



Research report

The role of psychopharmacology in the medical abuses of the Third Reich: From euthanasia programmes to human experimentation

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ABSTRACT

German psychiatry and pharmacology both enjoyed an extraordinary international reputation prior to the promulgation of the Third Reich. However, with the triumph of eugenic ideas and the imposition of a "racial hygiene" policy by the Nazi regime, various organs of the German health system saw themselves involved in a perverse system of social control, in which the illicit use of psychopharmacological tools became customary. In the present work, we review, from the historical perspective, the factors that helped to bring about this situation and we analyze the abuses (known and documented) committed through the specific use of psychotropic drugs during the Nazi period. Among such abuses we can identify the following illegitimate activities: the use of psychoactive drugs, mainly sedatives from the barbiturates family, in the different euthanasia programmes implemented by the Nazi authorities, in police activity and various types of repression, and for purely criminal and extermination purposes within the so-called "Final Solution"; psychopharmacological research on the mentally ill, without the slightest ethical requirements or legal justification; and the use of psychotropic agents in research on healthy subjects, recruited from concentration camps. Finally, we refer to the role of poisonous nerve agents (tabun, sarin and soman) as instruments of chemical warfare and their development by the German authorities. Many of these activities, though possibly only a small portion of the total – given the destruction of a great deal of documentation just before the end of World War II – came to light through the famous Nuremberg Trials, as well as through other trials in which specific persons were brought to justice unilaterally by individual Allied nations or by the authorities of the new German government after the War.

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1. Introduction

During the first third of the twentieth century, German medicine, like other scientific fields, was held in the highest esteem throughout the world. Pharmacology and psychiatry were no exceptions to this. Indeed, both disciplines were led, as regards their different schools and currents, by German scientists and clinicians. However, this period of splendour was brought to an abrupt end with the coming to power of the National Socialist German Workers' Party (*Nationalsozialistische Deutsche Arbeiterpartei*, NSDAP). Successive Nazi governments built up a perverse system of the destruction of social conscience which, in the gen-

eral area of health and medicine, involved the institutionalization of criminal behaviours in the name of public health, racial hygiene and human research. Active participants in this abusive network included considerable numbers of professionals from medicine (general practitioners, gynaecologists, surgeons, paediatricians and psychiatrists) and from related scientific disciplines, such as pharmacology. Some such specialists, apart from other criminal acts, did not hesitate to make use of the psychotropic agents available at the time in their criminal activities and in their repeated violations of basic human rights. Nor could it be said that other actors related to the health sector (in nursing, the pharmaceuticals industry, universities, etc.) were without involvement in such activities.

In the present work, we set out to explore the circumstances that led to German medicine and science, from its position of world leadership and prestige, into this profound abyss. From there we go on to analyze all the abuses (known and documented) committed through the specific use of psychotropic agents during the Nazi regime. Among these we can distinguish the following illegitimate

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Table 1

Illegitimate use of psychopharmacological agents during the Nazi period in Germany.

- Wild euthanasia programmes: use of sedatives at high doses (barbiturates).
- Programmes of mass extermination of certain groups of subjects (purely murderous purposes).
- Research projects with the mentally ill (sleep cures with barbiturates, etc.).
- Research projects with healthy human subjects (concentration camp prisoners, etc.).
- Police interrogation techniques (mental control techniques with barbiturates, mescaline, etc.).
- Development of toxic nerve agents as weapons of chemical warfare (tabun, sarin, soman).

activities and use of the neuropsychopharmacological tools available at that time (Table 1): the use of psychoactive drugs, mainly sedatives from the barbiturates family, in the different euthanasia programmes implemented by the Nazi authorities; the illegitimate use of these types of drugs in police activity and various types of repression (as tools for obtaining information); their use for merely criminal and extermination purposes, within the auspices of the so-called “Final Solution”; the development of psychopharmacological research on the mentally ill, without the slightest ethical requirements or legal justification; and, going one step further, the use of psychotropic agents in research on healthy subjects recruited from concentration camps. Finally, we consider the role of poisonous nerve agents as instruments of chemical warfare and their development by the German authorities.

Many of these activities, though possibly only a small portion of the total – given the destruction of a great deal of documentation just before the end of World War II – came to light through the famous Nuremberg Trials, held by an International Military Court between 1945 and 1949. Of the total of 13 Nuremberg Trials, two were closely linked to the goals of the present work: the so-called *Doctors Trial* and the trial of the directors of the chemical company I.G. Farben. In addition to that provided by the Nuremberg Trials, much of the available information on the matter that concerns us here derives from the trials in which specific persons were brought to justice unilaterally by individual Allied countries or by the authorities of the new German government after the War.

2. Historical antecedents

First of all, it should be stressed that the discovery of the majority of the psychotropic drugs available in the first half of the 20th century or of their therapeutic applications saw the substantial involvement of German scientists – leaders of pharmacology on the world stage – either in university laboratories, including the medical faculties and their research institutions, or in industrial laboratories belonging to pharmaceutical companies, or indeed in cooperative projects between the two. Moreover, it should be borne in mind, as we shall see presently, that during the Nazi era academic science, military power, industry and clinical medicine, including psychiatry, were woven together so tightly that it would be difficult to isolate the real and specific implication of some of those from each sector, not least because one of their principal goals was to construct a system of additional mutual benefit. We shall now attempt to analyze the historical development of these different elements up to their definitive integration in the National Socialist structure.

2.1. The birth of modern pharmacology

Modern pharmacology was born, in the opinion of most specialists, in 1847, in the former German city of Dorpat (now Tartu, Estonia), when Rudolf Buchheim (1820–1879) was appointed Pro-

fessor of Medicine, Dietetics and Medical History at its university, where he founded, in 1860, Germany's first Institute of Pharmacology (*Pharmakologische Institut*). Buchheim's great contribution lies in the study of the actions of the drugs available at the time with an experimental physiological approach, in contrast to the traditional empirical-observational one [43]. It was one of Buchheim's disciples who would definitively change the course of pharmacology, Oswald Schmiedeberg (1838–1921), who is indeed considered the true founder of modern Pharmacology. At the University of Strasbourg, Schmiedeberg founded an Institute of Pharmacology and created, in the course of his 46 years' teaching, a school that would nourish practically the whole of modern European pharmacology; in fact, he had almost 200 research pupils, who would end up in charge of the majority of the university departments in German-speaking countries [98]. Schmiedeberg studied the pharmacology of chloral hydrate and chloroform, and in 1885 introduced urethane as a hypnotic agent. His scientific thinking embraced two concepts of the utmost importance from the perspective of pharmacology today: the notion of the biological target and the selective recognition of the chemical structure of the drug [52]. Thus, Schmiedeberg can be considered as the man primarily responsible for German leadership of international pharmacology up to World War II.

It should also be borne in mind that in German academic laboratories crucial research was carried out on basic aspects of neurochemistry and neurophysiology. Of particular importance in this regard was the work of Otto Loewi (1873–1961), who completed his doctorate under Schmiedeberg at Strasbourg and worked in Graz (Austria) until, in 1939, under political pressure from the Nazi government, he was forced to seek exile and settle in the United States. Between 1921 and 1926, Loewi developed an experimental model through which he demonstrated that stimulation of the vagus nerve in the frog heart released a substance – *vagusstoff* – which, appropriately collected, was capable of reproducing on another, isolated heart the same effects as on the original organ [56]. Together with Ernst Navratil (1902–1979), Loewi eventually identified this substance as acetylcholine [57], whose existence in mammals would be demonstrated in 1933 by Wilhelm S. Feldberg (1900–1993). Loewi's findings won him the Nobel Prize for Medicine and Physiology in 1936, jointly with Henry H. Dale (1875–1968). His research also enabled Hermann Fühner (1871–1944) to discover the enhancing effect on acetylcholine of physostigmine [30], a discovery that would subsequently be of great relevance in the development of neurotoxic agents as chemical weapons by the Nazi scientific apparatus.

The accession to power of Adolf Hitler (1889–1945) actually facilitated the work of German scientists enormously, fundamentally of those who in every way supported the Nazi regime, and provided them with opportunities they had never had previously. On the contrary, at the same time, it totally eliminated the Jewish scientists' creative power. However, academic pharmacology, in contrast to the case of university psychiatry, as we shall see later, was one of the disciplines most negatively affected by the advent of the Nazi regime, being severely purged. By way of example, seven of the 29 professors in this discipline were dismissed, and many promising figures in this field were obliged to seek exile in the face of racial ideology or political intolerance [98], including Marthe L. Vogt (1903–2003), Herman K.F. Blaschko (1900–1993), Hans W. Kosterlitz (1903–1996) and Feldberg.

Finally, it should not be overlooked that German pharmacologists were also the veritable pioneers of psychopharmacology; for example, it was Germans who isolated mescaline, a powerful psychedelic drug (Louis Lewin, 1850–1929, and Arthur Heffter, 1859–1925), and synthesized the barbiturates (Adolf von Baeyer, 1835–1917), the family of psychoactive drugs *par excellence* in the first half of the 20th century (Fig. 1) [63]. The first of the barbiturates



Fig. 1. Different preparations of barbiturates used during the first third of the 20th century: (A) Box and jar of Luminal® tablets, produced by E. Merck (Darmstadt, Germany) and sold in Spain from 1921. Museu de la Farmàcia Catalana, Barcelona. (B) Jar of Evipan® (10 0.25 g tablets), produced by the German firm Bayer-Meister Lucius (Leverkusen) and distributed in Spain from 1933. Museu de la Farmàcia Catalana, Barcelona. (C) Package of Somnifen®, produced by the Swiss firm Hoffmann-LaRoche and customarily used in so-called “sleep cures”.

to come onto the market was diethyl-barbituric acid, also known as barbital, malonal and gardenal. Its properties were hypnotic, sedative and anticonvulsant, and it was introduced as a clinical tool in Germany by the E. Merck company (Darmstadt) in 1903 and F. Bayer and Co. (Leverkusen) in 1904, thanks to the work of Emil Fischer (1852–1919) (who won the Nobel Prize for Chemistry in 1902) and Josef Freiherr von Mering (1849–1908). By means of small modifications of the chemical structure of the barbituric acid molecule, researchers succeeded in synthesizing over 2500 different agents. The first analogues of barbital, numbering some 18, were synthesized and tested by Fischer's group, and notably included phenobarbital, synthesized by Heinrich Hörlein (1882–1954) in 1911 on substituting one of the ethyl groups by a phenyl radical. Phenobarbital was marketed in 1912 by F. Bayer and Co., under the name Luminal®, and rapidly became “king of the barbiturates” [91] (Fig. 1A). In the years that followed, new barbiturates continued to become available. One of these, injectable sodium hexobarbital (Evipan®) (Fig. 1B), introduced by Helmut Weese (1897–1954), would revolutionize the field of anaesthesiology, and would be one the drugs most abused, from the illicit and criminal perspective, during the Nazi regime, as we shall see later.

