

A Chemical Revolution as Seen from below: The 'Discovery' of Neuroleptics in 1950s Paris

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Summary. The 'success story' of chlorpromazine on an international level has been told over and over again. The prominence of Sainte Anne in Paris often features in these depictions. It played a critical role as a 'laboratory' between 1952 and 1954 in the narrative of the 'invention' of chlorpromazine as an antipsychotic. This paper intends to complete these global narratives by taking a closer look at the local therapy practice. The sources explored—from the systematic analysis of publications by Sainte-Anne psychiatrists and patient records—enable us to go beyond overused labels such as 'discovery', 'revolution' and 'invention' and glimpse inside the black boxes that these terms actually conceal. An analysis of the use of therapeutic tools reveals the level of 'tinkering' that occurred in medical practice. While the therapeutic arsenal was unquestionably diverse at the beginning of the 1950s, it was even more so by the end of the decade.

Keywords: chlorpromazine; Sainte Anne; antipsychotic; therapy

At Ste. Anne's, the windows facing the street were opened in the spring and summer, and the clamor of patients would normally be audible along the rue d'Alésia in the fourteenth arrondissement. After June 1952, the local merchants began pulling aside Jean Thuillier, one of Delay's assistants, and asking him with wonder: 'Doctor, what are you doing with the patients up there? We don't hear them anymore.'¹

It was with these words that Edward Shorter and David Healy, two specialists in the history of psychiatry, began their account of the invention of the first neuroleptic in the 1950s. The institution where this chemical 'revolution' was taking place was the Centre psychiatrique Sainte-Anne, located on rue Cabanis in Paris' 14th arrondissement.² During the summer of 1952, two psychiatrists working at the Clinique des maladies mentales et de l'encéphale (CMME), one of France's most prestigious psychiatry departments, presented their preliminary findings on a medication which at that point was still known under its industrial name RP 4560 and was subsequently marketed under the name of Largactil in France, Thorazine in the United States and Megaphen in Germany. The

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¹Edward Shorter and David Healy, *Shock Therapy: A History of Electroconvulsive Treatment in Mental Illness* (New Brunswick, NJ: Rutgers University Press, 2007), 166.

²Throughout this article I have used the term 'Centre psychiatrique Sainte-Anne'; today the institution is called the 'Centre hospitalier Sainte-Anne'.

occasion they chose to present their initial findings was the *Congrès des médecins aliénistes et neurologistes de France et des pays de la langue française* held in Luxembourg in July 1952. They described the administration of RP 4560 on 38 patients with a variety of diagnoses. They situated this ‘medicinal method’ within the broader context of hibernotherapy. Their findings were inconclusive: the medication mainly appeared to be effective for confusional states of mind. For schizophrenia, they reported ‘only remissions’.³

Sainte-Anne, which celebrates its 150th anniversary in 2017, partly draws its fame from this pharmaceutical discovery. As can be read on the institution’s website: ‘In 1952, psychiatry made a spectacular breakthrough thanks to the work of physicians at Sainte-Anne with the implementation of the first antipsychotic, an event that revolutionised therapy on a global scale.’⁴ This article aims to compare a local story—namely, that of a Parisian hospital—with an often told global narrative—a planetary revolution.⁵

A Paradoxical Historiography

While the history of neuroleptics in France in general, and at Sainte-Anne in particular, is at once acclaimed and challenged, it ultimately remains a little-known episode in the medical annals. Chlorpromazine’s story—from the synthesis of its core molecule in the dyestuff industry during the latter half of the nineteenth century to the trials on phenylethylene and its analogues by Rhône-Poulenc, its introduction into the medical field by the military surgeon Henri Laborit, its transition from surgery to psychiatry and, ultimately, its marketing by Rhône-Poulenc as a neuroleptic—has been told on multiple occasions by the protagonists themselves, by physicians and by researchers in the social sciences and humanities.⁶ Chlorpromazine is probably one of the medications whose trajectory has come under most scrutiny. It is hardly surprising that amid the abundant interpretations, there are diverse currents of thought. The history of chlorpromazine, and, in a broader sense, that of neuroleptics, remains a disputed one. Three salient historical

³Jean Delay and Pierre Deniker, ‘38 Cases of Psychosis Treated by a Prolonged and Continual Cure of RP 4560’, *Congrès des médecins aliénistes et neurologistes de France et des pays de langue française. 50th session—Luxembourg (21–27 July 1952)* (Paris: Masson, 1953), 503–13.

⁴‘Centre Hospitalier Saint-Anne’, *Historique*. <<http://www.ch-sainte-anne.fr/Etablissement/Historique>>, accessed 29 June 2015.

⁵See the classic by Charles Rosenberg, ‘The Therapeutic Revolution: Medicine, Meaning and Social Change in Nineteenth-Century America’, *Perspectives in Biology and Medicine*, 1977, 20, 485–506, and a contemporary reinterpretation: Nicolas Henckes, ‘Magic Bullet in the Head? Psychiatric Revolutions and their Aftermath’, in Jeremy Greene, Flurin Condrau and Elizabeth Siegel Watkins, eds, *Therapeutic Revolutions. Pharmaceutical and Social Change in the Twentieth Century* (Chicago: University of Chicago Press, 2016), 65–85.

⁶For the protagonist, see Pierre Deniker, ‘Qui a inventé les neuroleptiques?’, *Confrontations psychiatriques*, 1975, 13, 7–18; Jean Thuillier, *Les dix ans qui ont changé la folie* (Paris: Robert Laffont, 1981); Thérèse

Lempérière and Roger Ropert, ‘La révolution neuroleptique, le congrès de 1955’, in Jacques Arveiller, ed., *Psychiatries dans l’histoire* (Caen: Presses Universitaires de Caen, 2008), 233–40. A physician’s account can be found in Gérard Massé, ‘50 ans de découverte des neuroleptiques’, *Nervure*, 2005, 18, 1 and 9–10. For the work of researchers, see for example Judith P. Swazey, *Chlorpromazine in Psychiatry* (Cambridge, MA: MIT Press, 1974); David Healy, *The Creation of Psychopharmacology* (Cambridge, MA: Harvard University Press, 2002); Christian Bonah and Séverine Massat-Bourrat, ‘Les “agents thérapeutiques”. Paradoxes et ambiguïtés d’une histoire des remèdes aux XIXe et XXe siècles’, in Christian Bonah and Anne Rasmussen, eds, *Histoire et médicament aux XIXe et XXe siècles* (Paris: Glyphe, 2005), 23–61. Viviane Quirke, *Collaboration in the Pharmaceutical Industry: Changing Relationships in Britain and France, 1935–1965* (New York: Routledge, 2008), 197–206 for the influence of the pharmaceutical industry. Most recently Joanna Moncrieff, *The Bitterest Pills: The Troubling Story of Antipsychotic Drugs* (Houndmills: Palgrave, 2013), 20–38.

accounts, which do not reflect the usual divisions between histories written by medics or professional historians but transcend these different fields of knowledge, can be identified. I will elaborate on these accounts in this paper, using Sainte-Anne as a focal point. However, they are equally cogent for the general history of psychiatry after 1945.

