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Commemorative lecture at the 42nd Honda Prize
Award Ceremony on the 17th November 2021

Can Physics and Serendipity benefit to Clinical Neurosciences?

Dr. Alim Louis Benabid

Professor Emeritus of Joseph Fourier University
Chairman of the Board of Clinatec, Edmond J. Safra Biomedical Research Center

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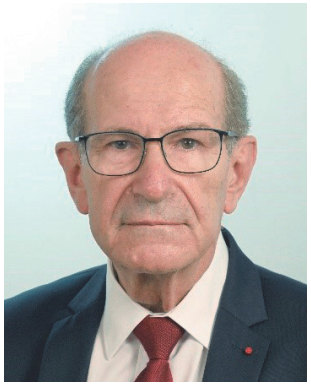


Dr. Alim Louis Benabid

Professor Emeritus of Joseph Fourier University
Chairman of the Board of the Clinatec, Edmond J. Safra Biomedical Research Center, France

■Born

May 2nd, 1942, Grenoble, France

■Education & Training

Medical Degrees (University of Grenoble)
1970: MD Thesis
1972: Staff Neurosurgeon
1978: Professor, Experimental Medicine
1984: Professor, Biophysics
1989-2007: Head of Neurosurgery

Scientific Degrees (University of Grenoble)
1973: Masters of Science
1978: Thesis (PhD) Physics

■Scientific Responsibilities

1978-2007: Director of LMCEC (Laboratoire de Médecine et Chirurgie Expérimentales et Comparées) and Laboratoire de Neurobiophysique
1984-1990: Director of IRMBM (Institut de Résonance Magnétique Biologique et Médicale)
1988-2007: Director of Research Unit INSERM 318 (Neurobiologie Préclinique)
1995-1997: Director of Center for Gene Therapy "Brain Tumors"
2007-: Director of the Clinatec Institute Project at CEA Grenoble
2008-2021: Chairman of the Board, Clinatec, Biomedical Research Center Edmond, afra, CEA, Grenoble

■Medical Responsibilities

1989-2004: Head of Neurosurgery Department – Coordinator of the Epilepsy and Movement Disorders Center "Claudio Munari", Niguarda ca Grande Hospital,Milano, Italy

■Administrative Responsibilities

Scientific Council of:
1976-1986: Medical School Grenoble
1976-1986: University of Grenoble

Administrative Council of:
1989-1993: INSERM (appointed by the Ministry)
2006-2012: Science Advisory Committee of ESRF (European Synchrotron Radiation Facility) Special Advisor
2007-: Scientific Advisor of the Director of Research and Technology at CEA
2016-: Scientific Advisory Board of the WYSS Foundation, Geneva

■Major Prizes and Honors

2007: James Parkinson Award, Parkinson's Disease Foundation, New York,
2008: - Movement Disorders Award of the American Academy of Neurology
- Prix d'Honneur de l'INSERM
2013: Robert A Prizker Prize, Michael J Fox Foundation
2014: - Lasker Prize
- Breakthrough Prize for Life Sciences
2016: European Inventor Award Research
2021: 2021 International Brain Stimulation Award

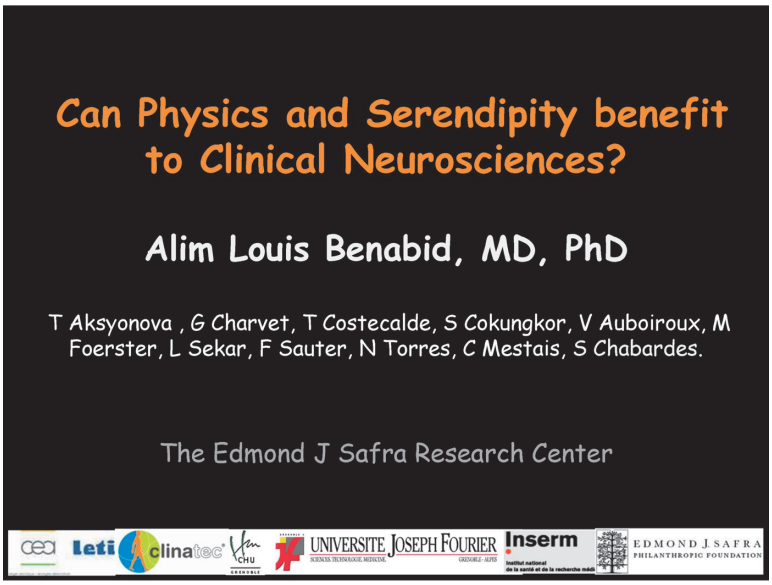
*over 30 awards and honors including the above

■Major Publications

- **Combined (thalamotomy and stimulation) stereotactic surgery of the VIM thalamic nucleus for bilateral Parkinson disease:** Benabid AL, Pollak P, Louveau A, Henry S, de Rougemont J: Appl Neurophysiol,1987, 50:344-346.
- **Stimulation of subthalamic nucleusalleviatestremor in Parkinson's disease**: Krack P, Pollak P, Limousin P, Benazzouz A, Benabid AL: Lancet. 1997 Dec 6;350(9092):1675.
- **Chronic stimulation of subthalamic nucleus improves levodopa-induced dyskinesias in Parkinson's disease**: Krack P, Limousin P, Benabid AL, Pollak P. : Lancet. 1997 Dec 6;350(9092):1676.
- **Electrical stimulation of the subthalamic nucleus in advanced Parkinson's disease:** Limousin P, Krack P, Pollak P, Benazzouz A, Ardouin C, Hoffmann D, Benabid AL: N Engl J Med. 1998 Oct 15;339(16):1105-1111.

This report is the gist of the commemorative lecture at the 42nd Honda Prize Award Ceremony on 17th November 2021.

Can Physics and Serendipity benefit to Clinical Neurosciences ?



Mr. Chairman, ladies and gentlemen, I want to say how impressed and honored I am to be designated as the winner of the Honda Prize 2021.

This is my pleasure to present mostly the results of what we have been doing for 30 years, the treatment of Parkinson's disease, extendable to similar neurodegenerative diseases, and I will present the results of deep-brain stimulation that we discovered in the late '80s, and more recently the introduction of infrared-light illumination, which we hope will be protective and might be a cure for Parkinson's and may be extended to other neurodegenerative diseases.

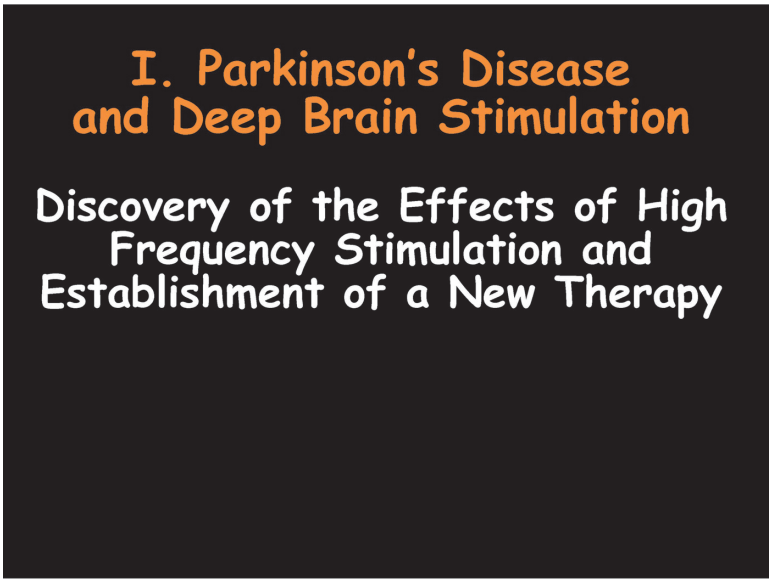


Fig. 1

〈Fig. 1〉 Parkinson's disease and deep-brain stimulation is based on the discovery of the effects of high-frequency stimulation, from which we established a new therapy.