2.2. The German chemical-pharmaceutical industry: the I.G. Farben empire

As early as the mid-nineteenth century there were instances in central Europe of pharmacists interested, at the individual level, in the discovery of new medicines, such as, in the German case, Heinrich Emanuel Merck (1794–1855), who would synthesize papaverine, and even of firms devoted to the production of standardized vegetable extracts, such as Chemische Fabrik, founded in 1869. However, the pharmaceutical industry properly emerged in the latter years of the 19th century, also in Germany, as a consequence of the expansion of the country's chemical industry (especially in the field of dyes and pigments), which was seeking to diversify its business into the world of medication [97]. During the first decades of the 20th century, numerous companies, such as E. Merck (Darmstadt), F. Bayer and Co. (Leverkusen), Hoechst AG (Frankfurt) or E. Schering (Berlin), built research facilities, stimulated above all by the desire to take advantage of the discoveries made in university laboratories, especially those of insulin and penicillin. Moreover, the 1920s and 1930s saw the construction of a close-knit network of collaboration between academic laborato-

ries at several universities and the pharmaceutical industry, leading to the launch of various clinical research projects [32], aimed primarily at combating infectious diseases, to which end a variety of antitoxins, vaccines, sulfonamides and penicillins were developed, in addition to alkaloids, hormonal preparations, and so on. However, neuropsychiatric disorders attracted little research attention, possibly due to the scarce clinical efficacy of the drugs available at the time and to the view that these types of disorder were of an incurable nature.

The German pharmaceutical industry, in the first twenty years of the 20th century, was dominated by two powerful companies, Hoechst (Farbwerke vorm. Meister Lucius und Bruening) and Bayer (Farbenfabriken vorm. Friedrich Bayer & Co.), which constituted the pharmaceutical core of a new industrial corporation, I.G. Farben (Interessen-Gemeinschaft Farbenindustrie AG) (Fig. 2). This conglomerate of companies, founded in 1925, monopolized the country's chemical production, and initially included 6 pow-



Fig. 2. German postcard from the 1930s showing the headquarters of I.G. Farben with the official flag of the Nazi regime.

erful chemical firms: Badische Anilin und Soda-Fabrik (BASF), Bayer, Aktiengesellschaft fuer Anilinfabrikaten (AGFA), Hoechst, Weiler-ter-Mer and Griesheim-Elektron. The two men primarily responsible for the construction of this industrial empire were Carl Duisberg (1861–1935) and Carl Bosch (1874–1940), though its financial architect was Hermann Schmitz (1881–1960), who received substantial backing from Wall Street [95]. I.G. Farben incorporated into its structure many of Germany's most prestigious scientists and engineers, turning the corporation into something more than an industrial giant. Indeed, few universities in the world could boast among its teaching staff as many Nobel laureates as I.G. Farben (Paul Ehrlich, 1854–1915, Gerhard Domagk, 1895–1964, Fritz Haber; 1868–1934 and Carl Bosch himself).

Despite Bosch's initial anti-Nazi stance, above all in defence of scientists of Jewish origin, the relationship between Schmitz and the new Nazi regime was extremely close [40,86]; indeed, the company had financed, to the tune of 400,000 marks, much of the electoral campaign that swept Hitler to power in March 1933. In the years that followed, the influence and presence of I.G. Farben in the apparatus of political decision did not cease to grow, to the extent that people spoke of "a State within the German State". And vice versa: the Nazi political doctrine became established in I.G. Farben as a corporate creed. On the outbreak of war in 1939, I.G. Farben was already the largest industrial chemical conglomerate in the world, having acquired 380 German and more than 500 foreign companies, broadening its business base (electrical and petroleum plants, coal mines, research units, metallurgical works, armaments and explosives factories, and even banks) [15]. Furthermore, in the wake of successive invasions of neighbouring countries by the Wehrmacht, I.G. Farben began "annexing" the leading chemical companies in the occupied territories.

During the Second World War, I.G. Farben became involved in numerous episodes related to the criminal activities of the Nazi executive, including the use of slave labour in installations constructed near concentration camps, such as the synthetic rubber and petrol plant in Buna, close to the Auschwitz camp, and whose director was the I.G. Farben chemist Otto Ambros (1901–1990). Going one step further, I.G. Farben's had its own con-

centration camp constructed at Monowitz, also in the vicinity of Auschwitz (Auschwitz-III), which began functioning in September 1942 (Fig. 3). A total of 300,000 slave workers were employed by this camp and the Buna installation, of whom some 25,000 died. It should also be borne in mind, in relation to criminal activity, that during the course of World War II, I.G. Farben produced 95% of Germany's total production of toxic gas intended for chemical warfare. Moreover, all of the infamous pesticide Zyklon-B (prussic acid or pure hydrogen cyanide), used systematically in gas chambers at the concentration camps, was manufactured and distributed by two subsidiaries of the industrial group called Degesch (*Deutsche Gesellschaft für Schädlingsbekämpfung mbH*) and Tesch (*Technischer Ausschuss für Schädlingsbekämpfung*) (Fig. 4). Indeed, sales of Zyklon-B came to constitute approximately 75% of Degesch's business [95]. I.G. Farben's implication in war crimes and crimes against humanity brought about a special trial after the War, within the framework of the Nuremberg Trials, in which 24 prominent members of the firm were charged.

2.3. German psychiatry in the international vanguard

Throughout the second half of the 19th century German psychiatry began to acquire an increasingly relevant and prestigious international role, gradually taking over from the predominant French school, whose postulates on moral questions were growing less and less acceptable to many, and guiding psychiatry toward a more somaticist approach, which soon imposed itself within the different European currents. The somatization of psychiatry was also favoured by the rise of other currents, such as the criminological positivism of the Italians and the theory of degeneration from the French school [46], as well as by the advance of the anatomo-clinical mentality, marvellously exemplified by the excellent German neurohistologists and neuropathologists [62]. Among the key figures in this change of orientation, which viewed mental disorders as a direct consequence of certain organic lesions, were Wilhelm Griesinger (1817–1868), Emil Kraepelin (1856–1926), who made the first description of schizophrenia in 1899, and Carl Wernicke (1848–1905), who in 1900 published an accurate descrip-

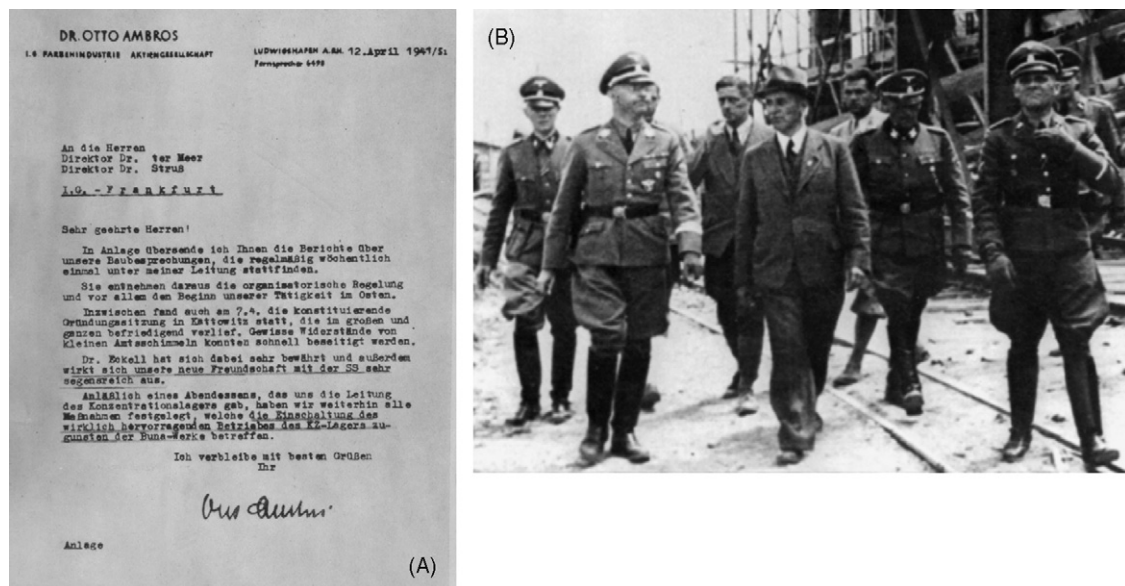


Fig. 3. Relations between I.G. Farben and the Nazi hierarchy and their implication in crimes against humanity: (A) Letter from the director of the I.G. Farben Buna plant (Auschwitz-II), Otto Ambros, dated 12th April 1941, and addressed to his colleagues in the corporation, in praise of the excellent negotiations carried out with the SS authorities at the death camp for the supply of slave labour for the new factory. FNDIRP Collection. (B) Inspection visit by Heinrich Himmler to the construction site of the I.G. Farben camp, Auschwitz III-Monowitz, in July 1942. The photograph shows the managers from the chemical-pharmaceutical company accompanying the SS *Reichsführer*, Auschwitz-Birkenau Museum.

