FONDATION PARALYSIE CÉRÉBRALE

15 years of research on Cerebral Palsy, part 1

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Research Letter

Since 2005, when the foundation was created with the ambition to give more extent to research on Cerebral Palsy (CP) in France and in Europe, the understanding of its mechanisms as well as medical practices have made important progress. This 27th Research Letter, and the following letter which will be published in spring 2021, is dedicated to the evolution of knowledge made possible by these last 15 years of research.

SUMMARY

1- From Cerebral Palsy to developmental disorders after early brain lesions

Interview with Dr Stéphane Chabrier
Pediatrician, Physical and Rehabilitation Medicine
Saint-Etienne University Hospital

The definition of Cerebral Palsy evolved through time and continues to be the subject of discussion. Overview with Dr Stéphane Chabrier, Pediatrician

Warning:

This research letter was written on the basis of phone interviews that took place during summer 2020. Many thanks to the seven distinguished researchers working on CP for their availability.

Words of Cerebral Palsy through time

1827: Jean-Baptiste Cazauvieilh, psychiatrist, describes congenial paralysis.

1834: Claude-François Lallemand, surgeon, makes the connexion between Cazauvieilh's clinical observations and the results of the autopsies he performs himself on brains.

1853: William John Little, surgeon, develops an expertise in the treatment of orthopedic deformities. He states that some forms of paralysis result from brain lesions caused in particular by premature births. His name will be given to a form of bilateral CP in the 1960s, the Little Syndrom.

1877: Pierre Marie, neurologist, describes spastic hemiplegia in children.

1888: Sir William Oster, with others, uses in conferences the term of Cerebral Palsy. In the following years, Sigmund Freud publishes his works on infantile cerebral palsy and submits one of the first descriptions of this condition, taking into account different troubles associated with paralysis.

1950s: Guy Tardieu proposes the term « infirmité motrice cérébrale » IMC (cerebral palsy) to describe mainly-motor troubles resulting from early non-evolving brain lesions.

1964: Martin Bax describes CP as a set of behavioral disorders and gait disturbances resulting from a lesion in the immature brain. Until the 2000s, the brain lesion prevails in the definitions of CP. But progress

Since when has CP has been recognised?

CP has been known for about 200 years, even if we didn't use this word. At the beginning of the 19th century, physicians spoke of congenial (today we would say congenital) paralysis to describe this form of handicap.
With the evolution of medicine and its techniques, we tried to describe the cause – the lesion – and the treatment of CP, but that wasn't enough.
Today we move towards a more global approach, not strictly medical, but also social we place CP in a context that includes living conditions. It is considered a developmental disorder, which concerns a given child in a given environment.
Many remain focused on the brain lesion, waiting to « repair » the brain. But limiting ourselves to the lesion and its motor consequences is simplistic: the child's development doesn't depend only on the lesion, but also on how he or she plays in the park, for instance.

It is a quite original approach ?

Indeed, and it is not well known even by practitioners: health is more global than the absence of disease, and care is only a part of child development. In the social model promoted by the WHO, amongst others, health and development build themselves under the influence of what caused the handicap, but also, just as much, of the environment. We then speak of salutogenesis. Because of the brain lesion, the child starts with a handicap, but his or her development path follows the rules of the other children. It is a model of resilience.

Does this way of defining CP have effects on research ?

Considering CP as a developmental disorder and not just a motor trouble leads to a more transversal analysis of the state of health while preserving a longitudinal approach of child development. But it is not clear-cut. Some wish that this notion of developmental disorder would appear in the definition of CP, whilst others are comfortable with the current definition on which the care system is built.
But considering the patient without his or her environment cannot make complete sense. And as long as we don't know how to repair the lesion that caused CP, we don't have the choice.
To improve the development of all children, we must intervene at the level of society and improve its global state of health. As much as the curative aspect, the « cure », we must take into consideration the « care ». Helping the most vulnerable is everyone's job.
So we shouldn't focus on the motor aspect of CP indeed it is the easiest way to represent ourselves this condition, and motor deficiency seems a thing we could more or less compensate for. But it is not necessarily what troubles the most the persons concerned. For people who have difficulties locating themselves, what is the use of walking if they do not know where they are going ?
So we shouldn't speak of « associated » troubles for troubles other than motor since it relegates them to the background both in care and research. Development is a whole: everything is developing at the same time and everything impacts everything. It's like the chicken and the egg.
What determines the child development thus takes place at three levels, beyond a strictly medical vision at the individual level, there is the lesion, at the family level the richness and the quality of interactions, like shared reading, and at the social level everything

in neuroimaging and neurology plus the evolution of the concepts of health and handicap inside the WHO bring out the need for more global studies, not only medical, of the patients' needs (see Peter Rosenbaum).