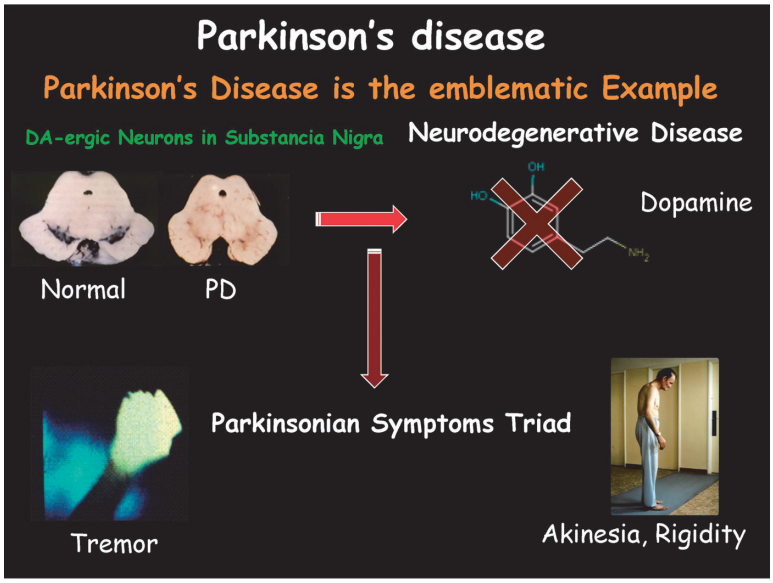


Fig. 2

〈Fig. 2〉 This is typically an example of the approach that doctors, surgeons and neurologists may have in front of the problem raised by the appearance of disease in a patient. In the case of Parkinson's disease, it is essentially related to the appearance of dopaminergic neurons in the substantia nigra. The substantia nigra takes its name from the presence of melanin, associated with dopamine, and this is why this place is black in normal patients. During the process of degeneration, what we see is the disappearance of those cells, which normally produce dopamine, and when they disappear the patient loses anatomical control at the end of the disease, meaning that all the neurons producing the dopamine have been destroyed and disappeared. As a consequence, this induces the Parkinson's symptom triad, which is made of tremor, first, and second akinesia and rigidity—the three elements essentially impacting the capacity of the patient to perform movements.

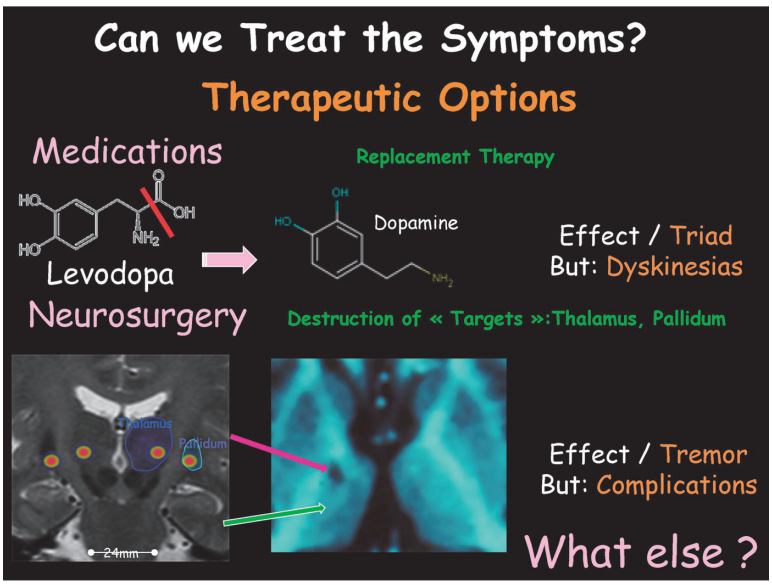


Fig. 3

〈Fig. 3〉 What are the therapeutic options? There are three. The first one is medication, meaning replacement of what is missing. This is possible thanks to the invention by Arvid Carlsson of levodopa, which is a precursor of dopamine, which can cross the blood-brain barrier and then in the brain is decarboxylated, producing the dopamine molecule, which is the efficient molecule for the effects. The effects cover the components of the triad—tremor, akinesia and rigidity—but those beautiful effects are plagued by complications, which are dyskinesia. The second approach is neurosurgery, consisting of destruction of targets, the thalamus and the pallidum, and we have different targets available, either the thalamus or the pallidum, here, the problem being that we have to be correctly placed. The lesion, which is made by—electrolytical assay and electrical current induces a lesion that has to be in the right place, which is not the case in this case, it should be more posterior. The effect when the electrolytical lesioning is sufficiently well placed is suppression of tremor, but it has complications, particularly when we are not correctly placed. So in front of these two options, is there anything else which could produce the same effects but not having the complications?

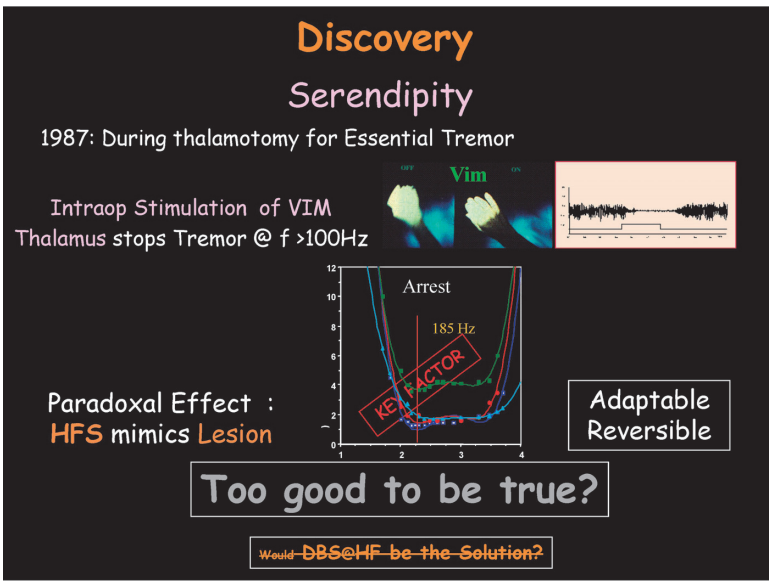


Fig. 4

〈Fig. 4〉 This is where we come to the discovery that has led to high-frequency stimulation. It is in the area of what we call serendipity. Serendipity is essentially discovering something you have not foreseen, you did not intend to see it by itself, but because your mind is preoccupied by the problem you have, which is for instance suppressing the tremor, an unintended effect or unintended event would be taken as a possible source. This is the famous "aha!" situation: What I see is not what I expected, but it could be a solution for what I need. For instance, during intraoperative stimulation of the ventral intermediate nucleus of the thalamus before making the lesion, checking that we are in the right position by taking a photo, you see that it is blurred by the tremor. And when we are in the right place and with the right parameters we have this suppression of the tremor, which allows us to take a good picture. The importance is that these tremor arrests happen at frequencies that are higher than 100 Hz, which is considered high-frequency stimulation, as compared to the 50 Hz of classical stimulation. We see here that the tremor, when we turn on the stimulation at high frequency, suppresses immediately and irreversibly the tremor. This arrest happens in the window of frequencies between 115 to 130 Hz up to several thousand Hz of frequency and in this place, we have this situation, the absence of tremor. This is paradoxical as we know, teaching students that electrical stimulation induces excitatory effects, while here atypically it mimics the effect of lesion, having the same effect as a lesion with the difference that a lesion is not reversible. The interesting thing about high-frequency stimulation is that it is adaptable, that it is reversible, and those beneficial effects with the lack of complications makes it an ideal situation. As we say, could it be usable? It looks like it is too good to be true.