The first account reflects an undeniable sense of achievement. Nowadays, most historians and physicians would concur that chlorpromazine was first used as a psychoactive substance at the Clinique des maladies mentales et de l'encéphale (CMME) at Sainte-Anne.⁷ In 1952, the CMME was directed by Jean Delay, who—along with his assistant Pierre Deniker—is generally considered as the inventor of the neuroleptic. The third protagonist, J. M. Harl, who co-authored most of the early scientific papers on chlorpromazine, is often overlooked.⁸ Reflecting the strong hierarchy in the medical profession, which was particularly pronounced at the CMME, this account reduces the medication's history to that of a single key figure, Jean Delay, the acclaimed 'protagonist of the latest psychiatric revolution'.⁹ The introduction of chlorpromazine is presented as an indicator of a biological revolution that 'has been a smashing success'.¹⁰ Today this is undoubtedly the dominant narrative within the medical sphere.

The second narrative is somewhat more ambiguous in its judgement. Admittedly, the significance of neuroleptics is emphasised. Likewise, the pivotal roles played by Delay and Deniker are given due prominence. Unquestionably, the expansion of the use and dissemination of chlorpromazine is considered to have been 'extremely swift', but this current of thought also alludes to the 'failure of neuroleptics' from as early as the 1960s. The analysis underlying this verdict is severe: 'Even the most experienced psychiatrists in biological psychiatry now think that neuroleptics cannot, in themselves, heal.'¹¹ Some commentators went even further in their criticism, either by labelling neuroleptics as a 'chemical straitjacket' or a form of 'social restraint', or by viewing them as a gateway for pharmaceutical companies, a situation which was considered to be extremely problematic.¹²

⁷A lively and prolonged discussion ensued as to whether Laborit or Delay/Deniker should be recognised as 'the inventor' of the first neuroleptic. This controversy would have prevented the Nobel Foundation from awarding a prize for the discovery of neuroleptics. E. M. Tansey and D. A. Christie, 'Drugs in Psychiatric Practice', in E. M. Tansey, D. A. Christie and L. A. Reynolds, eds, *Wellcome Witnesses in Twentieth-Century Medicine* (London: Wellcome Trust Centre for the History of Medicine at UCL, 1997), 131–205. In 1957, Pierre Deniker, Heinz Lehmann and Henri Laborit received the Lasker Prize for their discovery of chlorpromazine's clinical properties.

⁸Jean Delay, Pierre Deniker and J. M. Harl, 'Utilisation en thérapeutique psychiatrique d'un phénothiazine d'action centrale élective (4560 RP)', *Annales médico-psychologiques*, 1952, 110, 112–17; Jean Delay, Pierre Deniker and J. M. Harl, 'Traitement des états d'excitation et d'agitation par une méthode médicamenteuse dérivée de l'hibernothérapie', *Annales médico-psychologiques*, 1952, 110, 267–73; Jean

Delay et al., 'Traitements d'états confusionnels par le chlorhydrate de diéthylaminopropyl-N chlorophénothiazine (4560 RP)', *Annales médico-psychologiques*, 1952, 110, 398–403.

⁹Jean-Pierre Olié and Henri Lôo, 'Jean Delay (1907–1987), compositeur et acteur de la dernière révolution psychiatrique', *Psychiatrie française*, 1989, 20, 87–9.

¹⁰Edward Shorter, *A History of Psychiatry: From the Era of the Asylum to the Age of Prozac* (New York: John Wiley & Sons, 1997), vii.

¹¹Jacques Postel, *Éléments pour une histoire de la psychiatrie occidentale* (Paris: L'Harmattan, 2007), 329–43.

¹²Commentators who felt chlorpromazine was a form of restraint are quoted by Pierre Deniker, 'Trente ans de chimiothérapie neuroleptique en psychiatrie (Évolution du concept et de la pratique)', *Bulletin de l'Académie nationale de médecine*, 1982, 166, 117. On the opportunities it afforded pharmaceutical companies, see for example the early research

The third narrative completely circumvents neuroleptics. In a series of articles entitled 'Life in psychiatric hospitals from 1947 to 1959' published in *Nervure*, a psychiatric journal largely produced at Sainte-Anne, neuroleptics are entirely absent from the narrative.¹³ From this particular perspective, these years are described as a prehistoric age before a great shift took place in France—namely, sectorisation.¹⁴ Unlike other western countries, the breakdown of psychiatry into different sectors in France from the 1960s onwards resulted in a potent 'counter-narrative' to the pro-neuroleptic approach.

Yet despite this historiographical profusion, a rather surprising observation persists: more often than not these accounts end at the hospital gates.¹⁵ The Centre psychiatrique Sainte-Anne, the medical institution at which chlorpromazine was 'invented', is no exception.

And that is where this story begins. How was the introduction of a drug within a local context—albeit widely considered as having major consequences at the transnational level—experienced at the local context where it occurred? Chlorpromazine's 'global' dimension has been discussed on numerous occasions in the history of psychopharmacology. The first ever international conference organised in 1955, which brought together researchers from a dozen countries in order to establish a common terminology for the newly invented drug, is well documented. The local context, however, in which the drug standing as a neuroleptic was 'stabilised', is hardly known, if at all.¹⁶ How was chlorpromazine first introduced to Sainte-Anne? What were the circumstances under which

undertaken by David Healy on the history of psychopharmacology.