2007: according to the International Classification of Functioning, Disability and Health (ICF), the needs regarding the interactions of patients with their environment describe their state of health better than their medical diagnosis only.

2015: Michele Shusterman, the mother of a child with CP, theorizes about developmental disorders after brain lesions and supports the idea of a definition that would integrate the historical definition of CP (around early brain lesions) and the ICF one.

that concerns politics (school, transportation, urban design etc). All these elements are decisive.

2- Premature birth, still a major risk factor for Cerebral Palsy

Interview

with Pr Stéphane Marret
Pediatrician, Neonatology and Reanimation Service
Pediatric Neurology, Interhospital Federation of Neurodevelopment Eure-Seine
University Hospital Rouen-Normandie

Despite progress in the care of newborns, especially those who are premature, we don't observe a reduced risk of CP for these children. The explanations of Pr Stéphane Marret, pediatrician.

The prevalence of CP decreases in a general manner, but you say that the numbers concerning premature births are not good.

Indeed, that is what the results of Epipage 2 show us (see the framed text on the next page). Since 2008/2010, we have observed a general decline in the number of births in France, with a rate of very premature newborns that remains still, around 1.5 or 2%.
Their survival rate has improved since there are centers that know how to take care of children from 24-25 weeks of amenorrhea (WA). But these extremely premature children are at risk of important sequelae, in particular neurodevelopmental troubles. Among the 60% who will survive, only 30% will grow up without sequelae. And 5% of children born before 32 WA have a CP, these children representing 40% of children with CP.

How can we explain this ?

There has been considerable progress in care for very premature children, it is less aggressive and allows earlier autonomy for respiratory functions and nutrition. But it doesn't reduce the risk of neurodevelopmental troubles. Among them, CP is the least common, but the most severe.

However it is said that the prevalence of CP for these children decreases.

We should be precise and put in perspective this data, even if it is correct. Indeed for 20 years we have observed a decrease in the prevalence of CP in premature children. In the 1st Epipage population (children born in 1997), close to 9% of children born before 32 WA had CP. This number fell to 5.4% for children born in 2011. But this decline concerns the least severe forms of CP (grade 1 if we follow the Gross Motor Function Classification System GMFCS). Moderate to severe forms remain important, around 2-3%. Protection

strategies for the brain improved, but there are still frequent sequelae.

Screening and care made progress though.

Indeed we screen better and earlier today, since we learned to better examine children. But these progresses don't concern uniformly the whole territory and remain globally insufficient.
Knowing how to detect subtle signs of damages in motor skills allowed to make earlier diagnosis and to start treatments likely to reduce late sequelae like hypertonia or joint problems. CP is diagnosed early since motor and sensory deficits are detected early, but it is accompanied in premature children by a greater risk of minor behavioral problems (more rarely major disorders like autism) and by cognitive disabilities.
We often hear that lesions involved in CP are non progressive. It is an inaccurate term that we can criticize since developmental concepts appeared. CP is first characterized by sensory and perceptive problems that will disturb motor and cognitive development.

In which fields can we observe progress ?

A better understanding of the mechanisms in CP gave us leads to improve the prognosis of developmental delay in childhood.
If very early (those younger than 6 months) preventive physiotherapy did not prove its efficiency for very premature children at risk of CP, however medicinal (drug) strategies seem more interesting. In particular, magnesium sulfate prescribed to the mother facing premature birth showed a neuroprotective effect. Also, the risk of periventricular leukomalacia was reduced by the administration of corticosteroids, even if questions remain about the risk-benefit balance of these molecules.
Our hope mostly lies in support and intervention programs, in early parental guidance, in home-based neonatal care before the end of the hospitalization period to encourage child development and to reduce limitations for the newborns.
Following up and supporting families is essential to prevent treatment breaks, delayed diagnosis often leading to severe sequelae. It is the reason why coordination and orientation platforms were implemented in the frame of the 2017 Autism Program. General practitioners as well as maternal and child protection practitioners must be able to direct children to these platforms as soon as developmental troubles are detected. Then they hand over to teams of disability specialists in early medico-social action centers (CAMSP).