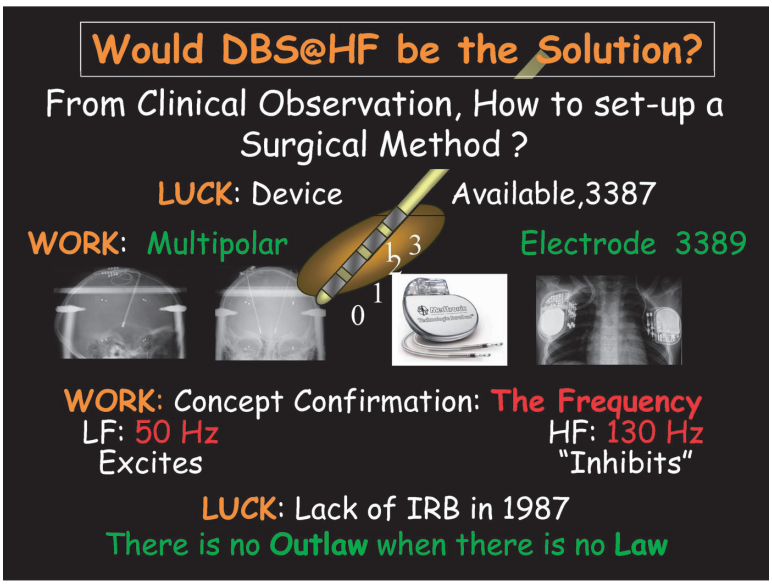


Fig. 5

〈Fig. 5〉 Then the question is, would deep-brain stimulation at high frequency (DBS@HF) be the solution? From clinical observation, how can we work to set up a surgical method? In this situation, we have positioned electrodes where we used to make a lesion and the contact that we had at the period, the electrode we had at that period had only one contact and it was associated to stimulate made by Medtronic Society at that time. We could do it bilaterally, or even have several electrodes. Then we were lucky because the device was available for the indications so we wouldn't have to develop it at that time, and to make it better than that we had to ask the company to make more electrodes. In the meantime, we had confirmation of the concept, which is that the frequency is a critical element. At low frequency we still have excitation, that is known, while at high frequency, at 130 Hz, this induces inhibition, which is what we used to see normal. Then we went to a multipolar electrode to increase the specificity. We had to convince the makers that they could develop a new electrode, which is called 3389, which has four contacts, meaning that we have the possibility, by playing with the settings, to modify the position of the place where we put in the electrode current, this being more precise and more efficient for what we want to do clinically. The luck, the essential luck we had at that time, was that there were no, at least in France, no internal review boards, meaning that we didn't have to go in front of an ethical committee, didn't have to present complicated pre-clinical data in animals. And we took advantage of what happened, which is the fact which allowed us to develop the method very quickly. There is no outlaw when there is no law to break.

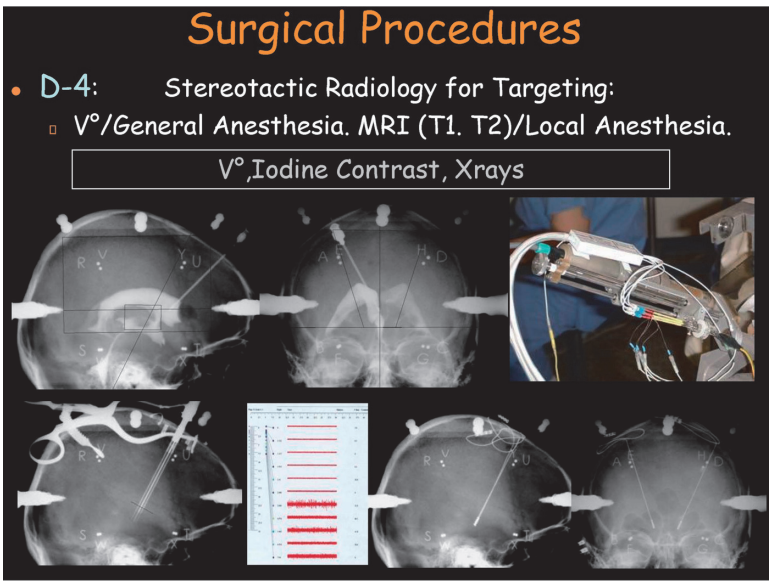


Fig. 6

〈Fig. 6〉 The surgical procedure to achieve that is based on, in fact, localization of the target. Here, using ventricular radiography by injecting iodine contrast and making some geometrical constructions, we can see ways the average position was adapted to the patient of the targets and bilaterally separated from the midline by 15 mm. We used during the surgery a Microdrive which allows us to descend microelectrodes recording the electrical activity along the track. On the superior part of the track there is no electrical activity here. We start entering the basal ganglia, we reach different frequencies and different patterns along the end of the track, which is the important place where we are going to put electrodes. When we have seen where we decide to put the final electrode, this is what we have, we see its place, this is a four-contact electrode placed in the thalamus or another target site. We can make it perfectly symmetrical and then observe the patient clinically.

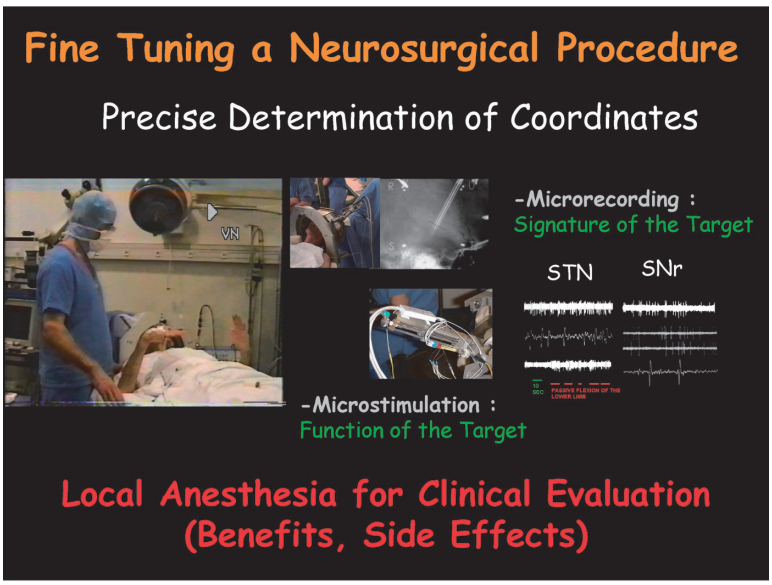


Fig. 7

〈Fig. 7〉 During this procedure we have to do precise determination of coordinates and when we are in some place we can turn on or off the stimulation, checking the symptoms and immediately after that there was an effect, unilateral here, because the electrical stimulation is unilateral, we stopped it and the tremor reoccurred. During this process we can do microrecording, which seeks the signature of the target here in the subthalamic nucleus. The firing is totally different from the substantia nigra reticulata, which allows us to check that we are at the proper place, this is where we have to be. We can also observe some other effects, particularly when we manipulate the patient, we can see changes in the firing to the microstimulation which is done afterwards, which shows the function of the target as you will see, and we can see already that high-frequency stimulation in this place which stops the tremor. Lower than that, in the substantia nigra reticulata, we have a totally different pattern and also a totally different effect of stimulation. This is done under local anesthesia for clinical observation. It is very important to know that where we put the electrodes, we have to check the benefits: the disappearance of the symptoms and also the absence of side effects such as tingling, showing that we are in a sensory area, or movements, showing that we are in a motor structure.

