



Traumatic Brain Injuries

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One of the most common causes of death for young people

Traumatic brain injuries resulting from traffic accidents, accidental falls or violent assaults generally occur in young subjects. In France, around 60,000 traumatic brain injuries occur every year, of which 5,000 are considered severe. The human, familial, social and economic costs of such injuries are considerable. Along with subarachnoid brain hemorrhages, traumatic brain injuries are the most common cause of the loss of years of life in young people, ahead of all other medical pathologies.

The initial severity of a brain injury is estimated in terms of the Glasgow score (Glasgow coma score: GCS), which evaluates the consciousness of the patient on a scale of 3 to 15. A brain injury is said to be severe when the initial GCS is less than or equal to 8. Recent progress in the initial care of the patient with severe brain injury, an improved understanding of the physiopathological mechanisms that lead to neuronal death as well as new monitoring technologies for neuro-intensive care have helped improve prognoses.

Severe brain injury causes immediate primary lesions (diffuse nerve fiber lesions, hemorrhagic contusions, intraparenchymal hematomas, extra- or subdural hematomas, vasogenic edemas) and secondary, deferred lesions. With the exception of certain hematomas that require immediate surgical evacuation (12 to 15% of patients require an emergency neuro-surgical intervention), primary lesions are irreversible and cannot be treated. They can, however, be prevented (by wearing helmets, reducing driving speeds, preventing violence).

Secondary brain lesions appear in the hours and days following the trauma, and are the consequence, on

one hand, of an alteration in the functioning of the brain, which is the source of intracranial pressure and tissue hypovascularization, and on the other hand the existence of bio-chemical disorders characterized by the massive release of excitatory amino acids, free radicals and other neurotoxic metabolites. These phenomena support the extension of secondary lesions that lead to cerebral ischemia, which considerably aggravates the prognosis of victims of traumatic brain injuries.

The physiopathological processes that are at the origin of these lesions are being studied by numerous experimental and clinical research projects. Over the past few years, fifteen clinical studies have examined the neuroprotective effects of several molecules such as glutamate antagonists, calcium antagonists, antioxidants, etc. Unfortunately, none of these studies has shown an advantage in terms of an improvement in the prognosis of patients suffering from brain injuries. Any improvements in the prognosis of these patients must be based on the discovery of new therapeutic targets, in particular activators of neural re-growth, and on improvements in quantitative tools used to measure cerebral lesions, which can be used to go beyond clinical variability.

The physical, psycho-sensorial and neurocognitive consequences in patients who have suffered severe injuries have the most dramatic personal, familial and social impact. The mortality rate on the 28th day after an injury was measured at 44% in a study undertaken in the Ile-de-France region from July 2005 to May 2007 on more than 500 patients having an initial GCS less than or equal to 8 (average age: 38). Only 20% of the patients showed few or no after-effects one year.



The ethical stakes in the initial care of these patients are also very important. The question of the proportionality of the services administered, with regard to the neurological prognosis, is constantly raised for surgeons and anesthetists during the initial care period of these patients, and during the time spent in intensive care, when invasive substitution techniques are put into place. The questions of the "acceptable level of handicap" and of the involvement of the family in the decision is at the heart of the relationship between health-care professionals and family members. These questions will be increasingly important in the next few years, as MRI techniques develop that will allow doctors to predict the patient's long-term handicap.

Pharmacological research in the domain of severe brain lesions will also greatly benefit from quantitative MRI techniques (spectrometry, diffusion tensor, volume measurement). These techniques that are currently being developed will allow for the drastic reduction in the number of patients required for clinical tests. This reduction will lead to cost reductions, and thereby to the increase not only in the number of these tests, but also in the speed of research into treatment strategies or into neuroprotective, neuro-modulating or neurostimulating molecules.

→ AT A GLANCE

The Promenades du Cavallino: On April 26, 2009, 62 owners of Ferrari and other exceptional automobiles gathered as volunteers at Ficheux (close to Arras), for the "Promenades du Cavallino"; 2,500 people came to the event that was organized by the Sogno de Cavallino Association to support the ICM.

Football match at Chantilly: A friendly soccer match was organized on May 8 to support the ICM, made up of players from the Variety Club of France and political personalities; with the support of the mayor of Chantilly, the D&O and the OCIRP.

Trophée du Luxe : golf swings and philanthropy On June 29, the golfers and partners of the second edition of the Trophée du Luxe participated in an event organized for the benefit of the ICM during a day of golf at Joyenval.

CIFA: The ICM participated in the 7th international forum of the CIFA (Convention of Independent Financial Advisors), an occasion to present the Institute to an international audience.

HEC: Many thanks to the students who turned out for the annual HEC gala to organize a raffle for the benefit of the ICM.

Festival of Romantic Cinema at Cabourg: The opening dinner was organized for the benefit of the ICM, in the presence of Professor Gérard Saillant.

Tribute: We have just learned of the death of Mr. Dominique Jérôme (research director at the CNRS, director of the research mission at the Regional Council of the Ile-de-France) and we would like to convey our sincere condolences to his family and friends.

His early support was very important in making the ICM project possible. Many thanks to all those who, at the moment of his passing, generously showed their sympathy through donations to the ICM.



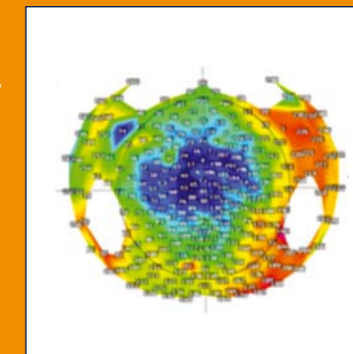
THE ICM CONSTRUCTION SITE

Construction is advancing; the walls and roof are in place, in accordance with the initial plans. On June 3, a topping-out ceremony was held on the construction site to celebrate the end of the structural work and the beginning of "finishing" work. A symbolic flag was raised on the roof of the building.



January 20, 2009, PNAS: the first publication for the ICM

While waiting for the 600 researchers selected by the ICM to be brought together in the 22,000m² building that is currently being built on the Pitié-Salpêtrière university hospital site, the ICM is financing extra-mural research teams. The research team of Dr. Naccache was chosen by the ICM, which has co-financed his work since 2006. The results of his team's research were published on January 20, 2009 in the very selective and prestigious scientific review PNAS (Proceedings of the National Academy of Sciences) which is one of the 5 most cited scientific reviews in the world. The authors have proposed a new test that permits the detection of the existence of conscious mental life, even in the absence of any clinical signs. This method, combining principles of the psychology of auditory perception with the measurement of electrical cerebral activity recorded at the patient's bedside, is an important contribution to the early care of many non-communicative patients (initially in a coma) for whom it is sometimes very difficult, if not impossible, to determine the level of consciousness on the basis of a traditional neurological examination. The method can still be improved in order to communicate even more accurately with the patients, using new tools such as the "Brain machine interface", another important subject for the transversal scientific program of the ICM. The perspectives of these scientific and medical advances are of the utmost importance, and the ICM is proud to have sponsored the team, whom it heartily congratulates.



Voltage topography of the "Mismatch Negativity" (MMN) in response to a rare auditory stimulus, by a non-communicative patient. This electric signature shows the reactivity of the brain to the auditory environment.