3- How to protect the fragile brain ?

Interview
with Pr Olivier Baud
Pediatrician, Neonatology,
Geneva University Hospitals
Development and Growth Laboratory, Geneva University

Preventing Cerebral Palsy mostly lies in protecting the brain when subjected to risks, as Pr Olivier Baud, pediatrician, explains.

Can you remind us what the important moments are to protect children at risk?

To prevent the occurrence of CP, the first imperative is to try to prevent its main causes. It implies preventing premature birth, in particular through better information for women during pregnancy on psychosocial lifestyle-related risks and on warning signs that should lead to seeking medical advice.
Then come prevention and care for the events that can occur during labor like perinatal asphyxia or some non-predictable causes like placental abruption, uterine rupture or umbilical cord prolapse. Teams must be ready to take in charge these kinds of situations.
In the neonatal period, we must prevent everything in relation to infections and inflammations that have a detrimental impact on the developing brain. Finally we need a good monitoring network for children so we don't lose sight of them before they enter school.
In France, regional monitoring networks are well organized, but care for developmental troubles is not always optimal in particular the initiation of interventions in psychomotricity, physiotherapy or speech therapy is often delayed.

Once CP is observed, what can we do?

When CP occurs and is confirmed, usually between 1-2 years and 4-5 years, we must see to screen any trouble other than motor (cognitive, neurodevelopmental etc) and to prevent troubles associated with a bad handling of the situation.

What were the main changes in prevention in the last 15 years?

15 years ago, CP was a bit « the tree hiding the forest ». Today it is less common, motor troubles are less severe, thus exposing other troubles (developmental, psychological, speech disorders...) that we observe more because we are looking for them better and earlier.
So interventions can be of different kinds: support in physiotherapy or psychomotricity is less important and we consider the child in his or her whole development, not only motor, but also cognitive and behavioral.

In terms of research, what does it change?

The spectrum of research is different. 15 years ago, we wanted to reduce brain injuries with medication. Today we look at the general microstructure of the brain, or the function. We have a physiological rather than a pharmaceutical vision, we consider developmental troubles globally: reducing inflammation of white matter, increasing neuroplasticity, improving the creation of synapses, activating neural networks...
For instance, we know that stem cells have an interest in neuroprotection, but we don't think that their role is to replace or repair anymore. Now we consider that they are regulating their environment, stimulating other mechanisms.
The big change is the following: we are not waiting for a miracle molecule to protect the brain. We know that perinatal brain lesions are complex, non monogenic, and that one molecule will only have very partial effects. So we adopted more global strategies.

What are medical practices today?

Our objective, through different interventions, is to restore the physiological state of the brain the closest to normal to counter the state of stress of the child. What we call NIDCAP* (developmental care including skin contact, personalised care, family involvement, creation of a less aggressive acoustic and light environment for the child) seems beneficial for the future of the very premature, even if we don't know exactly how. We can make the hypothesis that these interventions stimulate certain oxytocin neurons that reduce inflammation and stress hormones.
Hypothermia is now included in the standards of care for full-term babies in countries where nurse training programs make it possible. We also know that breast-feeding has a neuroprotective effect, it is therefore part of the recommendations.
Some avenues of research such as taking omega-3, DHA or EPO turned out to be disappointing, but like breast-feeding, these molecules can be considered in a « cocktail » of measures to reduce risks. What we finally know today is that the process leading to CP is a multi-factor and complex one.

So where will the next improvements come from?