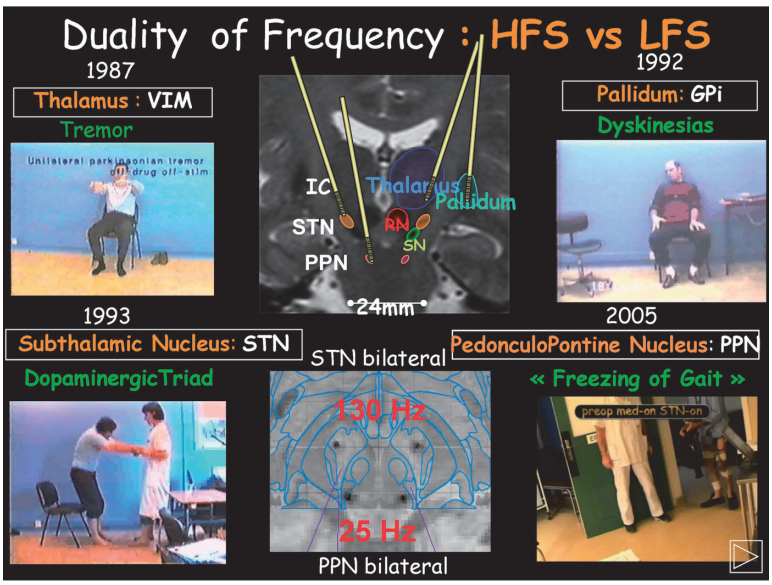


Fig. 8

〈Fig. 8〉 It is important to talk about the duality of frequency. We have said that HFS has an inhibitory effect versus LFS. We can see that in the thalamus area, (nucleus ventralis intermedius), the patient having Parkinson's tremor, I give my colleague a signal and he turns on the simulation, and the tremor disappears, reversibly. This is when we are in the thalamus. If we go into the pallidum, which is a bigger target, we see also that the dyskinesia making the clinical pattern of the patient will disappear when we turn on the stimulation and the patient tells you, "OK, it's gone", this movement will disappear but remains on the other side, which is not affected by the electrode. On the opposite side, when the pallidum is not treated continues to have dystonic movements. A third target, which is most important, that we addressed in 1993 and that is the subthalamic nucleus, is very low in the brain stem. Then the patient at the bottom left in Fig. 8, having the dopaminergic triad of symptoms: He is rigid, he is akinetic, he does not move easily, and then we ask him to make movements this is what happens: When the electrical stimulation at high frequency works, he gets normal movement of the hands and walking is normal. This is what we observe in those nuclei, the VIM, the GPI and STN, at high frequency, at 130 Hz. If we go to another set of targets, which are the pedunculopontine nucleus, which are posterior, and have been discovered by teams in Oxford, then it has a different effect and opposite to the high frequency. It has to be done at very low frequency compared to that at 25 Hz, which is excitatory, because this nucleus is becoming atrophic and has not to be inhibited, it has on the contrary to be excited, and this is obtained by low frequency. This is what you see in patients implanted in the PPN, they have disturbance of the gait, they walk and they eventually will fall, particularly when they are subjected to a stressful situation. And if we turn on the stimulation we can see in the same patient the same day, the difference between low frequency versus high frequency.

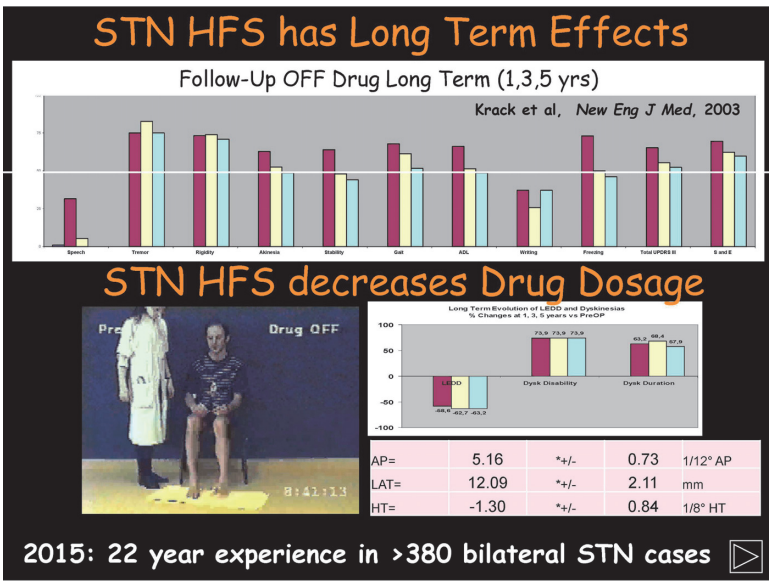


Fig. 9

〈Fig. 9〉 If we look now at the results of STN stimulation in Parkinson's patients, we have published already the follow up of five years, in an STN stimulated Parkinson's patient on different items. One can see that the improvement is above 50% except for a few items, particularly speech and on the other side the brain stimulation, the high frequency stimulation of the STN, allows decreasing the drug dosage and by the way also decreases the side effects occurring with the high drug dosage. And if we look at the patient, we see that, off drug, he has all the symptoms at a very high level, he is very slow in doing hand movements, he is slow at walking, we see that in the toes he develops a tremor, he's in a rigid position. When the drug is on, he has dyskinesia, typically on period dyskinesias, disability. When the drug is off and the stimulation is on, we see that the patient has no symptoms, he will do what is needed, asked by the neurologist. He has agility of the fingers and we can see that he can walk much better than he used to do. He could stand up from the chair, walk, go back and forth, in a very easy way. Because of the efficiency of the STN stimulation, we can also decrease strongly the drug dosage and as a consequence we decrease also the side-effects which mark the dyskinesias. We have a strong and long-lasting improvement. These are the coordinates in the stereotactic system, depending on the ventriculographic pictures, very precise for the implantation of the patient.

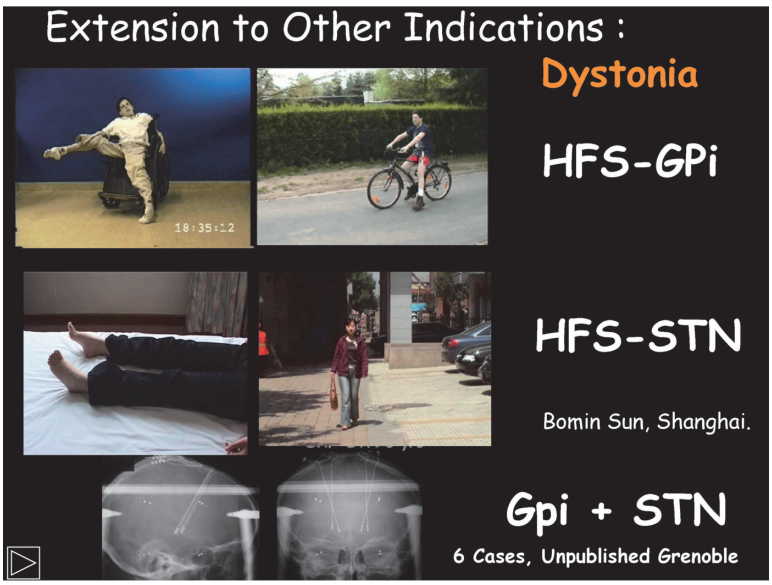


Fig. 10

〈Fig. 10〉 Then other indications are multiple. Here we have the effect on dystonia. This young patient at the upper left, has the DYT-1 mutation responsible for his lower-limb handicapping dystonia with abnormal movement and control. And when we turn on high frequency stimulation of the pallidum, we see that he recovers. What is usual at his age is biking. Here we have another patient, operated on by our colleague and friend Bomin Sun in Shanghai, and we see this young lady before surgery walking through the streets doing errands and here, we see this young lady biking, even though she's biking the wrong way. As the two targets are also equally efficient, she was operated on the subthalamic nucleus, which also provides beneficial effects as GPI. It's possible to have the combination of the two. See here the patient with two pairs of electrodes, outer in the pallidum and medial in the STN, with additional benefits. We have operated in six cases on the pallidum and STN, not yet published.

