LA FONDATION MOTRICE

FONDATION PARALYSIE CÉRÉBRALE

INFOMOTRICE N°22

RESEARCH PAPERS, May 2017

2017: A TURNING POINT FOR RESEARCH

BUILDING TOGETHER A GREAT PROJECT TO COPE WITH CEREBRAL PALSY

Presentation of 2016 research grants with Segolene Neuville, junior minister for Disabled People, and Andrea Casiraghi, the foundation's patron.

Dear Friends,

Those among us who experienced the announcement of a handicap remember the emotion that we felt knowing that our child, our ball of love carried in our arms won't walk. Those who didn't face this shock understand it easily. Then our child teaches us that life is beautiful and deserves to be lived, and that they want to live it. Our responsibility thus becomes clear: to free their way, to build a bridge above obstacles.

To this aim, with you, we created La Fondation Motrice more than ten years ago: in order for scientific progress to turn into concrete progress for the many children hit by Cerebral Palsy (CP). You will find in this letter the research we support in 2017: 8 projects selected by our Scientific Council among 60 international applications on strict requirement criteria. Words can be complicated, but ideas are simple: the goal is to understand the mechanisms of CP, to act from birth to reduce brain damage, then to act on children and adults to increase their autonomy and prevent complications.

In 2017, our research strategy is evolving to allow research to take a big step ahead. By launching an international call for projects concentrated on big projects, we set for ourselves a goal even more

ambitious, a first for us: that is to conduct therapeutic trials, which means large-scale studies to test, for instance, a drug against brain lesions at birth or to develop interventions that will prevent either Cerebral Palsy, either its complications on children and adults. To this end, we must collect from this year very important means: 500 000 Euros each year on three years.

Without you, without your donations and your commitment, this project won't see the day. With us, make this ambition a reality: make a donation, mobilize your friends or take part in the Heroes Race in May. If you want to have a long-term impact, think of legacies, and if you are subject to wealth tax, think of a tax-deductible donation. Companies you're working in can also become partners of our cause.

Dr Alain Chatelin, President

A REINFORCED SCIENTIFIC COUNCIL

In 2017, two leading experts join our 10 current members.

Jessica Dubois. Researcher in Neuroscience. INSERM, CEA/NeuroSpin, Gif-sur-Yvette. Specialist in Neuroimaging of early brain development, in particular in the premature infant.
Régine Scelles. Professor of Psychopathology. Nanterre University. Specialist in handicap and family relationships with a handicapped child.

FIVE PROJECTS SUPPORTED IN 2017

RESEARCH ON REHABILITATION: A LONG-TERM EFFORT

Are muscle disorders related to Cerebral Palsy reversible ?

Characterization of spastic myopathy at clinical, biomechanical, histo-immunological and radiological levels on adults suffering from spastic paresis after Cerebral Palsy and after a cerebrovascular accident.

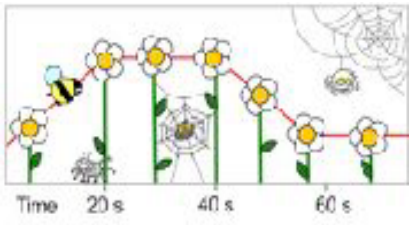
Cerebral Palsy (CP) results from a lesion in the central nervous system leading to paresis (motor loss) and from muscular hyperactivity restricting movement, and involves a less known muscle disorder called spastic myopathy. It is probably caused by a relative immobilization and underutilization of the muscles in the affected limbs and distorts in turn the movement's quality of command. The muscles concerned are, for instance, plantar flexors, whose extensibility decreases from the first years of the child's life. These mechanical and tissue changes in the muscle play a part in disrupting the quality of life in children and adults, but were little explored.

We noted the parallel development of a spastic myopathy comparable to the one observable in CP in adults having suffered a cerebrovascular accident: during the first weeks following the lesion, they often stay lying down with certain muscles, like those of the calf, the shoulder or the plantar flexors, in « short position ».

The objective of the study is thus to describe, in 40 adults with CP, genetic, histological (i.e. concerning tissues), radiological, mechanical, physiological and clinical changes in the calf muscle, and to study the reversibility of these modifications by comparing the effects of a conventional rehabilitation to those of an intense program of self-stretch (in the frame of a guided self-rehabilitation contract) during a year. These results will be compared to those obtained in a similar study led in adults after a CVA.