¹³Jean-Claude Bernard and Jean Morenon, 'La vie dans les hôpitaux psychiatriques de 1947 à 1959—Troisième partie: 1955–1956' *Nervure*, 17, 1, 8–10 and Jean-Claude Bernard and Jean Morenon, 'La vie dans les hôpitaux psychiatriques de 1947 à 1959—Quatrième partie: 1957–1959', *Nervure*, 2004, 17, 14–16.

¹⁴Sectorisation is characterised by two prevailing ideas: territorialisation of the mental health system and the establishment of alternative systems to hospitalisation: Nicolas Henckes, 'La psychiatrie de secteur, quelle histoire, quel avenir?', *Esprit*, 2015, 3, 28–40. In Nicolas Henckes' PhD on the reform of psychiatric hospitals in France post 1945, the question of neuroleptics is absent: Nicolas Henckes, *Le nouveau monde de la psychiatrie française. Les psychiatres, l'Etat et la réforme des hôpitaux psychiatriques de l'après-guerre aux années 1970*, (PhD, Ecole des Hautes Etudes en Sciences Sociales, 2007).

¹⁵This is especially true for France. In several other European countries, detailed studies on the introduction of antipsychotics in the 1950s do exist. For the United Kingdom: E. M. Tansey, 'They Used to Call it Psychiatry: Aspects of the Development and Impact of Psychopharmacology', in Marijke Gijswijt-Hofstra and Roy Porter, eds, *Cultures of Psychiatry and Mental Health Care in Post-war Britain and the Netherlands* (Amsterdam: Rodopi, 1998), 79–101;

Joanna Moncrieff, 'An Investigation into the Precedents of Modern Drug Treatment in Psychiatry', *History of Psychiatry*, 1999, 10, 475–90. For the Netherlands and Belgium: Toine Pieters and Benoît Majerus, 'The Introduction of Chlorpromazine in Belgium and the Netherlands (1951–1968): Tango between Old and New Treatment Features', *Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences*, 2011, 42, 443–52. For West and East Germany: Viola Balz, *Zwischen Wirkung und Erfahrung—eine Geschichte der Psychopharmaka Neuroleptika in der Bundesrepublik Deutschland, 1950–1980* (Bielefeld: transcript, 2010); Viola Balz and Matthias Hoheisel, 'East-Side Story: The Standardisation of Psychotropic Drugs at the Charité Psychiatric Clinic, 1955–1970', *Studies in History and Philosophy of Biological and Biomedical Sciences*, 2011, 42, 453–66. For Switzerland: Katharina Brandenberger, 'Psychiatrie und Psychopharmaka Therapien und klinische Forschung mit Psychopharmaka in zwei psychiatrischen Kliniken der Schweiz, 1950–1980' (PhD thesis, Universität Zürich, 2012).

¹⁶Lempérière and Ropert, 'La révolution neuroleptique'; David Healy, *The Psychopharmacologists: Interviews by Dr David Healy* (London: Chapman & Hall, 1996).

chlorpromazine was defined as a neuroleptic drug? And how was this drug administered in psychiatric practice? To which category of therapeutic methods did it belong?

Three categories of archival sources provide fundamental answers to these questions: first, the scientific output by the various teams working at the Centre psychiatrique Sainte-Anne. Here, the analytical approach will be twofold. Initially, it is important to observe how the output from the team working in conjunction with Delay on neuroleptics formed part of a broader practice of publishing their findings, and to determine the place chlorpromazine occupied in this process. Subsequently, consideration needs to be given to how the other physicians working at Sainte-Anne integrated this fresh data into their published papers. The second source is a series of reports by the *Commission de surveillance des hôpitaux psychiatriques de la Seine* (Committee for the Supervision of Psychiatric Hospitals in the Seine), kept in the City of Paris archives, that are particularly useful in terms of contextualising the emergence of chlorpromazine in a broader therapeutic setting.¹⁷ Thirdly, a collection of some 230 patient records covering 360 hospital stays by patients between 1949 and 1959 allows us to track the introduction of chlorpromazine by following developments in three units at the Centre psychiatrique Sainte-Anne. Before addressing these three aspects, a brief presentation is required of the Centre psychiatrique Sainte-Anne, a key location whose role in the history of chlorpromazine often remains elusive.

Sainte-Anne—A Unique Institution

Within the French context, the Centre psychiatrique Sainte-Anne is one of a kind. It is accountable to the Seine Prefecture, which administered a total of ten psychiatric institutions in the 1950s. Several of the hospital's departments form part of the Clinique de la Faculté de médecine. Sainte-Anne therefore also served as a training hospital, and it has enjoyed considerable prestige in both French and international psychiatric spheres from the late nineteenth century onwards. The medical journal *L'Encéphale: Journal des maladies mentales et nerveuses*, launched in the early twentieth century and predominantly edited and produced at Sainte-Anne, provided the institution with a significant mechanism for disseminating information. Jean Delay and Jean Lhermitte directed the journal, Henri Baruk and Julian De Ajuriaguerra handled editorial work, and Pierre Pichot acted as editorial secretary in the 1950s: all five were staff members who were working or had worked at the Centre psychiatrique Sainte-Anne.

Unlike at other hospitals, the individual heads of the various units at Sainte-Anne enjoyed considerable autonomy. It was the psychiatrists in charge of each of the seven departments—more so than the director of the institution—who left their individual mark on psychiatric practice. Departments at Sainte-Anne adhered to diverse traditions: one department was reputed to be more focused on psychoanalysis, for example, while another was known for taking a more biological approach.¹⁸

¹⁷Archives de la Ville de Paris, transfer 5037.

¹⁸Clément Fromentin, 'La fabrique de la clinique. Une histoire de la pratique psychiatrique (1850–1939)' (PhD, Paris VII—Denis Diderot, 2008); Michel Caire, 'Contribution à l'histoire de l'Hôpital Sainte-Anne

(Paris): des origines au début du XXe siècle' (PhD, Université René Descartes, 1981); *Sainte-Anne: 150 ans d'histoire à Paris* (Paris: Somogy éditions d'art, 2017).