In 15 years, we may have yet another view of the interventions I described. For that reason research must go on.
In particular, we lack large studies that would help us determine with adequate scientific evidence what brings significant clinical benefits and establish standards of care. For this reason we have ongoing randomised trials on one promising lead:association between hypothermia and molecules or other interventions.
What seems the most likely is that the next improvements will not come from a totally new thing, but by optimizing what we already do:reducing causes of stress, of pain and inflammation by improving the child's comfort, limiting iatrogenia* (alleviating ventilation for premature babies for instance), avoiding separation between the parents and their child, also nosocomial infections...
We know that improving care, generally speaking, is a preventive factor. Rather than waiting for a new thing, are we sure that our practices are always the best considering what we already know ?

* Newborn Individualized Developmental Care and Assessment Program
* iatrogenia refers to harmful effects on health of a medical or a medicinal intervention.

4- Will we ever know how to repair the brain ?

Interview
with Pr Pierre Gressens
Neuropediatrician
head of the research unit NeuroDiderot
Inserm, Paris University, Robert Debré Hospital

The causes of CP, brain lesions are the object of specific studies creating important expectancies: will we know how to repair injured brains one day ?
Overview with Pr Pierre Gressens, expert in neuroprotection and brain injuries in the newborn.

Is « repairing the brain » the right way to ask the question?

Repairing the brain is not a purpose in itself, what is important is to treat disorders that affect the person's life. However, we are making progress in knowledge of possible interventions at the level of lesions.
Until the beginning of the 1990s, we thought that we couldn't do anything once the brain was injured, thus work focused on how to take care of the damage. Then we moved towards the idea of trying to limit their extent.
The beginning of the 2000s was a real turn with the beginning of hypothermia (on full-term children), which helps reduce the likelihood of sequelae, even if we don't prevent everything. We consider that for one child that we « save », 10 will have sequelae, which is very imperfect, but better than for other conditions. So there is significant research effort. The idea of associating « hypothermia + molecule » in the hours following birth, in particular, seems interesting. So today, we have three approaches:

- preventing brain lesions
- preventing the progress of lesions once they occurred (it is particularly acute)
- finally repairing

Are there new research fields?

For children who didn't have access to hypothermia, for whom it was not indicated or didn't work, we now believe that it is possible to intervene later.
We learnt from the study of traumas in adults, which showed us that, contrary to what we thought, the pathology was not « fixed », but continued to evolve.
If we transpose to children, we can think that if the brain continues to move and evolve, there is without doubt a window of opportunity. We could use this plasticity and proceed with a remote intervention on the lesion (through medication, not just rehabilitation) to improve it. We know that rehabilitation works on brain mechanisms: if we knew them better we could make rehabilitation even more efficient.
There were studies in the 1970s that showed that rehabilitation improved motor and cognitive functions in children from disadvantaged backgrounds. We know that stimulating the child within the family is essential, but all children are not born in an ideal socio-cultural environment and rehabilitation allows to « get back » these less lucky children. Today we should integrate rehabilitation in our studies to improve our knowledge of its mechanisms and make it more efficient:until what age should we intervene? In association with which medication ? Can stem cells play a role ?

What are the other topics of study?

We have three main research areas:

1. **The mechanisms of the lesion**
   Until now, we implicated the lack of oxygen. Today we know that the origin is multifactorial, so we must identify all risk factors, among which inflammation, which is the « new enemy » at stake in many pathologies. But inflammation also has beneficial effects, so we must modulate it. For that, we are moving towards personalized medicine, at the level of the cell.

2. **Molecules**

   Besides melatonin, which is a serious candidate, which other molecules could intervene ? Alone or in association with hypothermia ? At what point after birth ?

3. **Stem cells**

   Stem cells are the ones that open the way for repairing the brain. There is an ongoing European study on this subject implicating 12 laboratories. The subject is not new, but our first hopes were dashed: indeed many stem cells die once transplanted. They locate the lesion and migrate there, but disappear. However we were able to observe functional improvements since these stem cells stimulate local cells. So we consider them « helping » rather than « replacing » cells.
   So there really is a theoretical potential that must be a research object, in particular to establish how much time after the injury we can act.
   We hope to move to human trials within the European project by associating also the Australian foundation Cerebral Palsy Alliance, which accepted to respect our validation steps. It is imperative to have a valid optimized protocol so our research teams won't have to stop trials because of accidents and fall behind in an area with a real potential, like it happened in gene therapy.
   In the next five years we should implement trials in non-premature then in premature newborns in 2025.

