physical activity during the day.

With this data, individualized suitable advice about physical activity will be offered to the people evaluated:

- Training exercises
- Recovery periods after an intense exercise
- Reduction of the time spent in sitting position

After eight weeks, physical activity and tiredness will be measured again, and a feedback will be given to the patient. A new evaluation will take place after 16 weeks of the physical activity program.

**Dr Raphaël Gross, Nantes Teaching Hospital (France)**

**EVALUATION OF THE IMPACT OF AN INCLINED PLANE ON WALKING FOR CHILDREN WITH CEREBRAL PALSY: WHAT LEADS FOR REHABILITATION?**



Building on children's capacity to adapt their walk to different situations, rehabilitation on an inclined plane is frequently used to foster the work of joints and muscle ranges of motion in the lower limbs, and of the trunk posture. This practice was not totally scientifically validated.

This study thus aimed at quantifying this therapy's impact, and the results are remarkable:

- We notice in children with CP as in valid children increased knee, ankle and hip flexion as the slope gets more important.
- And we observe in all children increased muscle activation, even if the muscle groups that are used to provide with the necessary energy differ according to children (valid or CP).

So we see that an inclined plane can be interesting to improve the range of motion in joints, thus leading to active maintaining of muscle lengths. We also note the importance of motor unit recruitment in this effort. This exercise can be achieved routinely in rehabilitation practice: it helps to prevent secondary and tertiary troubles associated with CP. We still have to validate the impact of this long-term rehabilitation by proving its 'after-effect' on level ground walking, thus its benefit for the child in everyday life.

*With the support of CI*

**Pr Yannick Bleyenheuft, Louvain Institute of Neuroscience (Belgium)**

**IMPACT OF INTENSIVE MOTOR LEARNING ON COGNITIVE CONTROL IN CHILDREN WITH CP.**



For around ten years, scientific literature has showed that therapeutic models built on intensive rehabilitation allowed significant changes in children with CP motor capacities. This rehabilitation consists of therapeutic training of 60 to 90 hours on two to three weeks, with a gradual adaptation of the games and tasks difficulties.

This therapy allows motor changes associated with modifications in brain regions that control paretic\* members. But we observed that children showing the same motor difficulties at the beginning could evolve differently during these intensive interventions. We thus made the hypothesis that for some of them, deficits could arise not only in the brain's motor regions, but also in regions that allow the learning of new motor tasks. This research project thus aims to investigate the impact of CP on the brain regions that allow the learning of new tasks, and the role that intensive rehabilitation might play in the development of these cortical regions dedicated to motor learning. Indeed this therapy, besides motor changes, might lead to changes in children motor learning capacities. If this is the case, this kind of therapeutic care could allow us to transform not only children motor capacities, but also their capacity to learn new motor tasks afterwards.

\*paresis: motor deficit with motor loss and partial paralysis

*With the support of Sesep*

### 3 projects supported in 2016

#### Better understanding and better preventing Cerebral Palsy

**Pr Stéphane Sizonenko, Geneva Teaching Hospitals (Switzerland)**

##### **CEREBRAL LESIONS IN INTRA-UTERINE GROWTH RETARDATION: THE IMPACT OF NUTRITIONAL SUPPLEMENTATION WITH LACTOFERRIN DURING GESTATION AND LACTATION.**



Works showed that lactoferrin, a milk protein with antioxidant and anti-inflammatory properties, could reduce cerebral lesions in the premature child.

On this basis, we wish to study the protective effects of lactoferrin in newborns with intra-uterine growth retardation, as this growth retardation can be a cause of neurodevelopmental troubles, and thus handicap.

Thus we will observe and measure – in an animal model – the effects of intra-uterine growth retardation on brain development, as well as the effects of lactoferrin as food supplement on mothers during gestation and

lactation on the same development parameters.

If we manage to highlight the beneficial effects of lactoferrin supplementation in this experimental frame, we will be able to move toward clinical trials to confirm this protective role for fetuses and newborns subject to intra-uterine growth retardation. The prospect is to reduce by this nutritional supplementation in mothers the handicaps associated with premature birth and intra-uterine growth retardation.

**Matthias Groszer, INSERM, Paris (France)**

##### **MOLECULAR MECHANISMS OF PROTECTION AGAINST LESIONS ASSOCIATED WITH HUMAN NEURONS HYPOXIA DERIVED FROM INDUCED PLURIPOTENT STEM CELLS.**



Oxygen deprivation in the period around birth can cause brain lesions and lead to Cerebral Palsy. Recent progresses have led to better care of the children concerned by a slight artificial cooling. This therapeutic hypothermia significantly improves clinical results, but underlying molecular mechanisms remain little-known.

Our recent publications on gene networks should allow us to help understand these mechanisms. The aim of this study is thus, firstly to develop a new model of cortical neurons derived from stem cells, then to expose them to oxygen deprivation (hypoxia), with or without hypothermia, and to evaluate the gene response to these two phenomena. A dynamic analysis of functional relationships between



molecular networks, as well as physiological studies, will be undertaken to check these networks' functionality.


This work should help identify complex underlying mechanisms of protection or vulnerability in the frame of CP and to interpret gene sequencing data to identify high-risk patients.

**Pr Kaat Desloovere, Louvain Teaching Hospital (Belgium)**

# IN-DEPTH ANALYSIS OF HYPERTONIA IN CHILDREN WITH CEREBRAL PALSY THROUGH BIOMECHANICAL AND ELECTROPHYSIOLOGICAL MEASUREMENTS ASSOCIATED WITH IMAGING IN PASSIVE MUSCLE STRETCH AND WITH WALKING: TOWARD A RENEWED CARE FOR TONE.



Cerebral Palsy is frequently characterized by hypertonia (increased muscle tone), limiting walking capacity. But this hypertonia remains difficult to evaluate, and the response to treatment is very variable.



Two factors intervene: spasticity (neuronal component associated with the central nervous system) and stiffness (non-neuronal component due to muscle changes), which play a different role depending on whether the muscle was stretched passively or in walking. This study thus aims at determining which components play the biggest part in hypertonia, and in what circumstances, by studying muscle behavior with ultrasonic imaging associated with simultaneous measurements of muscle activity, joint angles and strengths. Spasticity and stiffness will be quantified then validated by a treatment targeting either one or the other.

Results will allow us to better understand hypertonia and to adjust its treatment for every child based on their tone profile, thus facilitating individualized care.

More information on [www.lafondationmotrice.org](http://www.lafondationmotrice.org)

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