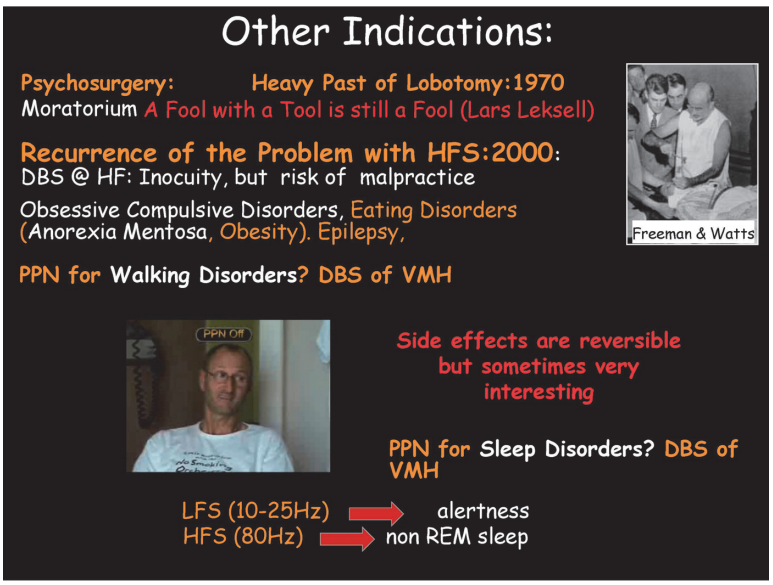


Fig. 11

〈Fig. 11〉 Then if we extend the application, the first one has been psychosurgery due to the heavy past of lobotomy, which was most formidable in Europe in the 1970s, prompting a moratorium. We have tried a different situation with high frequency DBS, because the innocuity has been easily accepted although it induces its own malpractice, because as it is less risky, we may have more surgeons tempted to do it. The most spectacular obsessive-compulsive disorder, also eating disorders (anorexia nervosa and obesity) and epilepsy. And also looking at the PPN where you saw the improvement in walking disorders, we have observed side-effects that are interesting. For example, when the patient wakes up in the morning, we have stopped the stimulator for the night to save the battery, and the patient reported that at 5 AM he was suddenly awakened and he felt something happening, and in fact it was that the stimulator turned on automatically. We wanted to explore more. There was an effect here, which was awakening.

What would happen if we stimulate PPN at high frequency, similar to Parkinson's? What we see, look at that in this patient, is that he looks normal but then he falls asleep very quickly, then wakes up after two hours' stimulation at low frequency. So those opposite effects of lower and higher frequency open the way to new applications and this has to be discussed but this is interesting to see: The same structure of high and low frequency has effects not only on waking but also on sleep, which tends to push us to explore what can be done for sleep disorders. Low frequency induces alertness, high frequency induces non-REM sleep.

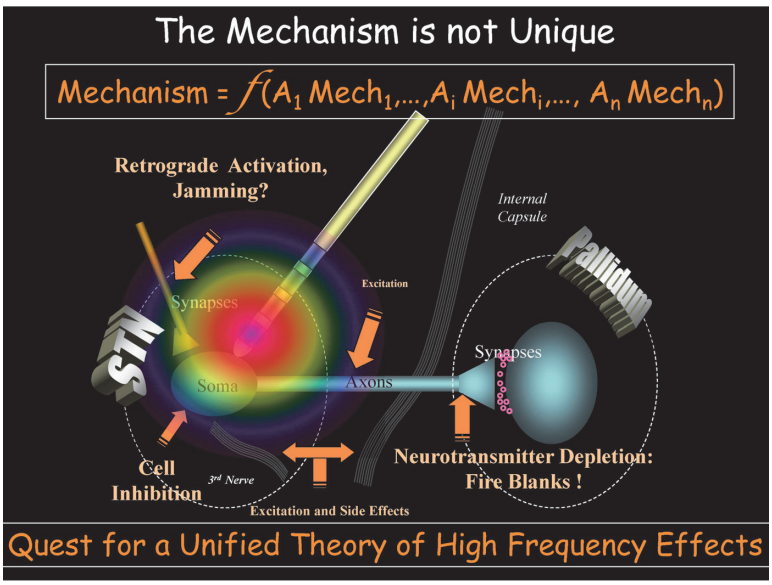


Fig. 12

〈Fig. 12〉 The mechanism is probably not unique. Without going into details, it could be a combination of cell inhibition, retrograde activation, also excitation and side effects and it's easy to understand fibers but it's also possible that the excitation of the axons, not on the soma of the neurons, would induce depletion of the neurotransmitters emitted by the synapse and then, when stimulated, the neuron would fire blanks.

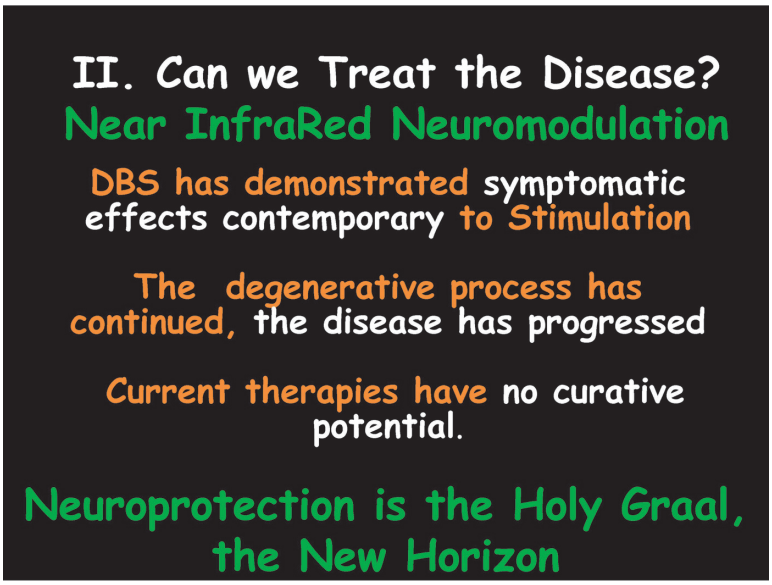


Fig. 13

〈Fig. 13〉 Now can we treat the disease? We have seen that DBS has demonstrated symptomatic improvement in the patient contemporary to stimulation, but during this the degenerative process has continued, the disease has progressed, and so current therapies have no curative potential from DBS for mitigation. Then the question is, we have to look in the other direction, which is neuroprotection, which is the Holy Grail now, the new horizon.

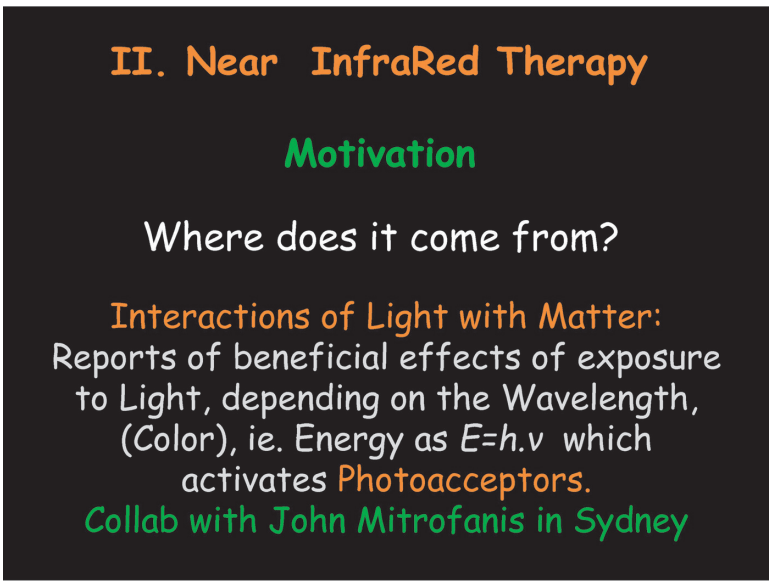


Fig. 14

〈Fig. 14〉 The motivation to go there is due to the knowledge we have of the interactions of light with matter and reports of beneficial effects of exposure to light depending on the wavelength, which has been reported based on the activation of photoacceptors such as cytochrome c oxidase. The work has been done through strong cooperation with John Mitrofanis who joined us in France.