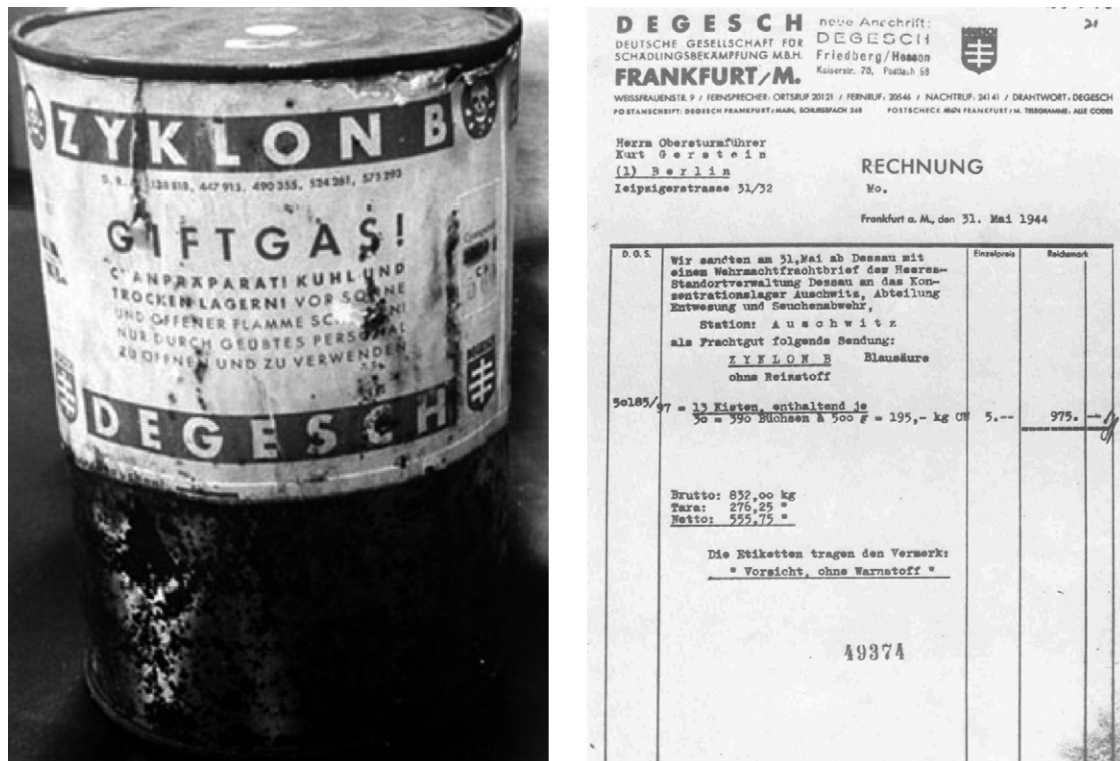


Fig. 4. Container of Zyklon-B manufactured by the Degesch company, a subsidiary of I.G. Farben, and invoice for purchase of the product by the authorities at the Auschwitz death camp.

tion of schizoaffective psychosis. Finally, in 1933, Oswald Bumke (1877–1950) published his *Handbuch der Psychiatrie*, an essential reference work at the time, and a symbol of the culmination of post-Kraepelinian psychiatry and the absolute predominance of German psychiatry in the inter-war years.

From the care perspective, German asylums at the turn of the century may also have been the best in the world, since the various States of the country subsidized them generously, and more importantly, they incorporated professionals from the university community, whose scientific mentality constituted an added value. Moreover, these professionals were steeped, from the outset of their university careers, in the culture of *Herr Geheimrat*, implying a motivation to excel and to gain honours through their professional activity – a concept virtually unknown in other European countries [91]. In fact, in 1911 Germany boasted 16 university psychiatric clinics (in addition to 187 public and 225 private asylums). The prestige of these institutions was increased, furthermore, by their substantial contributions in diagnostic material (electroencephalography) and therapeutic techniques, the latter being known as biological treatments (pyretotherapy through paludization, insulin shocks, convulsive therapy with cardiazol, etc.).

Thus, we can conclude by stating that German psychiatry (and indeed, medicine in general) enjoyed an excellent international reputation before the accession to power of the National Socialist party in 1933, a date considered by some authors as “the year German psychiatry went bankrupt” [77].

2.4. The German university and academic community

German universities, in the pre-Nazi era, were also among the international vanguard for the quality of their teaching and their scientific contributions. By way of example, universities in Ger-

many were pioneers in uniting the components of education and research, by virtue of the obligation to write a Doctoral Thesis followed by a post-doctoral research project called “certification”, essential requirements for becoming a university lecturer. In such a framework, Germany soon became a world leader, especially in the two academic contexts under consideration here: pharmacology and psychiatry.

However, the harsh economic, political and social conditions imposed on the German empire after its defeat in World War I, and accepted by the Weimar Republic, led to the majority of university teaching staff being opposed to the early inter-war German governments, whom they held responsible for the loss of their corporate privileges (as well as their spending power) as one of the country's elites [33]. This collective feeling of frustration may have been behind the broad support of the university community (added to those of others, including medicine and business) for the incipient political movement led by Hitler in the 1920s. A conference for foreign students' courses at the University of Freiburg, delivered on 15th August 1934 by the Rector at the time, the celebrated philosopher Martin Heidegger (1889–1976), sums up this historical view:

“First, it was necessary to have the extreme pressure of the First World War. . . This pressure on the people slowly created new needs. And it began awakening in the people the need for a guide [Führer], he who would lead the people back from the loss of themselves toward their own definition/determination and to a new will to being [Daseinswillen]. . . The fundamental nature of the new political-spiritual movement with which the people are imbued is that of an education and re-education of the people for the people through the State. . . The task of the New University consists in a similar education for the highest echelons of knowledge. . .” [41].



Fig. 5. The University and the Nazi regime: (A) Public demonstration of support from German academics for the new Nazi government, led by Martin Heidegger, Rector of the University of Freiburg, held on 11th November 1933 in Leipzig. (B) Open letter from Martin Heidegger to university students and published in the German press on 8th November 1933. In it he appeals for students to support the new government and presents Hitler as “the present and future of the German reality and its laws”.

The support of a sector of the academic fraternity for the new National Socialist government (Fig. 5) was indeed rewarded, in the same year that Hitler took power, through the enactment, on 7 April 1933, of the Law for the Restoration of the Professional Civil Service, which forced the resignation of 55% of university teaching staff (many of them, incidentally, of Jewish origin), permitting the swift promotion of those sympathetic to the new regime [20]. In such an atmosphere of repression it is not surprising that some members of the academic community, including many students, were also participants in certain illicit activities of the new German regime.

3. Toward the convergence of science and politics in the Third Reich: the triumph of eugenicist theories

During the second half of the 19th century, the growth of somatist approaches led to the increasing popularity of the pessimistic hypothesis of degeneration, which proposed that mental disorders, as a prototypical expression of “degenerations”, were nothing more than degenerative morbid alterations transmitted by heredity [1,45]. This perspective based on incurability, and the substantial aetiopathogenic role attributed to heredity and to the action on the organism of certain toxic agents, such as alcohol, led to the possibility of their control being transferred to the field of prevention, and this represented the beginning of the socialization of psychiatry and its possible use as a tool of social control by certain governments. The role of psychiatrists here would be crucial, since they were the perfect consultants for implementation of the rules of mental hygiene, through the so-called Mental Hygiene Leagues, and for contributing the pertinent advice on eugenics. In addition, for the first time, psychiatrists were in possession of a possible aetiopathogenic explanation of madness, and could provide an authoritative interpretation of the problem of mental illness to the new industrial bourgeoisie holding the reins of power [24]. But moreover, psychiatrists would find such postulates of particular interest, since through them they could become social agents with enormous influence in the political context of the time (including the control of criminality, linked by the Italian positivist school to the concepts of degeneration and insanity) [16,75,79].

Thus, in the first third of the 20th century eugenicist conceptions gained more and more ground, especially in the Central Euro-

pean context, and it was the espousal of such conceptions that would eventually lead to the tragedy of the Holocaust. Prestigious German scientists, taking inspiration from popular Darwinist perspectives regarding natural selection among species and “survival of the fittest”, widely propounded such ideas after 1900 [27,87,103]. Indeed, the year 1909 saw the foundation of the German Society for Racial Hygiene, whose perspectives were defended by prestigious German scientists, such as Ernst Rüdin (1874–1952), Professor of Psychiatry at the University of Munich, who claimed in 1916 to have demonstrated the hereditary nature of schizophrenia (*dementia praecox*) [84], or Eugen Fischer (1874–1967), director, between 1927 and 1942, of the prestigious Kaiser-Wilhelm Institut für Anthropologie, Human Genetics and Eugenics in Berlin, and co-author of the textbook *Menschliche Erblchkeitslehre und Rassenhygiene* (*Human Heredity and Racial Hygiene*) [7], a seminal work of reference in the field. Another reputable psychiatrist, Alfred Hoche (1865–1943), Professor at the University of Freiburg, in a book published in 1920 and co-written with the lawyer Karl Binding (1841–1920) (*Die Freigabe der Vernichtung Lebensunwerten Lebens – Allowing the destruction of life unworthy of living*) [10], defended the active euthanasia of some mental patients. These documents have been considered to be the ideological basis of the Nazi euthanasia programs [25,50]. All of these scientists advocated “cleansing of the genes of the race” and the elimination of the “rotten matter of the social body” [101].

