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Cerebral Impaludation – An Ignoble Procedure between Two Nobel Prizes: Frontal Lobe Lesions before the Introduction of Leucotomy

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Keywords

Lobotomy · Leucotomy · Impaludation

Abstract

During the 20th century, only two persons have been awarded the Nobel Prize for psychiatric discoveries, Julius Wagner-Jauregg in 1927 for the introduction of malaria inoculation in dementia paralytica and Egas Moniz in 1949 for prefrontal leucotomy. According to traditional narrative, Moniz was inspired by a presentation by Carlyle Jacobsen on prefrontal lesions in chimpanzees at a congress in London in 1935. A few months later, he performed the first operations with the help of a young neurosurgeon. These leucotomies were done using injections of a small amount of alcohol into each frontal lobe through a single burr hole on each side of the skull, and the findings from the first 20 patients were published soon after that in 1936. It has, however, been difficult to reconstruct the path leading Moniz to frontal leucotomy, due to his unwillingness to acknowledge contributions from others. Maurice Ducosté, psychiatrist at Villejuif in Paris, France, started his work with psychiatric patients in the early 1920s with mechanical lesions in schizophrenia and contin-

ued with injections into the frontal lobes. Later, he focused on general paresis of the insane in neurosyphilis. Here, he introduced injections of malaria-infested blood into the frontal lobes – cerebral impaludation. Injections were used also in schizophrenia, mania, melancholia, and other psychiatric conditions. These injections were up to 5 mL in volume and could be repeated up to 12 times in an individual patient, which must have created significant lesions. Ducosté performed his procedure in hundreds of psychiatric patients before Moniz attempted leucotomy, and his work was presented in several publications before that by Moniz. Moniz basically used the same entry point, target depth, and technique in his first leucotomies. The major difference was that Moniz used alcohol with the clear intent of producing a lesion. Further, Moniz must have been aware of the work of Ducosté, since they presented papers, one after the other, at a meeting of the French Academy of Medicine in 1932. Even so, Moniz never acknowledged any contribution by Ducosté. In my opinion, it would be appropriate to acknowledge the contribution of Maurice Ducosté to the introduction of lobotomy.

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Introduction

During the 20th century, only two persons have been awarded the Nobel Prize for psychiatric discoveries, Egas Moniz in 1949 for the introduction of prefrontal leucotomy and Julius Wagner-Jauregg in 1927 for the introduction of malaria inoculation in the treatment of dementia paralytica [1]. Wagner-Jauregg's contribution has been largely forgotten, even though it was probably more beneficial to mankind, while Moniz has secured himself a place in history.

Moniz had very actively been pursuing the Nobel Prize earlier, for his work on cerebral angiography, relying not solely on his scientific skills but largely on social networking and promotional activities. In this quest, he had displayed some – for a scientist not too uncommon – less admirable manners. Many of his actions displayed an obsession with priority and a marked unwillingness to acknowledge contributions from others, and he would go “to extremes to avoid sharing any of the credit” [2]. In the end, he fell on the finishing line, partly due to an issue of priority.

This was a grave personal loss for him, and he would therefore pursue the Noble Prize for leucotomy with even greater zeal, displaying the same manners in this new quest [2, 3]. However, it has hitherto not been clear how well he succeeded in making the world disremember the link between leucotomy and Wagner-Jauregg – and the now forgotten cerebral impaludation (CI) of Maurice Ducosté – which is the topic of this paper.

Neurosyphilis and Wagner-Jauregg

Neurosyphilis, with dementia paralytica, more commonly known as general paresis (GP) (*paralysie générale* of the insane), was a severe health problem in the early 20th century. To take Great Britain as an example, it is estimated that 10% of the beds in asylums were occupied by victims of this disease and that about 80% would soon suffer an often horrendous death [4].

While we today consider this infectious disease to be in the realm of microbiologists, neurosyphilis in the pre-antibiotic era was perceived as a mental disorder of central importance in the field of psychiatry [5], a field which in many cases was the responsibility of the neurologist. Neurosyphilis was further known as “the great imitator” because of the diagnostic difficulties in differentiating it from other mental disorders.