The neuroleptic use of chlorpromazine was discovered at the Clinique des maladies mentales et de l'encéphale (CMME), whose directors, since the nineteenth century, have included esteemed names from the world of French psychiatry such as Benjamin Ball, Alix Joffroy and Gilles Ballet. Thanks to its pivotal role in training Paris's elite psychiatrists, the CMME was central to Sainte-Anne's work in the latter half of the twentieth century: Henri Ey, Jaques Lacan, Daniel Lagache, the child psychiatrist Pierre Mâle as well as Jean Delay, who became chief physician in 1946, were among the many notable practitioners who worked there. Delay, however, was often absent due to illness during the initial experiments with chlorpromazine in 1952.¹⁹ His actual role is therefore probably much less significant than originally presumed: the department was directed by his assistants Pierre Deniker and Pierre Pichot during the year in which he was absent.

In the early 1950s, the patient count at the Centre psychiatrique Sainte-Anne was approximately 1,000, which for a European university psychiatric hospital represented a fairly high number. In many respects, Sainte-Anne more closely resembled an asylum than a hospital. Yet unlike other psychiatric hospitals, Sainte-Anne enjoyed a significant turnover among its ward population due to the fact that many patients, once deemed 'incurable', were subsequently sent on to hospitals under the control of the Prefecture, either in the Parisian suburbs or in the surrounding countryside. With an average of 1,100 patients at any one time in 1952, Sainte-Anne actually had a total of 5,000 patients that year who had left or been discharged from the hospital; this offered those physician/researchers working there the advantage of an extremely broad variety of patients and symptoms on which to draw to enhance their medical articles.

Chlorpromazine, One of Many Scientific Concerns

Given that they were deeply embedded in the academic system and considered themselves part of an elite, the psychiatrists working at Centre psychiatrique Sainte-Anne were in the habit of writing scientific papers. They published not only in many specialist psychiatric academic journals but also in general medical journals, thus accessing a much broader readership. Moreover, several of them were also the authors of textbooks. Their prolific scientific writing enables us to trace the earliest mention of RP 4560. Between 1952 and 1955, Jean Delay (co-)authored 78 papers in 14 separate journals.²⁰ This substantial body of published work in itself allows us to advance a more qualified chronology of the discovery of neuroleptics, whilst also underlining the prevailing internecine divisions at the Centre psychiatrique Sainte-Anne (Table 1). An analysis of the publishing strategies by its various medical teams enables us to formulate hypotheses on three levels: (a) on the relative importance accorded to chlorpromazine; (b) on the early results—deemed ambiguous—with regard to chlorpromazine; and (c) on the evolving definition given to chlorpromazine as a 'specific therapeutic treatment for a specific condition'.

¹⁹Archives de la Ville de Paris, transfer 5037, report from 2 March 1953.

²⁰Thirty-four articles in the journal *Annales médico-psychologiques*, fifteen in the journal *L'Encéphale*, five in *La Presse Médicale* and four in English-language journals, one of which appeared in *Science*. For an

analysis of the academic output of the psychiatrists at Sainte-Anne's, I referred to the data bank PubMed (consulted on 2 September 2009). This data bank, focused on the English-language sphere, undoubtedly does not contain all the articles published by the teams at Sainte-Anne.

Table 1. Heads of department with publications on neuroleptics (1952–1958)

Department head	Georges Daumezon	René Bessière	Emmanuel Martimor	Xavier Abély
Neuroleptics	Admissions	Men's-1st Section	Men's-2nd Section	Women's-1st Section
Main subjects	None	None	None	None
	Emigrants, Social Psychiatry, Lobotomy	Art-therapy, Pick's Disease, Rorschach	Alcoholism, Delirium	Electro-shock, Dementia

Department head	Paul Abély	Jean Delay CMME	Yves Porc'her Centre
	Women's-2nd Section		Henri Rousselle
Neuroleptics	Yes	Yes	None
Main subjects	Insulin Cure, Alcoholism, Schizophrenia	Neuroleptics	Mental hygiene

Two conclusions can be directly inferred from an analysis of these publishing strategies. First, of the seven departments concerned, only two published articles on chlorpromazine between 1952 and 1958. Furthermore, only the Clinique des maladies mentales et de l'encéphale devoted a substantial number of its publications to this topic. Another fact to be taken into consideration is that even in this medical department, the content of the scientific papers was not exclusively limited to neuroleptics. Of the 133 papers Jean Delay published between 1952 and 1958 in various scientific journals, 23 were devoted to neuroleptics, of which 15 concentrated on chlorpromazine. During that same period, Delay published, *inter alia*, 13 papers on personality tests and 8 on electro-shock therapy. Hence, chlorpromazine by no means occupied Delay's entire academic thinking, despite the fact that it was at a crucial phase in its development: it was just being transformed into a psychiatric medication, its nosology had been stabilised and lively discussions on how to evaluate its effectiveness were ongoing.

Delay's team was not alone in experimenting on chlorpromazine at Sainte-Anne at that time. A month after their first paper appeared in *Annales médico-psychologiques*, Paul Abély's department published its findings in the same journal, drawing a rather mixed assessment. Abély played a crucial role in introducing psychoanalysis in France.²¹ He branded chlorpromazine as a 'mere potentiator for barbiturates'.²² He challenged Deniker's findings on two fronts: first, he stated that chlorpromazine worked better in combination with other therapies; and second, he stressed that other chemical substances were more effective than chlorpromazine. Over the following months, Deniker and Abély engaged in animated debates at meetings of the Société médico-psychologique. Over time, the discussion focused predominantly on the question of whether the slumber induced by chlorpromazine resulted in an improvement, or whether chlorpromazine was beneficial per se. Abély advocated the former opinion, and was to find allies in the psychiatric world, notably Paul Sivadon and Henri Baruk, as well as within Joseph

²¹On Paul Abély: J. C. Dubois, 'Allocution nécrologique à la mémoire du Dr Paul Abély, ancien Secrétaire général et ancien Président' *Annales médico-psychologiques*, 1980, 138, 155–8.

²²Paul Abély *et al.*, 'Suite aux essais thérapeutiques de rééquilibration instinctivo-affective: Essai de traitement par le bromure tétraéthyl d'ammonium en comparaison avec le R.P. 45–60 et le C. 92–95' *Annales médico-psychologiques*, 1952, 110, 266.