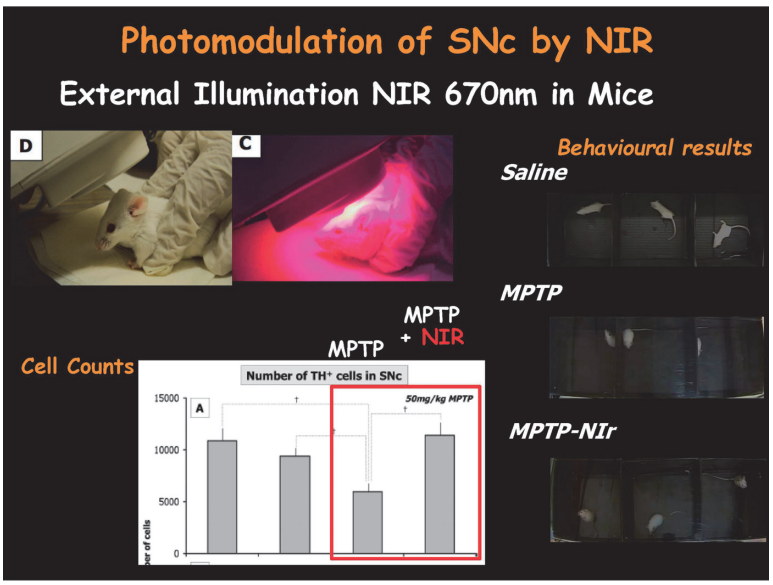


Fig. 15

〈Fig. 15〉 So if we take mice injected with MPTP then we make them “Parkinson’s” quote unquote. Their activity is reduced biologically so they have deficits at the level of the mitochondria and at the level of dopaminergic cells. So the treatment of those animals could be easy, just by exposing them to 670 nm NIR, using a lamp if you want, and we see that as compared to the behavioral result, we checked it with saline which are very active exploring in their cage, the MPTP treated animals are very akinetic. I think they don’t move too much, while those that have been irradiated with Nir did not record the same activity, the normal ones did much better. On the biological side, if we look at the number of TH cells in the substantia nigra reticulata, this is normal animals injected with saline, here the animals treated with MPTP-NIR have very significant loss of their TH-stained cells, while those that received MPTP have been preserved clearly as compared to normal animals.

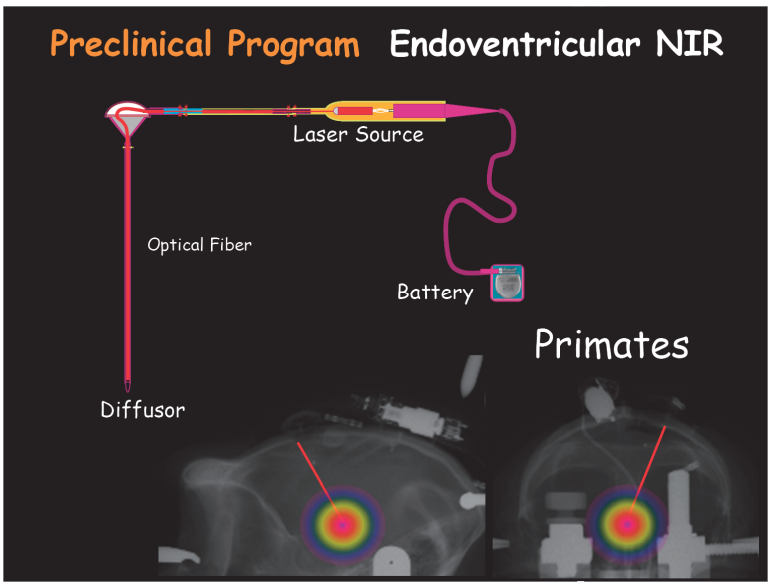


Fig. 16

〈Fig. 16〉 So then we designed a prototype to be used in patients. This prototype is made of a battery, the one we use for DBS, which powers a laser source, which is connected to an optical fiber which is introduced by tracing a way close to the substantia nigra sites. This system has been implanted in monkeys. We see the track of the laser fiber and when you turn on the stimulation, we display into the endoventricular space, the infrared light which encompasses the two substantia nigras.

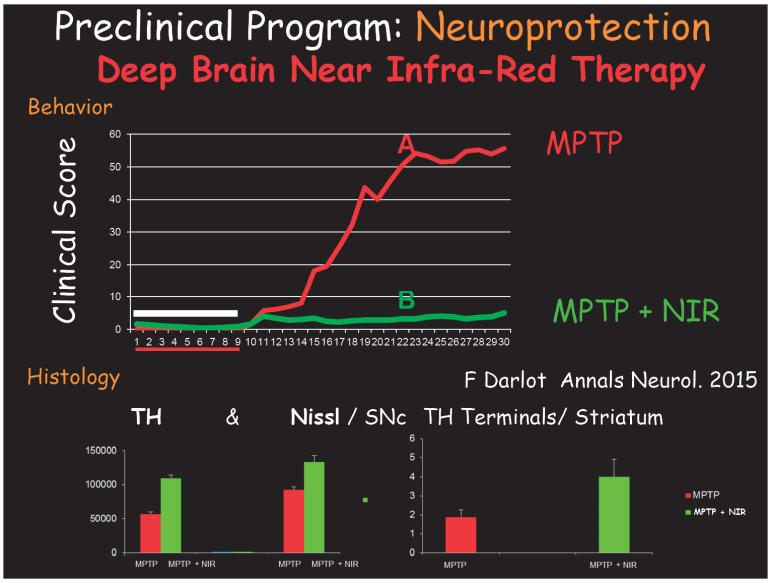


Fig. 17

〈Fig. 17〉 Look at the data of the monkeys that have been treated this way. Those who have received MPTP only are extremely disabled. This is a score of disability. We see that it increases to a higher level. Here the animals have to be treated, nursed, even given drugs, while those animals treated the same way but treated with MPTP and NIR are still exhibiting behavior which is close to normal. At the level of histology, we see again that MPTP treated plus NIR animals have TH-stained cells close to normal as compared to those which received MPTP. Same at the level of striatum, where the number of TH terminals is relatively preserved as compared with the untreated animals.