Many different therapies had been tried, but with limited success, until the Austrian Julius Wagner-Jauregg

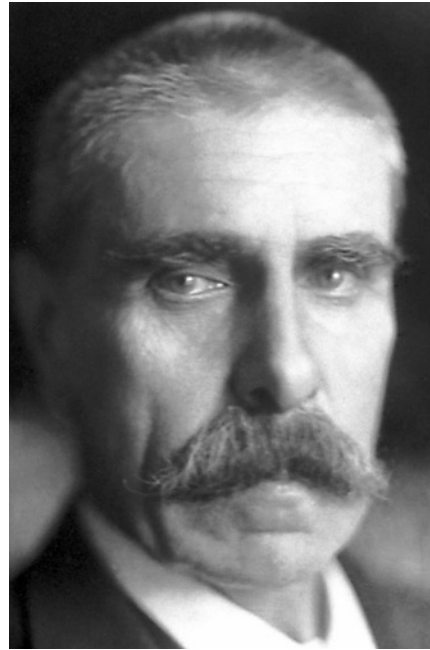


Fig. 1. Julius Wagner-Jauregg. From the Nobel Foundation archive.

(Fig. 1) discovered the therapeutic effects of malaria [6, 7]. Wagner-Jauregg was the successor of the well-known Richard von Krafft-Ebing at the Neuropsychiatric Clinic in Graz, Austria, and in 1893, he succeeded Theodor Meynert at the Clinic for Psychiatry and Nervous Diseases in Vienna, Austria. His main work was focused on pyrotherapy, and he discovered that patients inoculated with malaria-infested blood (impaludation in French, from “*paludism*” the French name for malaria) had a high rate of remissions, and the fatality rate decreased to around 5–10% [4]. This was the first effective treatment available, and it soon became the standard treatment. It remained so until the introduction of penicillin in the mid-1940s, but it was in continuous use until the 1970s [8].

The exact mechanism of action of impaludation is not known, but it was not considered to be confined only to the fevers induced by malaria. This lack of understanding, in combination with a suboptimal result in many treated patients, led to a search for alternative treatments, with different substances being administered with or without malaria-infested blood through various means [9]. The procedure of Wagner-Jauregg was also used for other psychiatric conditions, but with limited success. (It is also of interest to note that even if the use of lobotomy was

reported in GP [10], it never became widespread, probably since lobotomy became common only after the introduction of antibiotics.)

Early Psychosurgery

Our ancestors have displayed a keen interest in making holes into the heads of their fellow humans since Neolithic times, presumably sometimes for psychiatric conditions [11]. Trephinations specifically for such conditions are further mentioned a few times in the written sources, from medieval times and onwards [12, 13].

However, with the possible exception of posttraumatic disorders, the first modern publication on trephination for a psychiatric disorder appeared in 1889, when Claye Shaw introduced “the surgical treatment of general paralysis” [14]. Craniotomies with dural openings were performed, in order to lower intracranial pressure, mainly in GP, but also in other psychiatric conditions. This procedure saw a brief period of some popularity, with followers both in continental Europe and in the USA [15–23], before vanishing into oblivion (see Berrios [3] for a detailed account).

Two years later, in 1891, the Swiss psychiatrist Gottlieb Burkhardt published his work on so-called topectomies. He removed various cortical areas in six schizophrenic patients, chosen quite randomly, and without much success [24]. In 1910, Ludvic Puusepp cut parietofrontal connections in three patients with manodepressive psychosis, with poor results. However, this was not reported until 1937, as a consequence of the introduction of prefrontal leucotomy by Moniz, and hence Puusepp’s report had no importance for the future of lobotomy [25]. Thus, according to the traditional accounts, nothing happened in the field of psychosurgery during the period between 1891 until the introduction of leucotomy by Moniz in 1936.