Hamon's team at the military hospital in Val-de-Grâce. This opposing stance championed by Abély maintained a certain visibility over several years. In 1957, he once again offered a rather critical assessment. In his view, chemotherapy did not come into existence in 1952, but rather with 'the emergence and the use of derivatives of diethylmalonyl urea, ammonium salts, ergot derivatives and amphetamines', thus well prior to the 1950s.²³ Abély also highlighted how this new medication utterly failed to fulfil the hopes it had spawned at the outset. 'Perhaps we sounded somewhat prematurely the death knell of electro-shock therapy and insulin coma therapy. We have had to come back to it, particularly when it comes to treating genuine melancholy. ... And this has proved to be the case for several neuroses, because failures were frequent.'²⁴

This was, however, merely a rearguard action. In 1957, Delay and Deniker succeeded in imposing chlorpromazine as a specific therapeutic tool in psychiatry. Initially, their approach was circumspect. Until 1953 they situated their approach alongside that of hibernotherapy, which had previously been practised by other psychiatrists and considered as a 'therapy of French origin, made possible thanks to new drugs developed in France'.²⁵ Hibernotherapy was developed for surgery in order to induce a state of sleep in the nervous system; its objective was to limit the body's reaction to the shock produced during surgery. From as early as the 1920s, psychiatrists had been experimenting with profound sleep therapies, cold therapies, etc., with the hope of sedating psychotic patients.

Unlike some of their predecessors, however, Delay and Deniker gradually stopped advocating the administration of a cocktail of chemicals, instead championing the exclusive use of chlorpromazine. This usage of a 'single neuroplegic medication' was the real novelty.²⁶ At a later point in 1953, they differentiated between a 'neuroplegic' cure and hibernotherapy. They saw the action of chlorpromazine as being similar to that of shock therapies: 'that of a central neuroautonomic shock coinciding with the initial phase of neuroplegia, followed by a long rest period for the nerves'.²⁷

This change of approach—the exclusive use of chlorpromazine—was recognised as such by some of their peers from 1953 onwards. Two psychiatrists from the Vosges region in eastern France began their presentation on chlorpromazine in April 1953 in the following terms: '21 patients given a long-term treatment of RP 4560 *following a technique inspired by that proposed by Messrs. J. Delay and P. Deniker*'.²⁸ Moreover, Delay's method also crossed national and linguistic boundaries in 1953, following the publication of an article in a Swiss-German journal, in which the authors refer to Delay's and Deniker's method.²⁹ Subsequently, chlorpromazine, hitherto considered as an indistinct

²³Paul Abély and Pierre Lab, 'De quelques enseignements sémiologiques et doctrinaux découlant de l'usage des neuroleptiques' *Annales médico-psychologiques*, 1957, 115, 754.

²⁴*Ibid.*, 750.

²⁵Jean Delay and Pierre Deniker, 'Les neuroplégiques en thérapeutique psychiatrique', *Thérapie*, 1953, 8, 362.

²⁶Jean Delay, Pierre Deniker and Yvan Tardieu, 'Hibernothérapie et cure de sommeil en thérapeutique psychiatrique et psycho-somatique' *La Presse Médicale*, 1953, 61, 1165–6.

²⁷One of many examples: 'Celle d'un choc neuro-végétatif central coïncidant avec la phase initiale de la neuro-plégie et suivi d'une longue période de repos nerveux', Delay and Deniker, 'Les neuroplégiques en thérapeutique psychiatrique', 361.

²⁸'Session of Réunion *psychiatrique de Strasbourg-Nancy* on 25 April 1953' *Annales médico-psychologiques*, 1953, 111, 84. Emphasis added.

²⁹J. E. Staehelin and P. Kielholz, 'Largactil, ein neues vegetatives Dämpfungsmittel bei psychischen Störungen', *Schweizerische Medizinische Wochenschrift*, 1953, 25, 581.

therapeutic aid, was transformed into a specific therapeutic agent, with hopes that the medication could be swiftly turned into a sort of 'psychiatric aspirin'.³⁰

In 1955, Delay and Deniker organised the *Colloque international sur la chlorpromazine et les médicaments neuroleptiques en thérapeutique psychiatrique* in Paris with financial assistance from Spécia, the pharmaceutical arm of Rhône-Poulenc laboratories that was responsible for distributing chlorpromazine.³¹ At this symposium, attended by hundreds of psychiatrists, Delay and Deniker succeeded in establishing chlorpromazine as a specialist psychiatric drug, and moreover in having themselves implicitly recognised as the 'inventors' of neuroleptics. And yet the 147 reports assembled the following year for the in-house journal *L'Encéphale* do not reveal a similar degree of enthusiasm as Delay's introductory remarks to the symposium in which he ventured to compare chlorpromazine with penicillin.³² Most of the speakers, from 20 nations and including such high-profile names as Manfred Bleuler from Switzerland and Henricus Cornelius Rümke from the Netherlands, nonetheless emphasised the novelty of these drugs and acknowledged Delay's input.

The Discovery Years—A Non-event?

What can the administrative documentation at the Centre psychiatrique Sainte-Anne tell us about how the various players involved experienced this therapeutic metamorphosis? The reports by the Commission de surveillance des hôpitaux psychiatriques de la Seine offer us a rough idea.³³

What is striking on reading these administrative reports is the prevailing therapeutic optimism, bearing in mind that they were published in the immediate aftermath of the Second World War. The emerging image is less catastrophic than the usual portrayal of (French) psychiatry as having emerged from the war in a pitiful state.³⁴ These reports reveal how widely the war experiences differed between Paris and the rest of the country, between town and country, between private and public institutions. At the end of the war, these summaries of activities at Sainte-Anne were brimming with enthusiasm and hope when it came to reporting therapies, although this was less so when the topic at hand was the material conditions and infrastructure or the nursing staff's motivation. The report covering the year 1945 is illustrative in this respect: 'We will not dwell on the remarkable therapeutic results obtained by Professor J. Delay, through the application of new methods of treatment: electro-shock, insulin therapy, narcotherapy, psychoanalytic treatment.'³⁵

³⁰This term was used, for example, by Henri Ey in 1955: Massé, '50 ans de découverte', 1 and 10.

³¹David Healy, *The Psychopharmacologists*, 1 and 172.

³²Jean Delay, 'Introduction au colloque international', *L'Encéphale*, 1956, 45, 305.