Pr Jean-Michel Gracies. Maud Pradines (PhD). Albert Chenevier Hospital, Créteil.

Can « serious games » involving muscle activity improve the walk of children with Cerebral Palsy ? The interest of electromyographic (EMG) feedback.



The height of the bee is proportional to muscle activity. The position and the height of flowers can be modified to get the muscle activation wanted

Who would have thought that video games would inspire us for the rehabilitation of children with neurological damage ? With « serious games », we aim at combining our scientific knowledge with the children's instinct of play to create a playful tool for rehabilitation on smartphone or tablet.
First we developed a very small, very light device (100 g for a few square centimeters) that measures the increase in electrical activity in the muscle according to its contraction (electromyography EMG) and passes on this information to the smartphone or the tablet. We are now about to develop a game who will help children with CP to reduce the hyperactivity of certain muscles intervening in the foot movement (in particular the plantar flexors) and to decrease paresis in other muscles. The regulation of the ankle muscles activity, activity they are for the moment incapable of, should improve their walk, but also avoid certain neuro-orthopedic deformities that we can only treat today with surgery.
This innovation is interesting in two ways: on the one hand, this playful aspect should help children to commit themselves to their rehabilitation, and on the other hand, the information passed on in real time by electromyography (EMG) during the game allows an effective regulation between the two groups of muscles, unlike conventional rehabilitation that only aims at reducing the spastic muscles hyperactivity.

The study will be led with two groups of children – one benefiting from virtual reality, the other following a program of conventional rehabilitation – for whom we will measure the dicrease in (opposing) plantar flexors hyperactivity, the decrease in (agonist) dorsiflexors paresis, and the regulation between them.

Pr Marco Gazzoni. Politecnico di Torino (Italy). Dr Christophe Boulay. La Timone Hospital, Marseille.

The impact of Cerebral Palsy on the appropriation of the body.

The appropriation of the body, this feeling that our body is ours, is based on the connexions between our sensations in the brain, giving sens to the multiple sources of sensory information (like sight and touch). The « rubber hand » experiment shows it well: people without brain lesions will have the impression that an artificial hand is their hand when we will make coincide the sight of the rubber hand with the sensation of touch of their real hand, which is hidden. This notion is important in movement, and could be one of the explanatory factors of motor impairment: young people with unilateral Cerebral Palsy have a tendency to conceal what their affected limbs are able to do and to describe their deficiencies in a way that may lead to think that the appropriation of their bodies is distorted (« I forgot my hand » or « this hand is not mine »)

with the support of

SESEP

SESEP is a society dedicated to research and care for children with motor handicap. It supports clinical research in pediatric rehabilitation. This beautiful project echoes one of our daily concerns.

Jeanne-Charlotte Carlier, President

Thus we will lead the « rubber glove » experiment on 15 teenagers with unilateral Cerebral Palsy and compare these results with those of 15 able-bodied teenagers, to confirm if their brain lesions have an effect on the appropriation of their bodies. Complementary use of medical imaging will allow to identify the neurological correspondences of this phenomenon. The goal is to improve existing therapies like mirror therapies, and to set up new intervention protocols.

Dr Christopher Newman. Dr Corinna Gerber. CHUV Lausanne (Switzerland)

Mictional rehabilitation in children with Cerebral Palsy.

Almost half of children with CP have urinary troubles, in particular urinary incontinence. This has important psychological consequences, particularly on self-esteem, but also on their relatives' behavior towards them. As much as it seems obvious to handle the problem in able-bodied children, usually through urotherapy (rehabilitation of the urinary function), with success, we are prone to consider incontinence in children with CP « normal » and inevitable. Therefore the idea of making them benefit from urotherapy was never studied.

This study thus aims at improving the treatment of urinary problems in children with CP and, beforehand, at analysing the factors influencing incontinence. Our goal is to improve their quality of life and their family and social relationships. Rehabilitation of micturition through urotherapy should allow to reduce pharmaceutical treatments, the use of diapers and hospitalizations at adult age.