Egas Moniz and the Introduction of Frontal Leucotomy

The history of Egas Moniz (Fig. 2) has been narrated many times (see Valenstein [2] for a detailed account), and I will here only report what is of interest for the present topic. He was beyond doubt a very gifted man, not least in his social and diplomatic skills. These were not only displayed within the field of science, but also in the world of politics, where he served as both ambassador and



Fig. 2. Egas Moniz. From the Nobel Foundation archive.

minister for external affairs in Portugal, before focusing on his career in neurology. Here, he created a name for himself with his pioneering work on cerebral angiography. As was not uncommon during this period, his patients suffered mainly from psychiatric disorders. His views on such conditions were of an organic nature, and he considered the current treatments to be unsatisfactory, with, as he wrote, “the exception of malarial treatment in general paralysis” [2, 26]. It is therefore not surprising that he would investigate treatments of a more organic nature. However, it has been difficult to reconstruct the path leading Moniz to frontal leucotomy, especially since he himself was very reluctant to acknowledge any influence, except for some studies on frontal lobe functions and frontal lobectomies [2, 3]. His theory on “fixed ideas” can hardly have been the foundation for his decision to perform these lesions in the frontal lobes. Further, no tests were performed in animals, and the technical preparations were allegedly limited to sticking a pencil repeatedly into one single human brain until a satisfactory approach was found [2].

According to traditional narrative [27], Moniz was inspired by a presentation by Carlyle Jacobsen [28] on prefrontal lesions in chimpanzees at the Second International Neurological Congress in London in 1935. A few months later, he performed the first operations with the help of a young neurosurgeon, Almeida Lima, and in

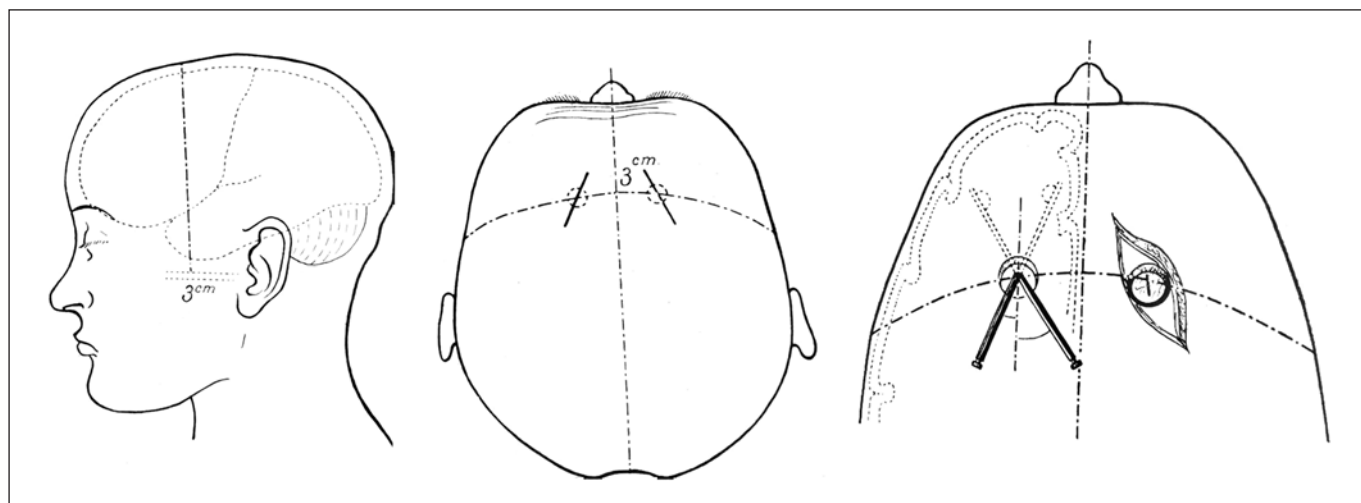


Fig. 3. Moniz's leucotomy. Entry point and injections (modified from Moniz [26]).



Fig. 4. Maurice Ducosté (courtesy of Michel Caire).

1936, he presented his findings in the first 20 patients [26].

The first leucotomies were done using injections of a small amount of alcohol into each frontal lobe through a single burr hole on each side of the skull (Fig 3).

A trepanation was done to the right and another to the left, 3 cm from the midline, and at a vertical line passing 3 cm in front of the ear at the base of the skull [...] [The needle] was introduced in order to reach the centrum ovale, at the level of area 9. A de

Martel ventricular puncture needle was used. The first injection, $1/10 \text{ cm}^3$, of absolute alcohol, was made 3.5 cm from the dura mater, and another, deeper, at 4.5 cm. Two other injections were made in the same lobe following another direction, more internal, not very far from the first, and at the same depths [26] (author's translation).