³³The history and role of this committee is not well known. It operated under the authority of the Office of Social Affairs at the Seine Prefecture and was composed of members of the Seine Departmental Council. The committee visited the various asylums under the authority of the Prefecture once a year,

compiling a report based, *inter alia*, upon notes written by the unit directors. In the 1950s, the committee was chaired by the former prefect and physician Francis Varenne, appointed in 1942. The rapporteur was the socialist President of the Departmental Council, the physician Jean Alessandri.

³⁴Isabelle Von Bueltingsloewen, *L'hécatombe des fous. La famine dans les hôpitaux psychiatriques français sous l'occupation* (Paris: Aubier, 2007).

³⁵Archives de la Ville de Paris, transfer 5037, report from 25 February 1946.

Over the following years such summaries frequently appear in the committee's reports. The report dating March 1952, for example, does not yet refer to neuroleptics, but expresses the prevailing optimism: 'Like his colleagues, Dr Guiraud [Director of the Centre psychiatrique Saint-Anne] specifies that the percentage of recoveries is much greater than was previously the case. This is due, he says, to the available modern treatments: malaria therapy, insulin therapy by administering the Sakel method.'³⁶ There had been the aforementioned new generation of therapies from the 1920s, for which the psychiatric community received two Nobel Prizes in Physiology or Medicine: in 1927, to Julius Wagner-Jauregg, for his discovery of the therapeutic value of malaria inoculation, and in 1949, to Antonio Moniz, for his work on the therapeutic value of the surgical procedure leucotomy.³⁷ From as early as the end of the nineteenth century, the use of drugs, mainly sedatives, became standard practice in most asylums.³⁸ In 1952, the year in which neuroleptics were introduced, administrative officials did not recognise a need for new therapies. The medications being administered were presented as adequate and effective: the situation is a far cry from the despondency or therapeutic nihilism often used to depict the period prior to the introduction of neuroleptics.³⁹

It is therefore hardly surprising that chlorpromazine was not immediately perceived as a break with the past. In the report compiled in 1953 covering the year 1952—the year that appears so pivotal in retrospect—the rapporteur noted:

Therapeutic attempts focused on biological treatments and psychotherapy. It is worth reiterating that 15 beds are devoted to insulin therapy—which is an extremely high figure if we take into account the complexity of the treatment—and that, in this regard, a novel method of protracted insulin-coma therapy was examined and developed. The therapeutic indications for ACTH [adrenocorticotrophic hormone] and cortisone were also specified for a certain number of psychiatric disorders. Finally, the earliest applications of a new medication in psychiatry were performed in this unit: the potent neuroplegic agent RP 4560, whose sedative effects enabled medical staff to completely eschew any form of restraint on agitated patients.⁴⁰

In early 1953, the priorities were thus clearly defined. First came insulin therapy and improved variants thereof. Developed in the early 1930s by the Viennese neurophysiologist Manfred Sakel, this method was widely applied in central and western Europe in the latter half of the decade. An insulin-induced coma administered by injection was considered therapeutic, even though its curative effects could not be explained. The patient was subsequently woken up following the administration of a glucose solution

³⁶Archives de la Ville de Paris, transfer 5037, report from 3 March 1952.

³⁷Jean-Noël Missa, *Naissance de la psychiatrie biologique: Histoire des traitements des maladies mentales au XXe siècle* (Paris: PUF, 2006).

³⁸Stephen Snelders, Charles Kaplan and Toine Pieters, 'On Cannabis, Chloral Hydrate, and Career Cycles of Psychotropic Drugs in Medicine', *Bulletin of the History of Medicine*, 2006, 80, 95–114. I have not come across evidence for the use of these drugs in

the sources used. It is not clear, however, if they were actually not used or simply not recorded in the patients' files.

³⁹Hervé Guillemain, *Chronique de la psychiatrie ordinaire: patients, soignants et institutions en Sarthe du XIXe au XXe siècle* (Le Mans: Editions de la Reinette, 2010).

⁴⁰Archives de la Ville de Paris, transfer 5037, report from 2 March 1953.

injection.⁴¹ At the end of the Second World War, this therapy was applied regularly at the Centre psychiatrique Sainte-Anne. It could not, however, be developed into a mass treatment, for it required considerable supervision to avoid fatal accidents. Patients had to be subjected to a thorough physical examination. During the coma and especially in the waking-up phase, the presence of at least two staff members was necessary to monitor a patient's condition.⁴² Despite the fact that in other European medical facilities, such as the Brussels Institute of Psychiatry, the method was already in decline due to its cumbersome nature, staff at Sainte-Anne nonetheless still believed in the potential of this therapy in the early 1950s.⁴³ The second priority was the use of ACTH and cortisone. While this practice is almost completely forgotten today, the use of cortisone in the early 1950s in psychiatry was considered as a serious option. Initially synthesised in 1948, this chemical element was manufactured on an industrial scale from 1950 onwards.⁴⁴ Papers on the subject were published in many countries.⁴⁵ Several teams at the Centre psychiatrique Sainte-Anne, including Jean Delay's team, were particularly interested in this approach, for two reasons. Following empirical observations demonstrating that both substances could trigger states resembling psychosis, psychiatrists began using them on their wards. By inducing psychosis, they hoped to come to a better understanding of the illness and how it operates. At the same time, after administering ACTH and cortisone, cases of swift recovery were recorded on a regular basis. This ambiguity—that a treatment could be at once pathogenic and therapeutic—posed problems on a practical level if the treatment were to be used on the wards. Delay nevertheless found the results 'significant' for their potential impact on theoretical research into psychosis.⁴⁶ These tests revealed the makeshift nature of psychiatric therapy. Chlorpromazine was given only third place in this report, and primarily as a sedative that helped calm agitated patients rather than as a therapeutic agent. It is also worth mentioning that this report highlights the vast sums of research funding granted to Delay's unit (a 30 per cent increase from 27 to 39 million French francs) to subsidise his research on cortisone, and not on chlorpromazine.

Over the following years, the reports remained decidedly circumspect with regard to the so-called revolution. For the year 1953, the report stated that the predominant therapies were 'insulin, encephalography, electro-shock [and] intra-cerebral injections'.⁴⁷

⁴¹Jean-Noël Missa, *Naissance de la psychiatrie biologique: Histoire des traitements des maladies mentales au XXe siècle* (Paris: Presses Universitaires de France, 2006), 97–138.