It was on these pseudoscientific bases that the Nazi government would later introduce a policy of “racial hygiene” (*Rassenhygiene*) in Germany, with extremely harmful political, social and scientific consequences [2,3,9,49,70,81]. Anthropological racism, medical somaticism, persecution of the abnormal or alien, and so on, were some of the constituent elements of the political-social programme of the Nazi party, which found fertile soil for the establishment of such ideas in the economic crisis of the late 1920s, in the sensation of oppression and victimhood among the German people in the wake of the Treaty of Versailles (1919) and in the neo-colonialist developments in politics in inter-war Europe. Thus, when Adolf Hitler acceded to the Presidency, in accordance with the electoral promises that helped bring him to power he began implementing racist policies in defence of a “master race” [5,104], bringing in legislation such as that relating to racial segregation and the

protection of the race, notably the *Gesetz zur Verhütung Erbkranken Nachwuchses*, or Law for the Prevention of Hereditary Diseases of Descent (better known as the *Sterilization Act*), promulgated on 14th July 1933. This law permitted, on the decision of a tribunal made up of two doctors and a judge, the forced sterilization of subjects (*Erbgesundheitsgesetz*) diagnosed with congenital mental weakness, schizophrenia, “circular madness” (manic-depressive psychosis), hereditary epilepsy, hereditary St. Vitus’ dance (Huntington’s chorea), congenital blindness and deafness, pronounced bodily malformations of a hereditary nature, severe chronic alcoholism, and so on [5,38,78,88]. The sterilizations began in 1934 and ended, in practice, on the outbreak of World War II, with a final total of 350,000 people sterilized (0.5% of the total population) and a death rate during the surgical interventions of 1–5%. As some authors have pointed out, “from enforced sterilization to the Holocaust was but a short step” [77].

3.1. The implication of the medical community in the eugenicist policies of the Nazi regime

In general, German medicine cannot be said to have dissociated itself from the eugenicist movements, and some members of the medical community became directly involved with this false and fanatical notion of racial science, closely bound up with a markedly racist ideology [81], which would up Pandora’s Box during the Nazi period [48,72], initially through the sterilization of the mentally ill and subsequently through generalized extermination [77,88], in a climate of what some have described as “the medicalization of anti-semitism” [81]. By way of example, the German Medical Association, in its official journal, not only failed to express any opposition to such legislation, but indeed openly praised it [28]; likewise, distinguished members of the medical community, such as Professor Rüdin himself, actively participated in the wide-ranging publicity campaigns of the Third Reich’s efficient propaganda machine in relation to the social benefits deriving from the application of these laws [11,17]. Moreover, it should be borne in mind that at one time during the Third Reich as many as 45% of German doctors were members of the Nazi Party [88].

However, it would be unfair to imply that all German doctors of the period were involved in these practices, or to attribute this type of activity exclusively to the German medical community. Eugenicist theories enjoyed a measure of general prestige in the first half of the 20th century, with eugenicist institutions and associations proliferating all over Europe, organizing many conferences and scientific meetings. Indeed, in the name of the eugenics concept, sterilization programmes were introduced in many Western countries, among them Denmark, Finland, Sweden and the United States [81].

Of all the medical specialties involved in the application of these laws, psychiatry had an especially prominent role, since they placed enormous political power in the hands of psychiatrists, insofar as it was they who had to diagnose whether patients were, for example, schizophrenic – and should therefore be sterilized – or whether they were free of any mental disorder [59]. Thus, prestigious professionals were sucked into this Nazi whirlpool that led inexorably to the Euthanasia Programmes [47]. However, although some psychiatry professionals gave their unreserved support to these programmes and many kept quiet after their introduction, we should also be fair to those who refused to participate in such “covert murders”. Of the 3000 psychiatrists practising in Germany in 1933, six hundred sought exile, either due to their Jewish origin or for other reasons [76], and many others stayed faithful to their healthcare duties, refusing to collaborate with the government apparatus (Karl Bonhoeffer, 1868–1948); some even went as far as protesting publicly, despite the professional and personal

risks involved (Gottfried Ewald, 1888–1963; Hans G. Creutzfeldt, 1885–1964) [88]. Ten psychiatrists were actually killed for these reasons, the most well-known being John Rittmeister (1898–1943), while others were sent to concentration camps, from which they managed to emerge alive (Viktor E. Frankl, Adalbert Kral, Jan Gross, Wanda Poltawska, etc.) [76].

4. Neuropsychopharmacology in the criminal abuse and illicit activities perpetrated by the Nazi regime

First of all, it should be pointed out that neuropsychopharmacology, understood as a scientific discipline in its own right, and even as a branch of the pharmacology that commands such presence and relevance today, did not exist at the time of the Third Reich. In reality, scientific psychopharmacology was born in the 1950s, an authentic “golden decade” [58], which saw the discovery and marketing of the principal groups of psychoactive drugs, as we know them today (antipsychotics, anxiolytics, antidepressants and mood regulators). Previously, the pharmacological tools available had been quite limited: on the one hand, there was morphine for controlling patients’ agitation and aggression, potassium bromide, to relieve worry and anxiety, chloral hydrate, to control insomnia, and finally, hyoscine (scopolamine) and paraldehyde, all isolated or synthesized during the 19th century; and on the other, the barbiturates, used as hypnotics or sedatives, nicotinic acid (vitamin B₃), and amphetamines and their derivatives, incorporated into therapy in the first third of the 20th century [6,91]. Of all these, it was primarily the barbiturates, and to a lesser extent the opiate derivatives, scopolamine and some amphetamine-type psychostimulants, that made up the nucleus of psychoactive drug use for illicit ends by philo-Nazi doctors and scientists.

4.1. The role of psychoactive drugs in the euthanasia programmes

With the antecedent represented by the enactment of the Nuremberg Laws, and given the imminence of war (which would require thousands of hospital beds to be freed up for wounded soldiers), Hitler signed, on 1st September 1939 (the day World War II broke out), a Decree specifying that “incurable patients, after a critical assessment of the state of their illness, will be permitted a euthanasic death” [77,92]. This Decree constituted the basis of the Programme of Euthanasia, *Gnadentod* (“mercy killing”), known popularly as Operation T4 or *Aktion T4*, due to the location of its administrative office at number 4 Tiergartenstrasse in Berlin [3,65,88], and marked the beginning of a process that would lead to the mass extermination of patients with mental “defects” or pathologies [94], and in which psychoactive drugs would play a central role. It should be borne in mind, in this regard, that the mentally ill were considered, even in scientific texts of the period, as inferior beings (*minderwertig*), actually being described in some medical circles as “empty human shells” (*Leere Menschenhülsen*) or “lives not worth living” (*Lebensunwertes Leben*) [29,55].

For the implementation of this project, Karl Brandt (1904–1948) (Fig. 6A), Hitler’s personal doctor and the director of operations in this case, called to Berlin the directors of all the psychiatric hospitals in Germany. There, they were informed about the procedures relating to the functioning of the programme, which began when the Reichs Task Force for Sanatoriums and Nursing Homes (*Reichsarbeitsgemeinschaft Heil-und Pflegeanstalten*, RAG) sent questionnaires to all the psychiatric institutions, to be filled out for each patient and returned for their study and assessment by a committee of experts made up of 54 prestigious psychiatrists (Fig. 7A). Once a patient’s death had been decreed, he or she was moved to one of the six regional extermination centres (Brandenburg, Bern-

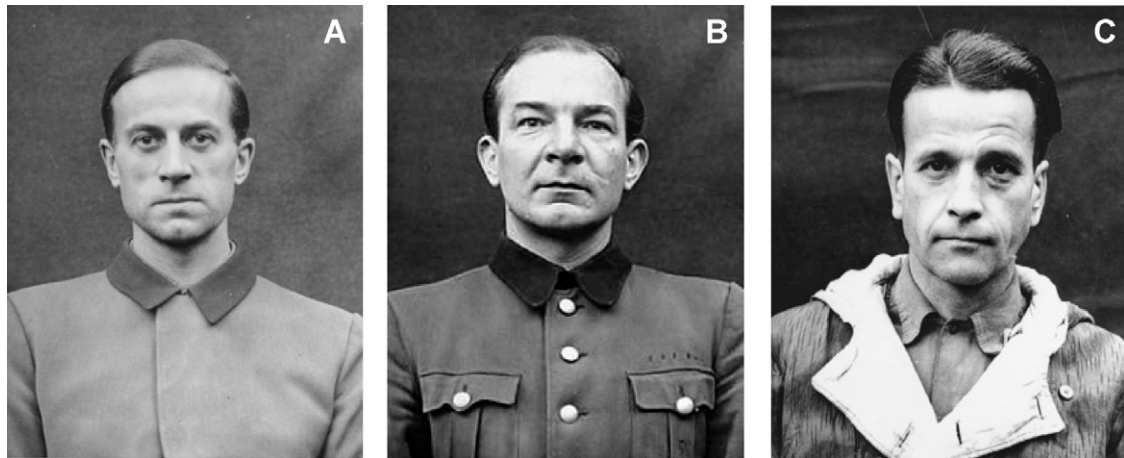


Fig. 6. Three of the most relevant doctors in the Nazi regime involved in criminal activities related to the euthanasia and human experimentation programmes. At the Nuremberg Trials they were sentenced to hanging, and executed on 2 June 1948 in Landsberg prison. (A) Karl Brandt, Hitler's personal doctor, General of the *Schutzstaffel* (SS), Reich Commissioner-General for Public Health, and organizer of *Aktion T4*. (B) Joachim Mrugowsky, Colonel of the *Schutzstaffel* (SS), Director of the *Waffen SS* Central Institute for Hygiene and Associate Professor of Hygiene at Berlin University. Mrugowsky was the man principally responsible for the medical research projects carried out in the Nazi concentration camps. (C) Waldemar Hoven, *Waffen SS* captain and chief doctor at the Buchenwald death camp. Hoven was found guilty of the murder of prisoners through the administration of lethal injections of aconitine, phenol and gasoline.

burg, Hartheim, Grafeneck, Sonnenstein and Hadamar) distributed throughout the Reich [65,94] – some of which were actually housed within psychiatric institutions – where they were routinely exterminated using various methods, among them carbon monoxide poisoning. The bodies were quickly incinerated in crematory ovens [35,77]. These practices served as a model for the subsequent implementation of the so-called “Final Solution” to the Jewish Question (*Endlösung der Judenfrage*) [2,78]. In the final part of this process, the doctors responsible for the patients' care signed a letter of condolence (*Trostbrief*) (Fig. 7B), prepared in a department created

specifically for this purpose, for their family, and issued false death certificates attributing the death to natural causes [55], such as icterus or different types of infections [8] (Fig. 7C). In total, it is estimated that *Aktion T4*, which was subsequently extended to other groups (concentration camp prisoners, political dissidents, common criminals, vagrants, etc.), was responsible for the deaths of more than 200,000 people [26,31,35,77], including 73,000 psychiatric patients [21].