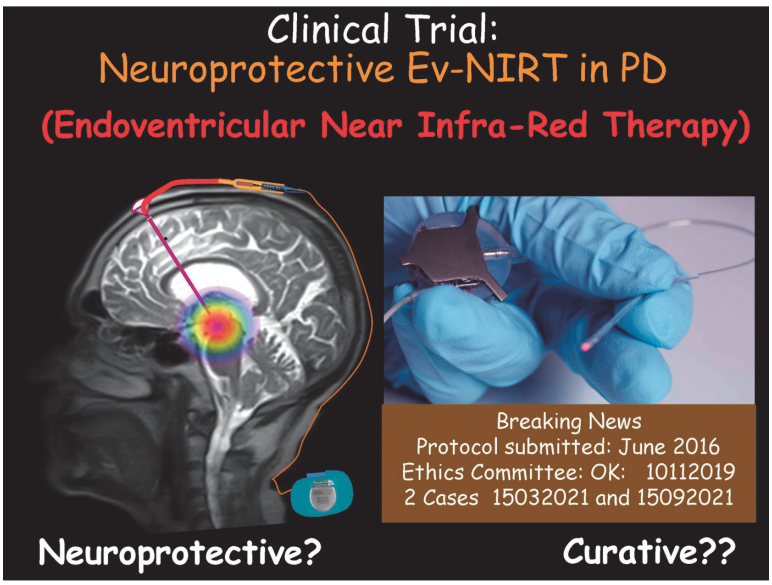


Fig. 18

〈Fig. 18〉 So this tends to substantiate the neuroprotective effect of near-infrared light and led us to go to human medical trials. You see here the device which is connected to a stimulator, such as the ones used in DBS which powers the device, with the fiber going into the third ventricle close to the substantia nigra reticulata. When we turn on the stimulation there is emission of infrared light which is visible here, the tip of the fiber coming out of the laser source which has been designed and produced at Clinatec. Then we went to the clinical trial, which was not easy to present and defend, but finally we obtained the clearance and protocol had been submitted in 2016 and three years later we had the OK from the committees. We implanted the first patient in March of this year, 2021, and the second patient was operated on very recently, in mid-September of the same year. The idea is to see if it is curative in addition to neuroprotective. For this first patient, and since we have observed, at three weeks after the beginning of the illumination, part of her symptoms was that she had difficulty putting on her shoes and tying the laces, now she is able to do it, this is not enough for publication but it is in a good direction.

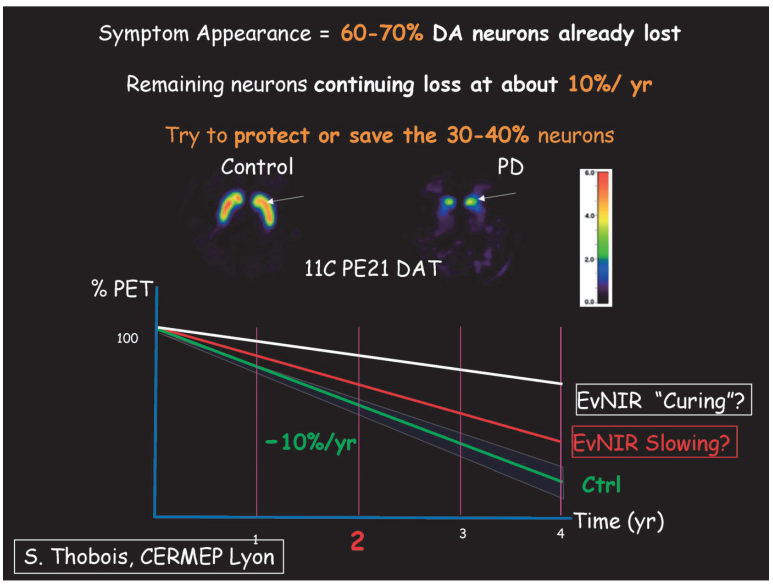


Fig. 19

〈Fig. 19〉 So the clinical trial will look using a PET scan at what may happen. PET scan PU2I is able to monitor the number of dopaminergic cells in the substantia nigra. In Parkinson's disease we know that patients lose about 70% of their cells at the beginning of the symptoms and they continue to lose them at a rate of 10% per year. So the goal is to protect, to save those 30% remaining dopaminergic neurons. The left image is a PET scan of a normal person and the right image is a PET scan of advanced Parkinson's. There are very few remaining. And normally, over the four years of the clinical trial, this is compared to the beginning, this is what we expected to see in untreated patients. With the infrared, the pessimistic approach would be that it does not improve significantly, so maybe this decrease of 10% being less, but what we hope is much more important, slowing of the decrease, coming close to curing this disease.

Fig. 20

〈Fig. 20〉 This is CLINATEC at CEA, linked to Grenoble University Hospital. This building is devoted to this kind of studies. We have the clinical area for the patients before and after surgery. We also have teaching rooms, the offices of the researchers, and buildings where the experiments are done.

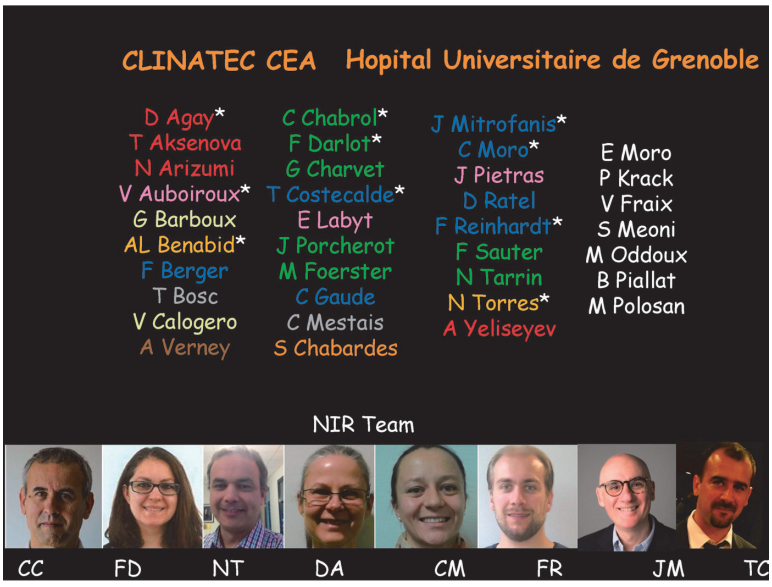


Fig. 21

〈Fig. 21〉 These are the people at CLINATEC CEA who are involved, in the NIR team, and they are responsible and I am grateful to them for all the data they presented to me. I thank you for your attention.

Regarding Recent Research: Brain Computer Interfaces

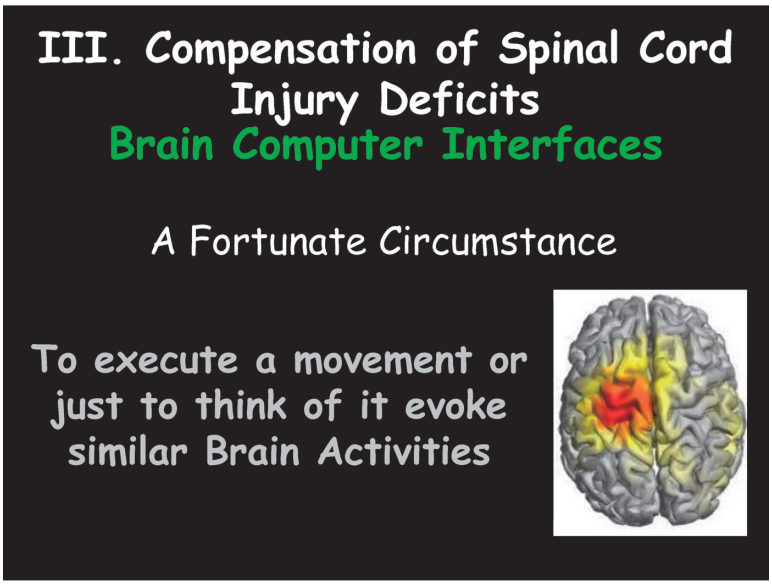


Fig. 22

〈Fig. 22〉 As we say we have a very fortunate circumstance, because the brain is very selfish. If I want to do something which activates cortical neurons in the expected motor area. But what happens is that if I want to do it or if I do it, the cortical neurons involved in this fire independently of what happens at the lower levels, particularly in the spinal cord. So I used to say that the brain talks and no-one listens.