5- Improving diagnosis, prognosis and our understanding of the mechanisms in CP with MRI

Interview
with Dr Lucie Hertz-Pannier
Pediatrician, Radiologist
NeuroSpin, CEA, Inserm, Paris University

Thanks to progress in medical imaging, we made great headway in the understanding of brain mechanisms, and thus of pathologies like CP. Overview with Dr Lucie Hertz-Pannier, expert in developmental neuroimaging.

What are the main progresses that MRI (magnetic resonance imaging) made possible?

The arrival of MRI was a true revolution. Until there, we had no (or few) technical means to see the child's brain. We did have ultrasound, but it didn't have the same power. Yet improving our knowledge of typical very early development of the brain gave us the capacity to see what was not physiological in other children and thus to sharpen our diagnostic capacity.
MRI made us understand the most important changes in the child's brain: its growth, the organization of neural networks, how they myelinate (which allows transmission of nerve impulses), etc.
Regarding CP in particular, this new knowledge led to a better understanding of brain anomalies liable to cause CP. We know for instance that all neonatal strokes do not cause CP, since all do not affect the motor area.
These improvements in diagnosis and prognosis resulting from systematic association of imaging and clinical data also improve parental guidance. Moreover it makes possible earlier care, which benefits children. Today, better than before, we are able to tell parents if their child is likely to develop a motor handicap and/or more. We see more, we see better, and we know to watch if the anomaly is focal (that is located) or extended. With more subtle measurements, we also learnt to detect brain anomalies distant from the lesion – the brain functioning in long-distance networks.

How does the lesion impact on the brain's development ?

The brain is a complex network of regions. And like musical instruments playing a symphony, functional networks synchronize themselves. MRI allowed us to better understand this organization; to understand in what order sequences are put in place in the typical brain. By observing subtle anomalies, we can deduce their remote consequences.

The developing brain maintains its capacity to organize itself differently if a lesion occurs: that's brain plasticity. During the development of the brain, both hemispheres « talk » together, they are connected: if one defects, it will necessarily have repercussions on the other. MRI and its measurement tools allow to « see » the connections between the different regions; to see how they organize and reorganize themselves in reaction to the lesion.
Seeing the alteration of the connections around the lesion allows to better understand what are or will be the child's difficulties.

**Research in imaging is expensive:
it requires images made following the same protocol,
on similar machines, with the same clinical expertise.
Retrospective studies using different clinical images
necessarily have biases.**

For instance ?

We can say that if the lesion affects the language networks in one hemisphere (most usually the left one in the right-handed), the child will be able to develop language in the other hemisphere, but it will happen at the expense of other functions. Plasticity has its limits, otherwise there wouldn't be any handicap.
Combination of breaches in several systems makes it impossible for the brain to learn and develop certain capacities. Knowing that allows to orientate prognosis and thus to quickly move towards early rehabilitation programs.
But there is much left to understand, in particular the variability of impairments depending on the person (I sometimes say there are « 50 shades of CP »). The ideal would be personalized medicine, we are still far from it but we're making progress.

Does MRI allow to evaluate therapeutic interventions like rehabilitation for instance ?

Now that we understand the mechanisms better, we can try to observe the modifications created in the brain by rehabilitation.
In a pragmatic way, we don't need imaging to see if rehabilitation works: there are goals, are they reached or not ?
However imaging will allow us to evaluate better than before what happens in the brain: what changes happen in myelin or in neural cells during rehabilitation ? That would allow us to understand why such rehabilitation is efficient or why it works for one child but not for the other.
Imaging is a tool for understanding what happens and for analysing the variability between methods or between patients.

What are the avenues of research for the future ?

Regarding knowledge of the child's brain, we have strong but incomplete bases. Current research uses big data and artificial intelligence methods to improve the sensitivity and robustness of our tools.

Databases in pediatrics are built up in Europe, in America and in the United Kingdom. They gather together hundreds if not thousands of children of all ages, some with typical development, some with neurodevelopmental troubles including CP. There, in these databases, we can include various complementary data (clinical, biological, genetic, from imaging etc), whose association proved to be fertile. These big data are accessible to all researchers (open data), which improves the richness and robustness of our studies and allows us to detect new prognostic or therapeutic markers with the help of artificial intelligence methods like deep neural networks.