Only later did Moniz introduce the core method with mechanical lesions using a leucotome and even later using multiple burr holes on each side [26, 29].

Maurice Ducosté and CI

The Sources

Maurice Ducosté (1875–1956) (Fig. 4), psychiatrist at the asylum of Villejuif in Paris France, [30] (Fig. 5), is today a name known by few, even among those currently working within the field of psychiatric neurosurgery. He is mentioned in a few papers, all but two of which seem to rely on the works of Valenstein [2, 31, 32], based on one paper from Ducosté [33], and an Italian source [34]. Ducosté is further mentioned in a paper on malaria therapy [4] based on meeting proceedings [35], and finally in a book by Michel Caire [30], adding an additional publication from Ducosté's group [9]. Of the 15 papers and monographs from Ducosté's group, and the 6 papers published by other groups on CI, the majority are in French, a few in Spanish and Italian, and only two in English [35, 36]. For the present paper, I have tried to consult all publications of interest to give a more detailed view on CIs and their relation to prefrontal leucotomy of Moniz.

Fig. 5. The asylum of Villejuif in Paris (courtesy of Michel Caire).

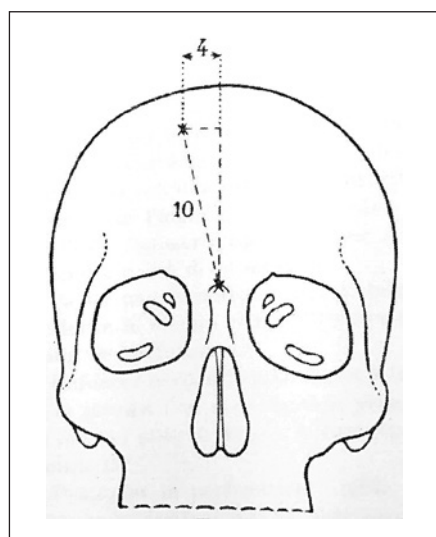


Fig. 6. Ducosté's cerebral impaludation. Entry point and trajectory (modified from Chavastelon [46]).

Surgical Technique

The operations were normally done under local anesthesia. A trepanation was performed at a point 10 cm behind the orbital arcade and 2–4 cm lateral of the midline (Fig. 6). This is roughly the same entry point typically used in stereotactic functional procedures. A needle was inserted 4–4.5 cm [37] into the frontal lobe using a special device (Fig. 7). In some early cases, 1 mL, but normally 2–5 mL [33], of blood or other substances were then injected into one or both frontal lobes [36]. The volume of the injections seems to have increased over time, and they could be repeated up to 12 times in staged procedures. This must have created significant lesions in the area.

Development of the Procedure

The information provided is sometimes difficult to interpret, since the different publications are sometimes referring to CI in general and sometimes to CI for specific conditions. The first publications date from 1932 [9, 33], and the historical development before this date must therefore be based on the retrospective information from the group itself. Ducosté reported that he based his therapy on a large number of animal experiments, before human trials [38]. He claims that the method was first introduced in 1920 [39] and that the first frontal procedures in schizophrenics were done the same year [40]. This must refer to the purely mechanical lesions he performed using a steel wire passed into the brain using a needle, and which preceded his experiments with injections [36]. In 1932, Ducosté wrote:

Before applying this method in the paralytics, I had used it a very large number of times in schizophrenics, encephalitics, maniacs. Since almost five years, I have done several hundreds of injections of various serums into the frontal lobes of the insane. Some have received up to twelve consecutive injections [33] (author's translation).