Two years after its inception, on 24th August 1941, *Aktion T4* was suspended, due to popular protests and to the needs of the

(A) Form sent to the RAG by health institutions during the selection process of patients for murder by euthanasia.

(B) Standard letter of condolence (Trostbrief) from the authorities at the health institutions responsible for euthanasia, after the murder of a patient.

(C) Death certificate of a patient from the Sonnenstein euthanasia centre.

Fig. 7. *Modus operandi* of the Nazi euthanasia project. (A) Form sent to the RAG by health institutions during the selection process of patients for murder by euthanasia. (B) Standard letter of condolence (*Trostbrief*) from the authorities at the health institutions responsible for euthanasia, after the murder of a patient. It reads: “We are sorry to inform you that your sister, . . . who was recently transferred to our hospital in accordance with the directive from the National Defence Commissioner, died suddenly on 7th December 1940, as a result of pancreatitis and subsequent peritonitis. . . . In accordance with the official regulations pertaining to war activities, the local police authorities have ordered the immediate cremation of the deceased. . . . in order to prevent the outbreak and spread of infectious diseases. In such cases the family's permission is not required. . . . Enclosed herewith are two death certificates, which you may need to present at official agencies.” (C) Death certificate of a patient from the Sonnenstein euthanasia centre. Alleged cause of death is generalized sepsis.

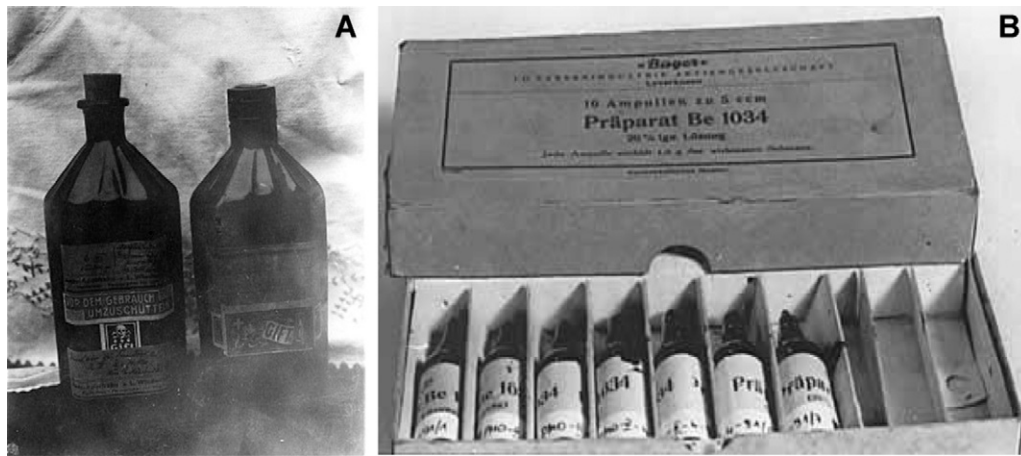


Fig. 8. Pharmacological preparations employed in human research at different health institutions and death camps in the Third Reich. (A) Bottles of morphine solution found by war crimes investigators at the Hadamar hospital. Holocaust Education & Archive Research Team (www.HolocaustResearchProject.org). (B) Box of vials of the experimental preparation B-1034, supplied by one of the subsidiaries of I.G. Farben for the experiments on prisoners at the Auschwitz concentration camp.

war effort on the Eastern Front, though this did not signal the end of the killings, which continued in furtive manner, out of sight of public opinion, typically using less violent methods, such as leaving patients to die of starvation [64]. Such procedures, carried out in the very health institutions in which the patients were being attended, have been described as “Wild Euthanasia”. Patients were murdered through the reduction to the minimum of food rations, which practically became limited to boiled vegetables (diet E), or by turning off the hospital’s heating system in winter [65,94,99]. In some cases doctors, psychiatrists and nurses accelerated the deaths of patients through the prolonged administration of barbiturates at low doses, resulting in terminal pneumonia [64], while elsewhere the murders were carried out less discreetly, through the intravenous injection of air or the lethal injection of various drugs, such as opiates (Fig. 8A) and scopolamine [8,73]. In this second phase of wild euthanasia it is estimated that as many as 110,000 patients may have been murdered [21].

A detailed account of the application of psychoactive drugs for this purpose was provided by a nurse, as von Cranach recounts, in the following way:

“...in the middle of April 1944 I was posted to the Kaufbeuren asylum with precise orders to carry out euthanasia on all the mental patients... I reported directly to the director of the hospital... Patients were given Luminal or Veronal, and sometimes Trional in the form of tablets, as well as morphine-scopolamine in liquid form when the effects of the barbiturates were not as desired. Modification of the dose was my responsibility... I normally began the treatment with two 0.3 mg tablets of Luminal per day and increased this dose according to the course of the ‘illness’. The final result of the medication was the induction of a deep sleep from which the patient never awoke. Sometimes death came quickly, even on the first day, though most commonly on the second or third. I received the medication straight from the director, who handed it to me personally...” [21].

Similar examples were reported as customary practice at other institutions, such as the Meseritz-Obrawalde hospital, where 10,000 patients were murdered [8]. The procedure followed there, according to the transcript of the trial against its healthcare staff in Berlin in March 1946, began with the selection of candidate patients, their installation in an isolation room and the administration of 10 tablets of Veronal® or Luminal® dissolved in water. Only when patients were incapable of swallowing the medication were they injected with morphine and scopolamine [8].

4.2. The mentally ill as pharmacological research material in the Third Reich

Apart from the involvement of the medical community in the sterilization and euthanasia programmes mentioned previously, the most worrying expression of the link between this sector and the Nazi tragedy was the forced participation of human beings, ill or otherwise, as research and laboratory material, not only in the infamous death camps, but also in hospitals and universities themselves [105], a situation in clear contrast to the great progress made and considerable interest on the part of doctors in ethical issues within biomedical research in pre-Nazi Germany, culminating in the publication of the *Guidelines for New Therapies and Experimentation in Humans* in 1931. That text already incorporated the legal doctrine of informed consent, prohibiting experimentation with the dying and with the financially or socially needy [100]. However, with the triumph of eugenicist and racial scientific theories, bioethics lost its very *raison d’être*, especially in the context of research, which, formerly “for the benefit of the patient,” became based on the principle of “for the benefit of the State.” Thus, medical experimentation became just one more tool of political power and social control, with increasingly evident military connotations. In such a framework, the physically and mentally handicapped affected by the euthanasia programmes became ideal recruits for medical experimentation projects, a situation justified by some of those responsible as follows: “If the patients have to die in any case, as a result of the expert assessment of one of my colleagues, why not use them while alive or after their execution for research?” [89].

Though less well known than research carried out in other medical fields, there is documentary evidence of some neuropsychiatric research projects. Among these was a wide-ranging programme (*Aktion T4*) on diverse forms of mental retardation and epilepsy directed by Carl Schneider (1891–1946), Professor of Psychiatry at the University of Heidelberg, involving the assessment and exhaustive long-term study of live patients from the neuropsychological, physiological and therapeutic perspectives, and culminating in the anatomopathological study of their brains after subjecting them to the Euthanasia Programme at one of the specific institutions mentioned above. Schneider’s correspondence reveals his great interest in obtaining the approval of the programme’s assessors, and there is evidence that at least 194 brains were analyzed in his department [102]. Indeed, in a letter to the Chief Assessor of *Aktion T4*, Paul Nitsche (1877–1948), Schneider

OFFICE OF U.S. CHIEF OF COUNSEL
FOR THE PROSECUTION OF AXIS CRIMINALITY
Doc. No. L170 APC 113 Date 23 August 1945
STAFF EVIDENCE ANALYSIS

DESCRIPTION OF ATTACHED DOCUMENT (Under following headings):

Title and Nature: Neuropathology and Neurophysiology, etc. in wartime Germany written by Major Leo Alexander, MD, STOUSA, published by CIOS, containing references to killing centers for the insane.

Date: Undated Original (x) Copy () Language: English

If not English, is translation attached: Yes () No ()

LOCATION OF ORIGINAL (also WITNESS if applicable) as of _____ 1945:

PERSONS IMPLICATED:

REFERENCES TO INDEX HEADINGS (Key to Par. nos. of Summary below):

ATROCITIES: Against Civilians (1)

NECESSARY PROCESSING TO PUT IN EVIDENTIARY FORM: LEADS:

Authentication by Major Alexander.

SUMMARY OF RELEVANT POINTS (with page references):

1. Patients in mental institutions were killed by gas in such large numbers that autopsies were impossible. The brains, however, were suspended in formalin and sent to laboratories for examination. Nurses and attendants selected the persons to be killed, and they degenerated to picking out the patients who looked sick, or who were problems, or whom they simply disliked. (20-21).