Dr Piet Hoebeke. Bieke Samijn (PhD). Ziekenhuis Gent University (Belgium)

The relationship between levels of physical activity and cardiorespiratory conditions in children with Cerebral Palsy

Today's children are less active than those from previous generations, and this lack of daily physical activity put their health at risk. This risk is in fact increased for those suffering from Cerebral Palsy. We also know that regular physical activity plays a part in (a better) psychological health and offers children – able-bodied as handicapped – opportunities of social integration. Recommendations regarding exercise and physical activity were emited recently for children with CP, but they were not introduced in clinical practice yet.

Thus we don't know the level of physical activity in children with CP in Flanders, since this is not part of a yearly clinical follow-up. Yet in order for health professionals to lead patients towards a more active way of life and improve their health, they must have access to (general as much as individual) information on their activity level and their physical condition.

This study thus aims to know better the way of life of people with CP, their cardiorespiratory health and the relationship between both, and to show that joint use of questionnaires and clinical tests is achievable and useful to monitor physical activity and shape in children with CP. The results we'll get will be used as a basis for discussion with clinicians in reference centers to set up recommendations.

Dr Patricia Van de Walle. Antwerpen University (Belgium)

THREE PROJECTS SUPPORTED IN 2017

BETTER PREVENT CEREBRAL PALSY

Neurocognitive disorders associated with intrauterine growth restriction: the regulation of neuroinflammation, a new target for neuroprotection.

A low birth weight, consequence of intrauterine growth restriction, happens in 10% of pregnancies and represents a high risk of neurological after-effects such as Cerebral Palsy or learning disabilities. This relationship is known, but remains badly understood. We hypothesize that brain inflammation, a known risk factor, could be involved.

We recently showed that intrauterine growth restriction associates itself with brain maturation abnormalities, and with a bad regulation of certain genes involved in the control of brain inflammation. This research project thus aims to study the control mechanisms of brain inflammation by determining, in particular with the help of innovative techniques, which genes are the most affected by intrauterine growth restriction, what is their role in the regulation of brain inflammation, and if they could be the target of treatments in order to reduce brain damage. Our work should introduce new ideas for the prevention of brain damage and its subsequent neurological aftereffects.

Dr Aline Rideau Batista Novais. Robert Debré Hospital, Paris

Could administration of carbetocin to newborns at risk prevent brain lesions ?

Early activation of oxytocin receptors and neuroprotection in regard to inflammatory damage in newborns affected by intrauterine growth restriction.

Low birth weight newborns present an increased risk of brain damage caused by postnatal inflammation. This (inflammation) results in lesions in brain's white matter (grouping of nerve fibers). Our previous works proved that postnatal administration of carbetocin, a molecule mimicking the effects of oxytocin (hormone necessary for a good cerebral development), allowed to reduce these lesions and to restore the normal development of white matter in animal models.

Thus we aim to study further the protective effects of carbetocin at the level of the motor cortex and of the corticostriatal circuitry (motor circuits), in particular with the help of a new very high-resolution ultrasound imaging technique, and their consequencies on motricity. First results are encouraging and pave the way for clinical utilization of carbetocin in low birth weight newborns.

Dr Jérôme Mairesse. INSERM, Paris

Is destruction of neurons in case of brain asphyxia preventable ?

Study of Na+K+-ATPase signaling pathways involved in neuronal death mediated by autophagy after perinatal hypoxia-ischemia.

Perinatal hypoxia-ischemia, a pathology characterized by a reduced supply of oxygen and/or blood flow towards the brain around birth is a major cause of death and of brain lesions causing troubles such as Cerebral Palsy. Despite the significant progress achieved, brain protection in newborns having suffered from this type of perinatal brain asphyxia remains a challenge.

We showed that autophagy (a cell « recycling » mechanism) can be involved in neuronal death when it is induced excessively by this brain asphyxia. This project thus aims at understanding how autophagy could be deregulated in neurons in order to be able to act in a targeted way on this destructive activity that plays a major role in the development of brain lesions.

Dr Julien Pierre Puyal. Lausanne University (Switzerland)

More information on www.lafondationmotrice.org

La Fondation Motrice, Research into Cerebral Palsy 67 rue Vergniaud, 75013 Paris, FRANCE Registered as a "government-approved and endorsed public foundation" in July 2006

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