The use of injections started in 1925 [36]. They were first done in non-GP (schizophrenics, etc.) [38]. These injections were initially also applied to the ventricles and other lobes than the frontals in a few patients, but this did not provide equally good results [36]. Injections with blood, and for GP, started in 1927 [36, 40, 41]. Ducosté performed some experiments with autologous blood injections [42], but he most often used malaria-infested blood [40]. After 1932, injections using equal parts of blood and tetanus toxin were the standard [40, 41]. It was claimed that this mixture resulted in better and faster effects [36, 41]. These were

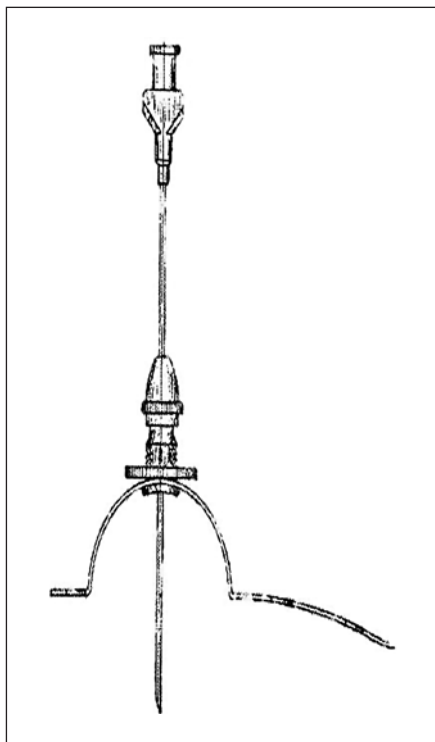


Fig. 7. Ducosté's device for injections into the frontal lobes (modified from Chavastelon [46]).

most often mixed, but sometimes delivered separately into each frontal lobe [40]. Diphtheria antitoxin was also tried [40] as well as anticobra serum [36]. Concerning other conditions than GP, such as schizophrenia, the patients were sometimes injected with blood and sometimes with antitoxins [40]. Both tetanus antitoxin and diphtheria antitoxin were tried in schizophrenics [43], as well as a combination of both [44].

Number of Patients

In 1932, Ducosté reported that he had operated on 108 patients specifically with GP [33]. In 1933, the number of patients was reported as 268. In the last publications from 1940, the group had done more than 1,000 procedures [37, 38]. At that time, they also reported that a total of 595 patients had been operated for GP at Villejuif [40]. It was further stated, already in 1932, that a very large number of patients with other mental conditions had been operated on [33]. Perhaps it can be assumed that these constituted the remaining 405 patients. Besides GP, schizophrenics, encephalitics, and maniacs are specifically mentioned in 1932 [33], and in later publications also melancholics, bipolars, and epileptics [40].

Suggested Mode(s) of Action

Ducosté acknowledged from early on that the trauma caused by the injection was “not without efficiency” [42]. Further, in a large number of patients, extensive biopsies were taken before the procedure and at two different occasions after the procedure, from different locations [40]. It was noted that the biopsies themselves seemed to have a beneficial effect on the symptoms [40]. The trauma was, however, never seen as the only, or even major, mode of action. The effect was seen as due to multiple modes of action [45], where the opening of the blood-brain barrier was of certain importance [42] and especially the increased microglia activity following the injections [36]. Further, in GP, a direct effect was assumed on the toxins of the spirochetes [36], while, contrary to normal impaludation, fever itself was seen as of only limited importance [33, 35].

Outcome

The results concerning GP were presented in several publications. In general, they were claimed to be superior to the results achieved by the method of Wagner-Jauregg, both in relation the published literature and to the experience of Ducosté's group. In an analysis of 435 patients with GP treated between 1927 and 1936, 81% were deemed to be cured [36, 46]. Cured was defined basically as patients being free from relapse for several years, appearing normal, and having returned to their previous life [36]. In contrast, among the patients who were admitted at Villejuif and were not treated with CI, 73% died during the first 6 months [36]. Ducosté stated that the effects of the treatment actually went beyond simply curing the disease:

This method has resulted in the cure of 250 paralytics, who not only resumed their normal life, but who have become superior to what they have ever been. It seems that the injection into the brain stimulates the intellectual faculties, modifies the character, provides youth and strength: many of these cured paralytics occupy positions which one would not have dared to confide them before their illness; many have become athletes, filled with energy and activity; a certain number among them, impotent for years, have procreated children of excellent shape [38] (author's translation).