Notes: This is only a small part of the report, but it might be used in connection with the report on execution of mental patients. (1-169)

Fig. 9. Detail of the L-170 Report on the Nazi doctors, drawn up by American psychiatrist Leo Alexander on 23rd August 1945 for the International Military Tribunal at Nuremberg. This report deals with wartime German medical research in the field of neuropathology. Harvard Law School Library Item No. 2451.

writes: “We should not miss the opportunity of using it [Aktion T4] in research on the mentally ill, especially from the therapeutic perspective” [90]. In 1940 Schneider actually founded a Research Institute in Wiesloch (*Forschungsanstalt des Reichsausschusses*), in which, in addition to the histopathological study of the brains of mentally ill victims from the extermination centres, he apparently experimented with drugs and electroshock techniques [3], though all the documentation from this institute was destroyed just before the end of the War.

A similar project was that coordinated by Professor Julius Hallervorden (1882–1965), sub-director of the Berlin-Buch Kaiser-Wilhelm Institut (KWI) for Brain Research and senior pathologist at one of the hospitals in the State of Brandenburg, who selected for his research the most interesting brains from patients at Brandenburg’s euthanasia centres, given his knowledge of their diagnosis prior to execution [29,35]. A report by the Combined Intelligence Operative Subcommittee (CIOS), catalogued as L-170, to the so-called Doctors’ Trial at Nuremberg (Fig. 9), specifies that “Dr. Hallervorden obtained 500 brains from the centres for the extermination of mental patients. These patients were murdered in various institutions through inhalation of carbon monoxide” [39]. In his testimony, Hallervorden stated that “there was wonderful material among those brains, beautiful mental defectives, mal-formations and early infantile diseases.” And following the line typical of the German medical class, he added “... Where they [the brains] came from and how they came to me was really none of my business.” [39]. However, it appears that Hallervorden was indeed aware of the euthanasia programme and of the murders committed at his institution, if we are to believe the testimony of his laboratory assistant, Werner-Joachim Eicke (1911–1988), made in an interview after the War [69].

Fortunately, a good deal of these projects had to be suspended, since in the wake of the German defeat at Stalingrad the majority of the doctors who participated in them were called up for military service. However, it is clear that many German doctors had abandoned their duties to their patients and renounced the ethical oath pertaining to their profession. Some of those responsible for these



Fig. 10. Container of metamphetamphetamine (Pervitin®), one of the psychoactive drugs most widely used in the pharmacological experiments of a psychiatric nature carried out in the internment camps.

projects, indeed, could not assimilate their guilt, such as Schneider himself, who took his own life after the War.

4.3. Psychopharmacological research without consent in forced prisoners

However, the evidence reveals not only research projects in subjects who were ill and in patients with mental disorders without their consent, during the Nazi regime, but also, in what was the utmost perversion of ethical principles, experimental programmes with healthy subjects from concentration camps. Although the deplorable human experiments by Nazi doctors were much more common in other areas of medicine, such as genetics, gynaecology, surgery or traumatology, and that it is these which are better documented and better known today (including those involving freezing, inoculation with tuberculosis bacilli, amputation of limbs, or surgical sterilization without anaesthetic) [74], they did indeed also take place in the specific field of neuropsychopharmacology. Concentration camp prisoners constituted the principal source of recruitment for pharmacological studies, in which other sectors of the Nazi regime’s health system played a substantial role – principally the chemical-pharmaceutical industry, also linked to medical research in the death camps, where they could test drugs practically unfettered [15,19]. As mentioned earlier, I.G. Farben actually set up a subsidiary at the Auschwitz concentration camp (called IG Auschwitz Industries) (Fig. 3B) [15], in which a variety of pharmacological substances were tested, including sulfamide and arsenical derivatives and other preparations whose composition is not precisely known (B-1012, B-1034, 3382 or Rutenol, 3582 or Acridine) (Fig. 8B). These tests were generally related to the treatment of infectious diseases, such as typhus, erysipelas, scarlet fever or paratyphoid diarrhoea, previously induced in the experimental subjects, and death rates were extremely high.

Among those responsible for these pharmacological projects were ex-IG Farben scientists, such as Medical Commander of the *Schutzstaffel* (SS) Helmuth Vetter (1910–1949), and doctors at the death camps, including the infamous Joseph Mengele (1911–1979) [19,55], though the ideologue of most medical experimentation in the camps, and the man with most responsibility for it, was Joachim Mrugowsky (1905–1948) (Fig. 6B), Colonel-Director of the *Waffen SS* Central Institute for Hygiene and Associate Professor at Berlin University. In the specific field of psychopharmacology, at the Buchenwald camp they studied the effects of combined administration of metamphetamphetamine (Pervitin®) (Fig. 10) and phenobarbital (Luminal®) (Fig. 1A) [93] and the anaesthetic properties of sodium hexobarbital and chloral hydrate in surgery on healthy subjects [37], and used lethal injections of aconitine and apomorphine [55]. At Dachau, whose chief medical officer was Sigmund Rascher (1909–1945), mescaline was administered to assess the hidden

schizophrenic behaviour of inmates or to actually induce it [51]. In another example of experiments of this nature, the psychiatrist Hans-Wilhelm König (1912–?), at the Auschwitz-Birkenau camp, studied the effects of applying high-voltage electric shocks, not only in schizoid patients, but also in healthy prisoners. After their death, the brains were removed for anatomopathological study [55].

The level of amorality and ethical degradation of the medical community during the Nazi time is reflected in a letter found among the files at Auschwitz, exemplifying the correspondence between the camp Commandant and certain departments of I.G. Farben. The chemical company was applying to purchase prisoners for research on a hypnotic drug: “We need some 150 women in the best possible state of health... We acknowledge your affirmative reply, but consider the price of 200 marks per woman too high. We propose paying no more than 170 marks per woman... The experiments were carried out. All of these persons died. We need a new delivery as soon as possible. . .” [19]. With regard to this type of pharmacological research, some of the doctors on trial at Nuremberg, such as chief doctor at the Buchenwald camp Waldemar Hoven (1903–1948) (Fig. 6C), claimed that the interest in demonstrating the efficacy of these substances originated not in official medical circles, but rather in the chemical companies themselves.

In any case, the real contributions to medical scientific progress of the all these research programmes founded on crimes by the State were practically non-existent. In the words of Leo T. Alexander (1905–1985), one of the American medical consultants for the prosecution at Nuremberg, and inspirer of the Nuremberg Code: “the result was a significant advance in the science of murder, or ktenology” [2].

4.4. The use of psychopharmacological agents as tools of murder

The utmost degree of perversion in the use of psychopharmacological agents corresponds to their application as instruments for the murder of healthy and innocent people, a circumstance that reaches even greater extremes of horror and amorality when it involves children. There were also examples of such atrocities in the darkest chapters of the medical history of the Third Reich. After the Second World War, at the trial by the Allies of the man who had been a senior doctor at the Auschwitz concentration camp, SS officer Josef Mengele (“the Angel of Death”), one of the prisoners forced to assist him, the doctor Miklos Nyiszli (1901–1956), described how Mengele himself murdered fourteen twins of gypsy race, and the procedure employed:

“... In the room adjacent to the dissection room, 14 gypsy twins were waiting, giving out some terrible screams. Without a single word, Dr. Mengele prepared 10 cc and 5 cc syringes for each one of them. From one box he took Evipal and from another chloroform, which was stored in glass containers of 20 cc, and laid everything out on the surgical instrument table. On bringing in the first twin, a 14-year-old girl, he ordered me to take off her clothes and lay her on the dissection table. He then administered an intravenous injection of Evipal in the girl's right arm, and when she became drowsy he marked the left ventricle of the heart and injected it with 10 cc of chloroform. After a slight contraction, the girl died, and Dr. Mengele moved the body to the mortuary. In this way all fourteen twins were murdered in the course of the night” [4].

According to Nyiszli's account, Mengele had already used this method in Auschwitz to murder four pairs of twins, all under the age of 10, as part of his genetic research, using hexobarbital (Evipan® or Evipal®) (Fig. 1B), a barbiturate with ultra-rapid action. It seems that the “Angel of Death” became interested in them on noticing that, despite being twins, they had different-coloured eyes. As men-

tioned previously, after their murder the eyes, together with other organs, were extirpated and sent for study to the KWI in Berlin. The label on their container bore the words “War Material – Urgent” [80].

Another documented example of these types of practice took place in the Buchenwald death camp, whose medical director, Waldemar Hoven, murdered an indeterminate number of Soviet prisoners through the administration of aconitine [2], the principal alkaloid of plants of the genus *Aconitum*. This highly toxic substance has the capacity to open the sodium channels of the nerve and muscle cells, leading rapidly to respiratory paralysis and cardiac arrest. For his involvement in these events Hoven was tried after the War and hanged in 1948.

4.5. The use of psychoactive drugs in police interrogations

Possibly the most relevant experiments carried out by Nazi doctors and psychiatrists with psychopharmacological agents were those related to mental control techniques, whose immediate antecedents could be found in the so-called “sleep cures” with barbiturates, developed in the 1920s for schizophrenic patients and agitated maniacs by the German psychiatrist Jakob Klaesi (1883–1980), assistant (*Privatdozent*) at the Psychiatric Clinic of Zurich University (Psychiatrischen Universitätsklinik, Burghölzli, Switzerland) [61]. These “sleep cures” or “prolonged narcosis” (*Dauerschlaf*, *Dauernarkose*), proposed by Klaesi in 1920, were widely advocated at the time, especially among psychiatrists in the German sphere of influence. They directly involved Somnifen® (Fig. 1C), a mixture of diethyl and dipropenyl-barbituric acid and diethylamine first marketed in 1920 by the Swiss pharmaceutical company Hoffmann-La Roche, and developed under the guidance of Max Cloëta (1868–1940), Professor of Pharmacology at Zurich University. The method introduced by Klaesi involved a pre-medication based on morphine (0.01 cm³) and scopolamine (0.001 cm³) administered subcutaneously, and the injection 30–60 min later, either intravenous or subcutaneous, for 6–7 days, of Somnifen® (2–4 cm³). However, there were numerous variations on this methodology, it being customary to prolong the state of narcolepsy for up to two weeks at a time [106]. Mortality rates with this procedure were very high, with deaths occurring particularly as a result of bronchopneumonia, a circumstance the Nazi authorities took advantage of, as outlined earlier, to implement their criminal programmes of “wild euthanasia”.