6- Enhancing brain plasticity in children through early interventions

Interview
with Pr Mickaël Dinomais
Pediatric Physical Medicine and Rehabilitation
Les Capucins Teaching hospital, Angers

Progress in knowledge of Cerebral Palsy leads us to intervene early in newborns, as Pr Mickaël Dinomais explains.

How does brain plasticity work ?

Brain plasticity is the capacity of the brain to (re)organize itself by creating neural networks connected to one another by synapses to support functions (motor, language etc).
It happens naturally during brain maturation or after a lesion. Natural plasticity is possible at all stages of life, but seems more intense during the first 1000 days of life.
There is a great number of synapses. They reach their maximum density at the age of 6, then they experience pruning during brain maturation, when only the most efficient persist: the most used stabilize themselves and become more and more efficient while the others destroy themselves, just as the cell bodies of the neurons they connect. This natural plasticity and its development depend on genetic factors and external factors like external requests: the more a neural network is used, the more it becomes efficient. It creates a virtuous circle: the more powerful the neural network, the more efficient its function; the more the function is used, the more the neural network can organize itself and be efficient.
Today we know that natural brain plasticity depends on the activity, and that to learn how to make a gesture, and to make it efficiently, one must repeat it in real-world conditions. We learn to swim by being in the water, not by imitating the movements an instructor shows us near the swimming pool. We showed that post-lesional plasticity follows this same rule, and also depends on the activity.

What happens after a brain injury ?

CP results from a brain injury that occurs before the age of two, when natural plasticity is important. Post-lesional plasticity, inherent in the lesion, affects natural plasticity: both interpenetrate.
I said capacity for post-lesional plasticity depends on the activity. It also depends on the moment when the lesion occurred and on the maturity level of the injured system: the less mature it was when the lesion happened, the more plastic it is. Yet all systems do not develop at the same pace: the motor system matures very early, the language system later, until 6/7 years, cognitive functions until adulthood. A stroke (CVA) in the left hemisphere, where the language areas are located, can lead to

aphasia in adulthood. It won't be the case if this same CVA happens in the neonatal period: at the time of birth, the language networks are located in both hemispheres (even if the left is already a bit more specialized than the right). If a lesion occurs, language networks located in the right hemisphere, rather than disappearing, will reinforce and continue to take care of language. But if the lesion occurs after 7/8 years, the language system having reached maturity, there will be no turning back. The right brain won't take over. We speak of critical period when the system matured so much that it can't go back in case of injury.
In short, brain has capacity for reorganization, but it can't do everything, and it remains very vulnerable during the development period. The lesion will shake its foundations and complicate its subsequent building. Assaults on one system will have consequences on others: a focal lesion will affect all neural networks differently, depending on the moment when the lesion occurs.

How can we encourage this plasticity ?

There are several avenues of research. The first one concerns molecules: synapses involving molecules called neurotransmitters, we study the use of molecules that could keep stable the synapses created by the activity; that would help them strengthen and reach their long-term potential.
We can also intervene through rehabilitation. Plasticity can be enhanced for instance by repeating a gesture, which must be objective-oriented and receive feedback. It can be explicit (remarks from the instructor) or implicit (when patients understand by themselves what works and what doesn't).
Another very important element is pleasure: the rewarding times that also help stabilize synapses. When children take pleasure in what they do, they become more efficient, then they take even more pleasure and get more involved in their gestures. Moreover, good sleep quality is crucial for synaptic stabilization and thus for natural and post-lesional plasticity.
Finally, the earlier we intervene, the more important potential plasticity seems to be, which leads to early rehabilitation programs like the CAP project, on the HABIT-ILE theory: short intense rehabilitation periods with objectives determined with families and feedback from therapists.

Connected soft toys to stimulate toddlers ?

How can we optimize rehabilitation ?

We need to better understand how (natural and post-lesional) brain plasticity works and how we can stimulate it to succeed in mapping and planning interventions adapted to each child, which are individual and personalized rehabilitation programs according to one's capacities and potentialities. But we don't have the tools that would allow us to determine perfectly everyone's potential and rehabilitation profile. Exploration methods like MRI, MEG or EEG will also allow us, hopefully, to make a prognosis about plasticity for every child to modulate rehabilitation the best we can.