The very positive descriptions of results and complications are similar to some early reports on lobotomy, and they should of course be interpreted with caution. However, despite all possible shortcomings, the group of Ducosté did at least follow and report the long-term outcome in some of their patients. Regarding complications, it was stressed that there were virtually no side effects [36, 45].

In 1,000 procedures, 3–4 deaths occurred, not deemed to be related to the procedure itself [38].

Regarding the outcome in other conditions, this was never reported in any detail, and the estimates vary considerably between different publications. The first interventions done in patients other than GP were less extensive, and hence the results were more limited [38] or even “without success” [36]. Later, the results were reported as “most valuable” [40].

CI outside of Villejuif

CI was mainly the work of Ducosté himself, but a couple of other persons performing the operation at Villejuif are mentioned [40]. The procedure was further performed by Thuillier in Amiens [40] and by Orticoni [42]. It is claimed that it was used in many psychiatric hospitals in Germany and also in Japan since 1933, as well as in other countries [40]. In Italy, CI was introduced by Mariotti and Sciuti for GP and schizophrenia based on the work by Ducosté. Inspired by the results of Moniz, they later operated on a group of schizophrenics, using the same technique with injections of autologous blood, but making two staged injections in each frontal lobe (and through two burr holes, instead of reaching both lobes from one side) [34, 47, 48]. Also Rizzatti and Borgarello are referring to Ducosté [49], reporting a number of leucotomies according to Moniz but modified according to Ducosté and performed with malaria-infested blood [49].

In Argentina, Ansaldi introduced CI for GP in 1934 [50] and published several papers on the topic [50–53]. In a paper from 1938, he describes the leucotomy of Moniz, and he considers the use of the leucotome to be a more purely surgical method than the injections previously used by Moniz, Ducosté, and others. However, even when following the example of Moniz and operating on a patient with depression, he retained the technique with injections of blood. Even Walter Freeman became, at a late stage, aware of Ducosté and tried such injections in a few cases, using the transorbital approach (unpublished manuscript) [2]. It seems as if, in these cases, leucotomy was seen as a variant, or further development, but not as something of a different nature compared with CI.

There are further a number of later publications on performing injections of various substances into the frontal lobes, but it was debated to what extent these were destructive, and hence should be considered as lobotomies or not (see Caire [30] for a detailed discussion).

Ducosté and Moniz

It is interesting to note that Moniz never mentioned the work of Ducosté. However, it is evident that he must have been aware of it. When Moniz presented his results in 1937 at the meeting of the Société Médico-Psychologique (session of July 26, 1937), the work of Ducosté was mentioned in the subsequent discussion [54]. Further, CI was discussed in early publications on lobotomy from other groups, as discussed above. However, more importantly, Moniz must have been aware of the work of Ducosté, well before the introduction of leucotomy, as pointed out by Valenstein [2]. At the meeting of the French Academy of Medicine in 1932, Moniz and Ducosté presented papers, one after the other, and these appeared together also in published form [33, 55]. Further, it is of interest to note that Moniz himself wrote that he had informed Almeida Lima about his ideas of leucotomy already 2.5 years before the meeting in London, that is, shortly after the 1932 meeting in Paris.

At this meeting, Moniz would have learned that more than 100 patients with GP, and a very large number of patients with other psychiatric conditions including schizophrenia and mania, had been operated on with favorable results using injections into the frontal lobes, and further, that this had been done without any serious complications. Additionally, Moniz – who was fluent in French – was a corresponding member of the French National Academy of Medicine, and it seems likely that he might also have read the subsequent publications from Ducosté’s group before 1936.

Thus, it seems strange that Moniz, independently and without being influenced by this information, would, within less than a year from this meeting, conceive the idea to perform injections into the frontal lobes of patients with schizophrenia, mania, and other psychiatric conditions, using a technique, entry point, and target depth very similar to Ducosté. The only major difference between Ducosté’s CI and Moniz’s initial leucotomies was that the latter used alcohol and made bilateral lesions during the same operation.