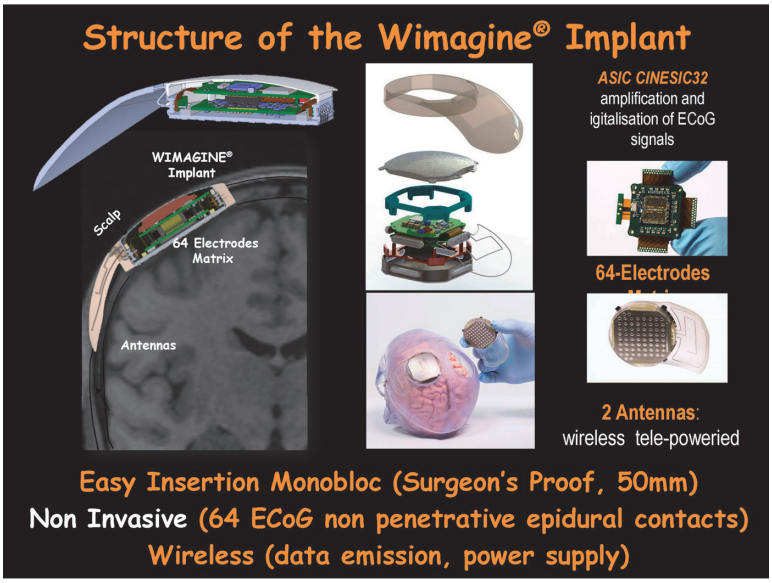


Fig. 23

〈Fig. 23〉 With the power of Clinatec in the CEA facilities, we have designed an implantable, cordless, wireless system which is implanted in front of the sensory motor area. It has the power of recording the activities on 64 electrodes and then it is digitized, transformed and sent away by radio module and you see that it looks like the visor of a cap, it is a silicon flap which comprises the antenna to emit the data but also an antenna which receives energy through a link which makes everything work without any external connection and there is no risk of infection. The implantation is extradural, epidural, which makes it safe in terms of infection. If some infection happens at a higher level, it will not go into the brain or even the subarachnoid place space because the implanted system just lies on the dura mater which is a very strong barrier. And we made it not only non-invasive but also surgeon-proof because it reduces strongly the possibility of malpractice.

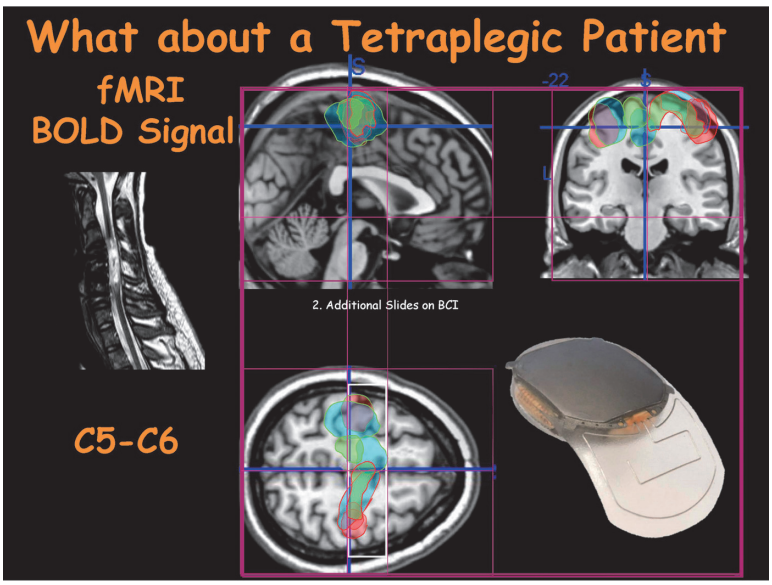


Fig. 24

〈Fig. 24〉 The three images on MEG analysis and functional MRI show us very nicely where the activity is happening on the level of the cortex when we ask the patient to move the leg or to move their hands, although they are tetraplegic (all indications for the moment are that they are tetraplegic patients). And you see the MRI of the patient on the three segments: the medulla and spinal cord at levels C5 and C6 are totally destroyed.

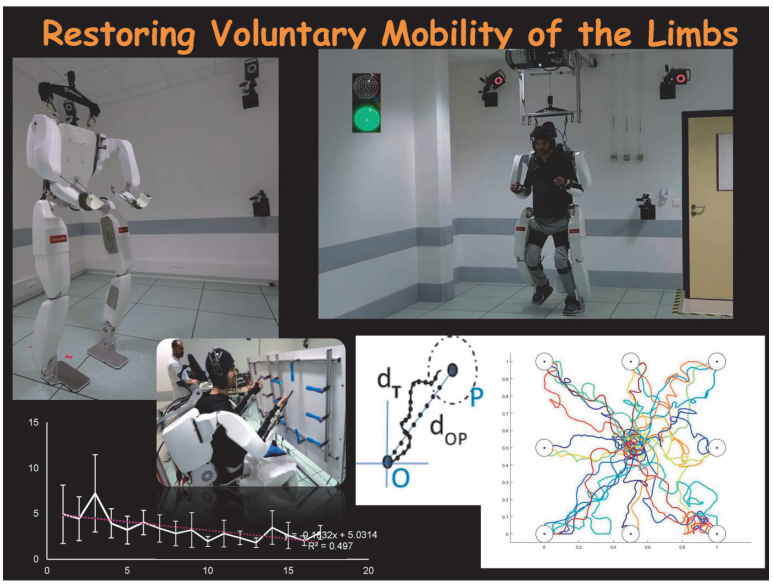


Fig. 25

〈Fig. 25〉 This slide shows that from that we designed an exoskeleton, as you can see in the upper left image, which is handling the patient. It does not have further movements for automatic equilibrium and when the patient is suspended from the ceiling for security reasons, when we ask the patient to walk, which is shown by the green light, then he initiates the walking sequence for the lower limbs and he will then stop when the light turns red. We still have a lot of progress to do, and for that we need a lot of administrative authorizations that we don't have for the moment. Then just lower than that you see the patient with the exoskeleton sitting in front of a panel which has different targets which are LEDs in red or green and he has to touch the lighted targets which become lighted in sequence. He can do that with his upper limb. We calculate the efficiency of that by measuring the distance done followed by the index of the exoskeleton from zero, which is the starting point, to P, which is the target. We can measure the actual distance which is followed and then calculate the distance from the direct trajectory. You can see on the right side what happens for different attempts. The lower left diagram shows the efficiency of this approach. With time, with repetition and with training, we see that after a few months of training the patient is able to do quite precise reaching. So I think it is one of the last.

Fig. 26

〈Fig. 26〉 This is the last slide and it's the same as the one before. The interesting thing about Clinatec is that you put in the same place medical and physiological techniques as well as engineering and technological solutions. It needs a different set of workers, and you see them there essentially showing the multidisciplinary approach which is realized in the system. We think that, although this is not necessarily understood or wanted by the upper layers of command, we think it is an important approach that we find a way, and Clinatec is this kind of way, where medical people, biomedical persons and technological persons are working together on the same project and fusing their own qualities and potentialities. This is easy to say but it is not easy to achieve and to run, but it is the motto of Honda Foundation. All of this, difficult or not, is mostly if not uniquely aimed at the better being of patients and particularly those who lost their motricity. And I'm sure this is what Honda has understood, because what they do is provide machines which allow us to change our place on the map of the earth and this is for their benefit and this is the same direction as you felt it, which is taken by Clinatec. And I thank you for giving us this wonderful prize because it means that you share—of course, this is your motto—this goal of improving the being of patients who have lost their motricity, particularly because of quite often traumatic events. I thank you again for this award, it rewards us, but I would say, further than that, you are doing wonderful impact which would be understood by the authorities handling and directing this institution that were working for the benefit of patients, giving them back what they have lost, which is important, it looks like stupid but motricity is very important.
I thank Honda Foundation for having backing this work. Thank you again. I'm very honored and very impressed and very humbled and very moved by this. Thank you.

HONDA FOUNDATION

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