⁴²The Centre psychiatrique Sainte-Anne would occasionally ask permission from the patient's family before proceeding with a given therapy. See, for example: ASA, 5th district, no. 341848. Chloé P. was at Sainte-Anne from October 1956 until August 1959.

⁴³Benoît Majerus, *Parmi les fous. Une histoire sociale de la psychiatrie au 20e siècle* (Rennes: PUR, 2013).

⁴⁴David Healy, *The Creation of Psychopharmacology*, 184–5.

⁴⁵'L'A.C.T.H. et la cortisone en psychiatrie. La notion de "stress" en psychiatrie', *Médecine et hygiène*,

1950, 8, 173; S. Katzenelbogen, 'Recent Developments in Treatments in Psychiatry', *International Record of Medicine and General Practice Clinics*, 1951, 164, 59–61; Paul Abély, Janine Cor and Jean Lemaire, 'Essais de traitement de la schizophrénie par la cortisone ou l'A.C.T.H. combiné avec les antibiotiques et la cure de Sakel. Premières indications et premiers résultats', *Annales médico-psychologiques*, 1954, 112, 394–8.

⁴⁶Jean Delay, L. Bertagna and A. Lauras, 'ACTH et cortisone en psychiatrie', *Annales médico-psychologiques*, 1954, 112, 538.

⁴⁷Archives de la Ville de Paris, transfer 5037, report from 29 March 1954.

Findings were similar at other psychiatric hospitals under the aegis of the prefectural authorities. For example, the 1954 report for the Chezal-Benoît hospital in the Cher department states: '22 patients received 120 electro-shocks with the same overall satisfactory results as in the past. 26 were treated with electro-narcosis (125 sessions). 13 patients were treated with insulin.'⁴⁸ Chlorpromazine was not mentioned.

It was not until 1956—four years after its first administration—that chlorpromazine, which hitherto had invariably been presented as a sedative therapy, assumed a certain significance in the field, first following its inclusion in the report published after the aforementioned international conference in Paris in 1955. Secondly, prescription of this 'still very expensive' medication was linked with the sharp rise in the pharmaceutical budget. After 1957, 'psychopathogenic medications'⁴⁹ began appearing more frequently in therapeutic reports at various hospitals throughout the Prefecture. Yet it was only from 1959 onwards that neuroleptics became more prominent, initially within the hospital structure, where neuroleptics were described as 'facilitating family reintegration', and later outside the hospital establishment thanks to the 'international reputation' Sainte-Anne had garnered in the world of psychiatry.⁵⁰ The decisive role played by Sainte-Anne was also reflected at a national level: Jean Delay, Pierre Deniker and Pierre Pichot were appointed to several ministerial committees on medications.⁵¹

Chlorpromazine in Therapeutic Practice

The third scale of application to consider is the use of chlorpromazine in therapeutic practice by physicians at Centre psychiatrique Sainte-Anne. Approximately 230 patient records from three units, spanning the period 1949–1959 and covering 360 hospital stays, were consulted (Tables 2a and 2b). The files come from three significantly different units.⁵² The first is the Admissions Service, directed by Georges Daumézon. Known as a psychiatrist who championed institutional psychotherapy, Daumézon's name does not feature prominently in publications on the topic of neuroleptics. The second unit is the Second Women's Section, headed by Paul Abély. The third unit is the CMME, headed by Jean Delay, who was absent due to illness in 1952 and replaced by his assistants Deniker and Pichot.

Drawn from patient files, the figures in Tables 2a and 2b are partially corroborated by a more detailed administrative report concerning biological therapies used at the CMME in 1955 Table 3).

Despite the difficulties related to establishing the sample, the figures in the tables do nevertheless enable several hypotheses to be proposed.

First, Largactil was introduced at a gradual pace. By 1952, the year in which traders in the neighbourhood were apparently perplexed not to hear the inmates any more, Largactil had already gained a foothold, albeit a minor one, among the biological arsenal

⁴⁸Archives de la Ville de Paris, transfer 5037, report from 7/8 June 1955.

⁴⁹Archives de la Ville de Paris, transfer 5037, report from 19 March 1956.

⁵⁰Archives de la Ville de Paris, transfer 5037, report from 13 April 1959.

⁵¹Delay and Deniker were appointed members of the *Comité de Neuropsychologie et Neuropsychophar-*

macologie de la Délégation Générale de la Recherche Scientifique, working alongside the prime minister. Along with Pichot, both were included on the list of experts designated for clinical trials on new neuropsychiatric medication.

⁵²This is a sample of files whose make-up remains unknown.

Table 2a. Usage of the three therapies (1949–1953)

	1949 (<i>n</i> = 7)	1950 (<i>n</i> = 13)	1951 (<i>n</i> = 22)	1952 (<i>n</i> = 28)	1953 (<i>n</i> = 40)
ECT	2	13	7	12	13
Largactil	0	0	0	1	10
Insulin	1	0	4	6	7

Note: *N* designates the number of dossiers on an annual basis. The dossiers may contain several therapeutic indications or none at all.

Table 2b. Usage of the three therapies (1954–1959)

	1954 (<i>n</i> = 46)	1955 (<i>n</i> = 47)	1956 (<i>n</i> = 29)	1957 (<i>n</i> = 32)	1958 (<i>n</i> = 51)	1959 (<i>n</i> = 91)
ECT	22	20	12	10	18	33
Largactil	11	18	14	17	32	56
Insulin	9	9	9	10	11	13

available to psychiatrists at the Centre psychiatrique Saint-Anne. It was not until 1956—some four years after its introduction—that Largactil was to become the most widely used means of therapy.⁵³