One of the consequences of the infusion of barbiturates in schizophrenic patients in a catatonic state was that they temporarily reverted to their state of immobility, which permitted them, for a few hours, to maintain conversations and interact with their environment, before lapsing once more into a state of lethargy. Moreover, William J. Bleckwenn (1895–1965) noted in 1930 that barbiturates, thanks to the reduced level of consciousness they induced, permitted the therapist to access unconscious information in the patient, who could thus free him or herself of anxieties associated with previous traumatic events [12,13]. This marked the birth of so-called “narcoanalysis” methods, whose extension to extra-therapeutic contexts would not be far behind.

Lifton recounts how agents of the German political police, the *Gestapo*, dissatisfied with the quality of information about the resistance obtained from torture session with Polish prisoners, commissioned the psychiatrist Bruno Weber (1915–1956), director of the Institute of Hygiene at Auschwitz, former employee (like Vetter) of I.G. Farben and close collaborator with Mrugowsky, to begin studies of “brainwashing” with pharmacological agents, as they assumed their Russian counterparts were doing. Weber,



Fig. 11. Key people and places in the synthesis and development of nerve agents during the Nazi era: (A) Gerhard Schrader, chemist at the I.G. Farben company, who developed, within the framework of research on new insecticides, a series of substances that became the first toxic nerve agents used as instruments of chemical warfare. This earned him the nickname in some quarters of “the father of nerve agents”. (B) Photograph from the 1930s of the Kaiser-Wilhelm Institute installations for Medical Research at Heidelberg, where some chemical warfare material was subsequently developed, including the neurotoxic agent soman. (C) Professor Richard Kuhn, winner of the Nobel Prize for Chemistry in 1938 and Director of the Chemistry Department at the Heidelberg KWI; the man responsible for synthesizing soman. Archiv zur Geschichte der Max-Planck-Gesellschaft, Berlin-Dahlem.

working with Victor Capesius (1907–1985), director of the SS's Pharmacy Services, administered chemical compounds based on different barbiturates and morphine derivatives to experimental subjects (in the style of Klaesi's barbiturate cures), resulting in high mortality rates [55]. Similar research was carried out at the Dachau camp, through the administration of high doses of mescaline, according to a report by the US Army Technical Mission. After administration of hallucinogenic substances to 30 prisoners, the researchers concluded that the results were far from satisfactory [53,55]. Unfortunately, the existing documentation on this research is extremely scarce, since its highly secret nature meant that it had to be destroyed in the event of any type of compromising circumstances, such as the advance of Allied troops in the final stages of World War II.

However, it would actually be after the War that these techniques reached their peak, precisely among the victors. Notable in this regard would be sodium pentothal, commonly known as “truth serum”, since its intravenous administration had a disinhibitory effect (enhancement of positive transfers) which made subsequent interviews more productive (through a phenomenon known as “cathartic abreaction”) [54]. Some authors referred to this technique as the “induced crepuscular method”.

4.6. The development of neurotoxic agents as instruments of chemical warfare

The use of chemical substances and biological material as weapons of war is as old as the very conflicts humankind has waged since prehistoric times [96], though the substantial development of this form of warfare coincides with the rise of the chemical industry in the 19th century, which permitted the large-scale production of the toxic compounds used as tools of mass destruction during World War I.

The year after the Nazis came to power in Germany, chemical giant I.G. Farben launched a research project on synthetic insecticides directed, at the Leverkusen plant, by the chemist Gerhard Schrader (1903–1990) (Fig. 11A), who, from 1936 onwards, focused his research line on the organophosphate agents developed a few years earlier by Willy Lange (1890–1976) and his pupil, the student Gerda von Krüger [43]. Krüger's team succeeded in synthesizing over 2000 compounds of this nature, notable among which were parathion, subsequently the most widely used insecticide of this type in the world, and malathion, which is still employed today. Another of these compounds was ethyl-N,N-dimethyl-phosphoramidocyanidate (tabun) (Table 2), synthesized on the 23th December 1936, and whose inclusion in the arsenal of

Table 2
Nerve agents developed by German scientists during the Third Reich.

Chemical name	Common name	Acronym ^a	LCT ₅₀ mg (min)/m ³	Topical LD ₅₀ (mg)	Chemical structure
Ethyl-N,N-dimethyl-phosphoramidocyanidate	Tabun	GA	400	1000	
Isopropyl-methyl-phosphonofluoridate	Sarin	GB	100	1700	
Cyclohexyl-methyl-phosphonofluoridate	Cyclosarin	GF			
Pinacolyl-methyl-phosphonofluoridate	Soman	GD	50	100	

^a Code used by US Army and Tripartite Pact (precursor of NATO). The initial G refers to its source (Germany). Modified from [44,83,96].

chemical weapons was the result, as is often the case in science, to the intervention of chance: an accidental contamination of the research personnel, including Schrader himself, led to the discovery of symptoms typical of poisoning by anticholinesterase agents, such as myosis and asthma [18]. Subsequent studies with experimental animals confirmed the highly toxic consequences of exposure to the vapours given off by this substance. On 10th October 1938 this same research team synthesized another substance with similar properties, isopropyl-methyl-phosphonofluoridate, dubbed *sarin* in honour of its discoverers (Schrader, Ambrose, Rudringer & Vander Linde) (Table 2) [60].

From the moment Hitler came to power in 1933, research programmes on chemical weapons, expressly prohibited by the Treaty of Versailles, were reactivated, through a substantial increase in the funds made available for the relevant research and through the reinforcement of a network of collaboration between the military authorities, the academic sector and the chemical industry, in a kind of general militarization of science [60,85]. In this context, a decree was passed by the Reich obliging the remittance of samples of any type of chemical compound synthesized in the country to the Chemical Warfare Section of the Wehrmacht's Armaments Office (*Wa Prüf 9*), in case of some potential military application. In accordance with this decree, I.G. Farben sent samples of the two insecticides synthesized by Schrader's team, their possible utility being recognized immediately, given their capacity for inhibiting cholinesterase, with the result that their application was declared a military secret [18,82] under the code-name *N-Stoff* [15]. Although, thanks to work by Schrader's group, there were already data on lethal dosages of tabun and sarin in diverse animal species, there was still no information available about their effects on humans. Responsibility for the study of such effects was given to Wolfgang Wirth (1898–1996), director of the Institute of Military Pharmacology and Toxicology at the Academy of Military Medicine (Berlin) [71], who performed experiments with low doses of these agents, ostensibly using volunteer soldiers who gave their consent in return for some remuneration, though possibly also to avoid being sent to the front. However, documents presented by the Allies provide evidence of experiments on human beings at high doses in I.G. Farben's Elberfeld laboratory [60,85].

From 1940 onwards, tabun was produced on a large scale at an industrial plant constructed jointly by *Wa Prüf 9* and I.G. Farben in Dyhernfurth (Silesia), while industrial production of sarin (in another factory built in Falkenhagen) was delayed until May 1943, due to problems in the handling of one of the chemical substances involved in the manufacturing process, fluorhydric acid, which is extremely corrosive. Up to the end of World War II, the two plants between them had produced 12,000 tonnes of tabun and 600 tonnes of sarin [42,82], substances produced under the trade name Trilone®. Fortunately, however, these nerve gases were not employed during the War, though Hitler was tempted to use them after the Allies invaded the continent in June 1944 [15].

In addition to the efforts of the Academy of Military Medicine, *Wa Prüf 9* set up a network of academic and university research centres with the aim of obtaining data on potential neurotoxic agents [60]. This network included most notably the KWIs for Medical Research, a conglomerate of more than 40 centres throughout the length and breadth of Germany. Of all of them, the Heidelberg Institute was the one most strongly involved in the development of new chemical warfare agents (Fig. 11B). The director of the Chemistry Department of this KWI was the chemist of Austrian origin Richard Kuhn (1900–1967), who won the Nobel Prize for Chemistry in 1938 for his research on vitamins (Fig. 11C). Kuhn's influence in the German-speaking scientific community was evi-

dent, and without his becoming affiliated at any time with the Nazi Party, he was appointed one month after war broke out, in October 1939, director of the Department of Organic Chemistry of the Reich Research Council (*Fachspartenleiter*). Kuhn's very work on the relationship between vitamin B₁ and brain metabolism, and his development of advanced models of the relation between the spatial chemical structure of molecules and their biochemical effects at the level of the nervous system, led him to the discovery, in 1944, of a new neurotoxic agent, pinacolyl-methyl-phosphonofluoridate (code 25075), known as soman (Table 2) [60].

Tests were carried out on this new chemical agent at the *Wa Prüf 9* laboratory in Spandau, which found it to be more effective than tabun and sarin. Likewise, at the KWI in Heidelberg, Kuhn's team launched a series of comparative studies on the effect of these acetylcholinesterase inhibitors on preparations of isolated human organs – among them, notably, samples of human brain. Although almost all the documentation on administrative and bureaucratic aspects of this research disappeared after the War, a note in the MPG-Archiv, dated 8th April 1943, and recovered by Schmaltz [85], indicates that these types of practice were habitual. In the note, Ernst Telschow (1889–1988), Secretary-General of the Kaiser-Wilhelm Society, the umbrella organization for the KWIs, after a visit to the Heidelberg laboratory, writes: "Professor Kuhn is currently carrying out various highly interesting experiments, for which he needs brains from young, healthy subjects. I have informed him that I shall pass on his proposal to the pertinent authorities". Telschow, in a letter dated 22nd April, tells Kuhn that he has discussed the matter with the Chief of the Criminal Law and Judicial Department and with a Supreme Court judge from the Justice Ministry, who told him that the Departments of Anatomy at Heidelberg already received a large quantity of organs from Stuttgart, and that Kuhn "should make a direct request for a share of them" and, if necessary, make use of his military contacts (Telschow E, Note for the file, 1943, MPG-Archiv, Abt. I, Rep 1A, Nr.2576, p. 309, and Rep. 29, Nr. 104, p. 19). This note opens up the worrying question of where the brains came from. If we exclude those deriving from the Nazi regime's euthanasia programmes (used, as it has been demonstrated, in neuropathological studies carried out at the KWI in Munich), then given the need for brains from healthy subjects, some potential alternative sources (apart from that of soldiers who died in field hospitals) would be executed prisoners of war or concentration camp inmates. Regrettably, no documents remain that would provide evidence of where these organs actually came from, but Telschow's exchange with the Chief of the Judicial Department at the Ministry of Justice suggest that they may have been from subjects executed by the Nazi judicial system. At the same time, it should be stressed that there is no documentary proof that the pharmacologists and chemists participating in the development of research programmes on neurotoxic agents during the Nazi period had been involved in experiments with human beings in concentration camps.