7- Population registers, an issue for the quality of care

Interview
with Dr Javier de la Cruz
Epidemiologist
University Hospital 12 de Octubre, Madrid

These data sources are a precious tool for following the evolution over time of the number and of the characteristics of a pathology in a population. Overview with Dr Javier de la Cruz, epidemiologist and expert in CP.

What is the role of a register ?

A register is a standardized data collection maintained over time. Population registers, called « population-based », cover the general population in a definite geographical zone.
A register is first of all useful as a matter of public health: it helps follow-up the evolution over time of a pathology in a population, to propose actions and to plan resources accordingly.
Moreover, in the field of research, a register is considered as a frame that can help answer questions for instance, what is the origin of CP ? What are its consequences ? In this case, epidemiology allows us to check hypotheses and to plan services.

How were born registers for CP ?

The first to implement registers for CP were clinicians who had clear ideas about public health and asked questions about the quality of care, in Denmark and in Sweden. Australia followed, then France, where two registers of disabled children were established in the 1990s, in Grenoble (RHEOP, register of childhood disabilities and perinatal data *) then in Toulouse (RHE31, Haute Garonne register of childhood disabilities**).
CP is not an easy pathology to work on, since it is less a disease than a condition, with a diversity of presentations and etiologies. Since the first registers, researchers stressed the importance of having quality rather than a big quantity of data.
A register must include the whole population concerned. In the case of CP, the difficulty lies in the fact that its identification in medico-administrative databases isn't automatic there isn't a test or a unique diagnostic code that would allow us to identify all persons with CP. It is thus necessary to work with several data sources to interpret clinical descriptions and to implement coding standards in a sustained manner.
Behind a register, there is always a specialized team of professionals from many disciplines, in close contact with institutions and networks of caregivers and researchers. And also, in the case of CP, with everyone related to the persons concerned by this condition.
To get comparable data from these registers, it was thus important to develop a common language between the different medico-social disciplines involved: obstetrics, pediatrics, rehabilitation, radiology, epidemiology etc.
This effort was made at the end of the 1990s on the initiative of Dr Christine Cans, Pr Ingeborg Krägeloh-Mann and Dr Ann Johnson. They were rapidly met by colleagues from Scandinavian registers and then from the rest of Europe to create the Surveillance of Cerebral Palsy in Europe

** https://rheop.univ-grenoble-alpes.fr*
*** https://rhe31.org*

(SCPE) network, whose president today is Dr Catherine Arnaud, RHE31.
Inclusion criteria, diagnostic algorithms and classifications of subtypes of CP were determined first with functional scales, or criteria in the field of neuroimaging allowing to share important databases.

What did these registers teach us ?

Every year, the scientists in charge of these registers publish a detailed report presenting recent local data put in perspective (evolution over time is also considered), which is a precious resource for planning social and health services.
SCPE showed us a global decrease in the frequency of CP. Changes in quality of maternal and neonatal care can explain part of it.
Data gathered by the network of European registers also allowed us to analyse the characteristics of subgroups of patients and to better understand the causes, in relation with subtypes of CP, prematurity, multiple birth or genetic anomalies.
Recent neuroimaging data on vast populations help establish the relation between brain lesions and functional manifestations.
These developments make it possible to think of measures that would reduce the severity of injuries direct patients towards the best therapies based on their profile; and mobilize the necessary means.

How can we still improve the usefulness of these registers ?

First they should be better known ! They would be a good basis for care programs, research studies or for decision-making in health and community services.
CP registers make a rigorous work, they benefit from a good evaluation while respecting data protection laws. Strengthening them would help them evolve and extend their influence.
They still face a number of challenges, among which:

- continuing to improve the quality of care
- integrating longitudinal (that is over time) monitoring of the registered, including adults
- building relationships with biobanks and other information systems.

Including the persons concerned in the board meetings of the registers leads to a review of the objectives, measuring and informing as to what is important for them. The most important is to continue to speak the same language.

The second part of this file will be published in Research Letter n° 28, Spring 2021. It will be devoted to life path from birth to adulthood: rehabilitation, technology, social life, participation etc.