Moniz rapidly published papers on frontal leucotomy in 6 different countries, 7 papers and a monograph in 1936, and 6 more papers and a book chapter in 1937 [2]. It was evident that Moniz aimed at forestalling any discussion on who was first [2, 56]. It is not known when Ducosté’s group became aware of the work of Moniz. However, considering that Moniz chose to give the first presentation on leucotomy at the French National Acad-

emy of Medicine on March 3, 1936 [29], and the second only two days later at the French Neurological Society, as well as printed his monography in Paris the same year [26], it seems reasonable to assume that it would not have taken long for Ducosté to become aware of the work of Moniz.

In 1938, Ducosté published an overview of his work. It was the first time he wrote in English, and the character of this paper makes it easy to see this as a first positioning regarding priority in relation to Moniz, even though Moniz was never mentioned. Only two years later, in 1940, Moniz is mentioned by name, and Ducosté's group wrote that they do not want to claim priority over Moniz, only to conclude that:

The method of E. Moniz is thus related to the method of Ducosté, of which it constitutes a variant, however interesting and original. If one systematic introduces the blood of the diseased himself, or other substances, into the frontal lobes, one will certainly in the favorable cases achieve – we can already provide several observations – cures faster and more complete than those achieved by Moniz [40] (author's translation).

We are here seeing the start of a battle of priority. However, this was not the only battle at that moment. France was at war with Germany, and this had already started to affect the CI work at Villejuif [40]. The last paper on CI was published in May 1940, one week before the German invasion of France. After this, we hear no more of impaludations, and the battle of priority died in its infancy.

The first leucotomies in France were performed in 1936 by Marcel David, the mentor of Jean Talairach, at Sainte-Anne Hospital with the assistance of Egas Moniz, but the results were not encouraging, and the procedure was abandoned for the moment [57]. However, the interest in psychosurgery seems to have been limited until after the war, by which time it had passed from the psychiatrists into the hands of the neurosurgeons [58, 30].

Conclusion

Should Ducosté Be Given Credit for the Introduction of Leucotomy/Lobotomy?

It is clear that Ducosté had performed his procedure in hundreds of psychiatric patients before Moniz attempted leucotomy, and his first two publications date from 1932 [9, 33], four years before Moniz, and an additional three publications were presented in 1933 [41, 42, 59]. Ducosté performed injections of blood and other

substances and did also try purely mechanical lesions. The injections were done into the frontal lobes and must often have caused significant lesions in the area where Moniz would later perform his leucotomies. Even if CI was most often done for GP, the number of patients with other conditions, such as schizophrenia and mania, seems to have well surpassed the number of patients reported by Moniz.

Moniz conceived the idea of leucotomy shortly after attending a session where Ducosté presented CI in 1932. He never acknowledged any contribution by Ducosté, even though his initial leucotomies used basically the same entry point, target depth, and technique. The major difference was that Moniz used alcohol with the clear intent of producing a lesion. However, later, also others would perform what was called lobotomies using injections of blood as Ducosté.

The reason why Ducosté has been forgotten must be ascribed to the disruptive effects of WWII, that his group published mainly in French, and that the further development of lobotomy occurred mainly in the USA, where the work of Ducosté was virtually unknown. More important was probably the fact that Moniz immediately flooded the scientific world with a large number of publications in many different languages and performed what can be described as a PR campaign, supposedly in order to avoid any competition regarding priority. This was most successful, and it can hardly be questioned that the spread of frontal lobotomy over the world was the achievement of Moniz. However, most features of Moniz's leucotomy were not new but to a large extent identical to, and likely based on, CI of Ducosté. This would also explain the much discussed question on how Moniz could decide to perform these frontal procedures on the flimsy grounds he himself presented. These procedures had already been done in hundreds of patients and reported as safe and in most cases efficient! In my opinion, it would therefore be appropriate to acknowledge the contribution of Maurice Ducosté to the introduction of lobotomy, however dubious this honor might be.

Limitations

The subject of this article may seem more proper for a book than for a short report. While the author believes that he has been able to document the central points in this paper, some claims, such as those describing the character of Moniz, cannot be satisfyingly substantiated in this article in the interest of space. However, the few references selected here will guide the interested reader to more detailed accounts. Concerning ethical consider-

ations, it may be safe to state that some of the early research in this field can be considered questionable even with respect to the ethical standard of that time.

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