Fortunately, there was not enough time before the War ended for the industrial production of soman to begin. However, despite the fact that this line of research with neurotoxic agents was also developed by British scientists, it would not be until after the cessation of hostilities that the victorious powers (the United States, Great Britain, France and the Soviet Union) gained detailed knowledge of the German military projects and began their own research on these compounds and their large-scale production [96]. As a result, from a combined Anglo-North American project in the 1950s, a new neurotoxic agent emerged, called VX (O-ethyl-S-(2-diisopropylamine-ethyl)-methyl-phosphonothiolate), which would come to constitute the most effective and powerful chemical warfare agent in ever known [44,83].

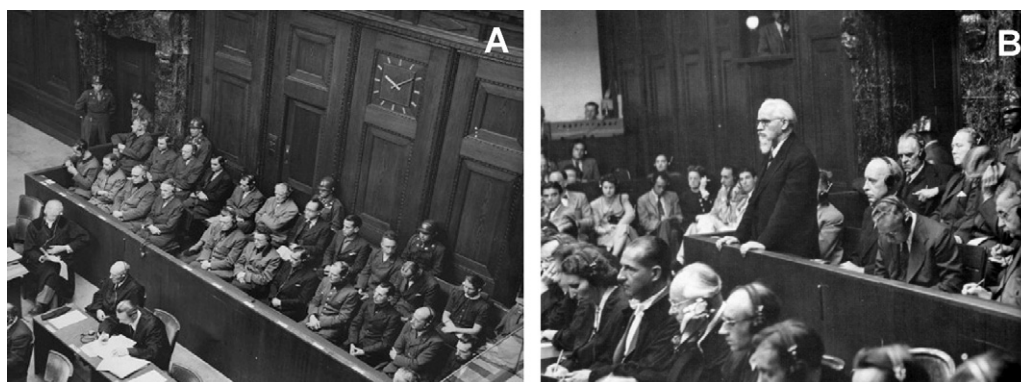


Fig. 12. Some of those responsible for the criminal activities in the fields of medicine and healthcare perpetrated by the Nazi regime, brought to justice: (A) Nazi medical officers during the Nuremberg Trials, 12th December 1946. (B) Bench with the 24 I.G. Farben directors accused of crimes against humanity, August 1947.

5. Nazi medicine brought to justice

After World War II, in the city of Nuremberg between 1945 and 1949, an International Military Tribunal made up of judges from the four allied nations, the United States, Britain, France and the Soviet Union, tried the former Nazi leaders, who were charged with war crimes [34,36,67]. At one of these trials (*The Doctors Trial*), 3 officers and 20 doctors were charged with, among other offences, “crimes against humanity” (United States of America vs. Karl Brandt et al.) (Fig. 12A); on 20th August 1947 the court passed death sentences on 7 of them (including Karl Brandt, Joachim Mrugowsky and Waldemar Hoven) (Fig. 5), giving prison sentences to another 9 and acquitting the remaining 7. However, as far as the euthanasia and mental health programmes and medical research were concerned, despite the fact that 3 of those sentenced were directly involved with them, those primarily responsible either committed suicide before they could be brought to trial, others were executed by Soviet troops (such as Paul Nitsche, after a death sentence at the Doctors Trial in Dresden, or *Dresdner Ärzteprozess*), or died in the course of the War, while others escaped justice [36,68], including Mengele, who escaped to South America where he drowned in a pond [22]. There were also cases such as that of Rüdin, one of the key players in the eugenicist policies of the Nazi regime, who, despite being arrested at the end of the War and tried by a local German court in 1947, was eventually acquitted on the grounds that his involvement with the Nazi crimes was purely circumstantial [34].

It is also relevant to mention that prior to the *Doctors Trial*, in October 1945, in the US-occupied zone of Germany, a trial took place specifically involving those responsible for the euthanasia programme at Hadamar (United States of America vs. Alfons Klein, et al.). Despite lacking the authority to pass judgement on the murder of 15,000 German subjects at this psychiatric institution, the fact that the victims included 476 Russian and Polish forced labourers made possible the so-called Hadamar Trial, in which the administrator of the institution, Alfons Klein (1909–1946), and two male nurses, Heinrich Ruoff (1887–1946) and Karl Willig (1894–1946), were condemned to hang. On the other hand, the medical director, Adolf Wahlmann (1876–1956), had his death sentence commuted in view of his advanced age, while the nurse Irmgard Huber (1901–?), who was directly responsible for administering drugs to thousands of patients according to the euthanasia protocol, though sentenced to 25 years in prison, was actually released in 1952. Similarly, on 25th March 1946 a court in East Germany passed death sentences on the doctor Hildegard Wernicke (1899–1946) and the nurse Helene Wiczorek for the murder of 600 mental patients at the Meseritz-Obrawalde hospital. Although other doctors were also tried after the war for crimes related to the

euthanasia programmes and condemned to death, their sentences would later be commuted; Wernicke was in fact the only German doctor to be executed after being tried by her compatriots [23].

The same year that the Doctors Trial at Nuremberg ended, another trial began there, in August 1947 (United States of America vs. Carl Krauch et al.) (Fig. 12B), popularly known as the *IG Farben Trial*, of 24 managers and scientists from the chemical-pharmaceutical corporation, for “crimes against humanity” (experiments with prisoners, use of slave labour, abuse, torture and murder of prisoners, etc.), among other offences (planning and preparation for war and invasion of other countries). Sentences in this case were considerably more benevolent (13 were acquitted and the rest sentenced to between 6 months and 8 years in prison). Among those given the heaviest sentences were Otto Ambros, director of the War Ministry’s Chemical Warfare Committee and Head of Production at Buna and Auschwitz (8 years), and Fritz ter Meer (1884–1967), Head of Department II and responsible for the chemical plant at Buna (7 years). The lack of incriminatory documentary evidence of I.G. Farben’s participation in different war crimes may explain the lightness of these sentences. In relation to this, from September 1944, as the Allied troops advanced, one of the most senior directors of the company, Fritz ter Meer, launched an operation to destroy all of its compromising files. Just before Frankfurt fell into American hands, more than 15 tonnes of paper was destroyed at the corporation’s headquarters; likewise, most of the documents relating to Auschwitz were disposed of before the Soviet forces arrived [15]. Less fortunate were two of the directors of Tesch, a subsidiary of I.G. Farben, Bruno Tesch (1890–1946) and Karl Weinbacher (1898–1946), who were tried and sentenced to death after the War by a British military court, for supplying the chemical products employed in the gas chambers at the concentration camps (Zyklon-B Trial, March 1946, Hamburg).

6. Conclusions

The contribution of German medicine to the development of psychopharmacology was fundamental during the 19th century and the first half of the twentieth. Indeed, the majority of the psychotropic drugs incorporated into the therapeutic *armamentarium* prior to the so-called “psychopharmacological revolution” [58], such as morphine, chloral hydrate, barbiturates or amphetamines, were developed by German researchers. However, this laudable scientific contribution was tainted from the very moment the Third Reich was proclaimed, ushering in a period in which psychotropic agents were used not only as therapeutic tools but also in a whole range of illicit and criminal activities, as described in the present work. But the most tragic aspect of all this is that despite such insti-

tutional abuses having been made public at the end of World War II, and the Nuremberg Code (1947) – the first international code of ethics for research with human beings – having been drawn up immediately afterwards, these types of activities and practices continued to take place subsequently, mainly in countries governed by totalitarian regimes, such as the former Soviet Union [14] and the People's Republic of China, essentially within the framework of political and religious repression. Nevertheless, the information available in relation to these countries is extremely scarce, since the activities in question have never reached public knowledge as they did in the West, so that those responsible have never been brought to justice.

In any case, it remains to ponder the motives and circumstances that led to the abuses described here, though this is *a priori* a rather difficult question to tackle. It is certainly true that, in the atmosphere of generalized enthusiasm in the early years of the Third Reich, the doctors involved in the application of eugenicist laws, and those who passively accepted them, argued that the norms were conceived for the benefit of the nation (*Volksgesundheit*) and not for the patient, if they were to leave a legacy of health for the coming generations [5,9], implying the invocation of such deceptive and coercive concepts as *cause majeure* or “sacred mission” [26,55]. However, there must also have been many other types of motivation in the members of the medical and scientific community for participating directly in the tremendous abuses committed during the Nazi regime [66]: some believed that everything was justified in the name of science, including the inhuman experiments carried out during the Second World War in the concentration camps [47]; others simply saw themselves as patriots, and justified their behaviour as acts of war; many became feverishly imbued with the perverse Nazi philosophy, while still others, more driven by ambition, became involved in such activities with a view to promoting their professional and academic careers. Finally, it is also important to stress that uncoupling oneself completely from the sinister Nazi machinery could become quite difficult for the health community in general, and for psychiatrists in particular [8], especially in an atmosphere in which fear was an essential tool of social pressure.

Conflicts of interest

The authors have no financial relationships to disclose, nor conflicts of interest.

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