Secondly, compared with other European psychiatric hospitals from which similar quantified analyses are available, two elements need to be highlighted. First, Largactil became part of the therapeutic arsenal at the Centre psychiatrique Sainte-Anne at a very early stage. At the Karl-Bonhoeffer-Nervenlinik in West Berlin, for instance, chlorpromazine was also in use from 1952, but in Belgium it was only introduced later.⁵⁴ The Brothers of Charity, a religious congregation that managed 30 per cent of psychiatric beds in Belgium, started using chlorpromazine in 1953. At the Institute of Psychiatry, the university department in Brussels, patients were first treated with Largactil in 1954, and in the Belgian capital's largest psychiatric asylum, the Centre neuropsychiatrique de Bruxelles, neuroleptics were not introduced until 1959.⁵⁵ Since the initial discovery had been made at Sainte-Anne, psychiatrists there had easier access to neuroleptics than their colleagues elsewhere. Yet comparisons with these other hospitals also reveal that the use of Largactil remained measured at Sainte-Anne, and that the medication struggled to become established there. From 1954 onwards, Largactil became the most widely used therapy in the Brothers of Charity hospitals in Belgium. Similarly, in the Karl-Bonhoeffer Nervenlinik, chlorpromazine—known as Megaphen in Germany—superseded other

⁵³See the article's introductory citation. This story has undoubtedly become a medical myth, given that the anecdote is regularly retold. Elaborating on the notion of an urban myth, but this would require further research on urban societies and the stories they tell about psychiatry.

⁵⁴Thomas Beddies and Andrea Dörries, 'Auswertung', in Thomas Beddies and Andrea Dörries, eds, *Die*

Patienten der Wittenauer Heilstätten in Berlin, 1919–1960 (Husum: Matthiesen, 1999), 236–398.

⁵⁵Benoît Majerus, 'Une stabilisation difficile. La chlorpromazine dans les années 1950 en Belgique', *Gesnerus. Swiss Journal of the History of Medicine and Sciences*, 2010, 67, 57–72.

Table 3. Biological therapies in the CMME in 1955 (*n* = 708)

Insulin cure	ECT	Pneumoencephalography	Chlorpromazine	Others
7%	27%	12%	37%	17%

Source: Archives de la Ville de Paris, transfer 1513, report on the clinic of the Faculty of the Centre Psychiatrique Sainte-Anne, p. 9.

forms of therapy from 1955. While it was swiftly introduced at Sainte-Anne, its use there was not as widespread as at other hospitals.

The third and final observation is that Largactil was part of an already amply endowed therapeutic arsenal. This observation, initially made on the basis of reports from the Commission de Surveillance, is borne out by a perusal of patients' records. The introduction of neuroleptics is often depicted as a break with past practices, a radical turning point in the psychiatric timeline, as though the twentieth century only began in 1952 or the twenty-first century had precociously arrived in 1952. The figures in Tables 2a, 3b and 3, however, reveal that prevailing biological therapies were impervious to chlorpromazine, at least at Sainte-Anne. The 1950s witnessed the continuation of a therapeutic practice that was characterised, at least it had been since the 1920s, by a rather heterodox combination of treatments. Between 1955 and 1959, in the three units mentioned above, 36 per cent of patients were given electroconvulsive therapy (ECT), 53 per cent were administered Largactil and 21 per cent received ECT and chlorpromazine.

The administration of Largactil varied enormously from one doctor to the next.⁵⁶ Largactil was often administered at the beginning of a period of hospitalisation at Sainte-Anne. Just as at the Institute of Psychiatry in Brussels, Largactil was primarily used as a potent sedative. In April 1955, Balto M., a carpenter by trade, was brought in by the police due to a 'delirious surge'.⁵⁷ The nurses' notes indicate difficulties controlling the 'patient from Admissions—quite agitated—restrained—put under monitoring'.⁵⁸ From day one, the patient was administered a large dose of Largactil. The medication's effective sedative potency also explains its use whenever the patient suffered seizures during a hospital stay. Balto M. was interned for depression at the end of June 1956. Initially, he did not pose any particular difficulties, but after ten days a dramatic change occurred; in the wake of this development the doctor prescribed Largactil for 'relapse, crying and screaming, was sleeping on the ground floor. Had Largactil in the morning. Calmer afterwards. Was agitated again at 1 o'clock, was restrained'.⁵⁹ The medical staff thus used chlorpromazine as they would previously have used the straitjacket or hydrotherapy.

⁵⁶In the absence of the nurses' notes, which are not kept at Sainte-Anne, the point of view of the guardians and nurses is not broached here. In his monograph on the asylum at Le Mans, Hervé Guillemain emphasises that the testimony provided by the carers and the nurses underlined the break with the past: Guillemain, *Chronique de la psychiatrie ordinaire*, 89–90. This can also be witnessed in the retrospective autobiographical account of a nurse at the psychiatric hospital in Ville-Évrard: André Roumieux, *Je*

travaille à l'asile d'aliénés, 2nd edn (Paris: Éditions Ivrea, 2009), 149.

⁵⁷The patients' names have been anonymised. I would like to thank my family and friends who were kind enough to lend their names to some of 'my' patients.

⁵⁸ASA, sector 16, no. 333427, nurses' record (5 April 1955).

⁵⁹ASA, sector 16, no. 334637, nurses' record (3 July 1953).

Furthermore, this 'calming' effect was also influential when it came to organising the release of patients from Saint-Anne. Jean-Christophe C. was interned in 1955 for schizophrenia. After a protracted stay of four years, during which he was given ECT on several occasions, he was given permission to transfer to a nursing home on condition he abide by his prescribed medication regimen: 'One of my patients asked me today if he could go to your unit. I'm of the opinion that this new life situation would correspond perfectly to his temperament and would be beneficial for him. [He's a] very conscientious worker and he's completely calm, provided he receives a daily dose of 200mg of Largactil, which he willingly takes.'⁶⁰

Other forms of treatment were still considered more effective than Largactil. Paul Abély, whom we previously noted was not necessarily keen on using chlorpromazine, described the situation of Manon P., a 29-year-old woman detained for 'very atypical *delirium excito*', in the following terms: 'Currently being treated with Gardénal and Largactil. ... But it seems that we find ourselves dealing with the acute phase of a discordant psychic state silently evolving over a long time. The [patient's] admission is much too recent to develop a clear opinion but schizophrenic development is to be feared. It strikes us that a Sakel cure will need to be envisaged when this acute state and resistance abates'.⁶¹ In other words, Largactil was used to control the acute phase and insulin was used as therapy.

A medical file from the CMME confirms this observation. For patient Stéphanie G., who was admitted to the unit in 1956 and underwent several Largactil treatments, the psychiatrist noted: 'Resuming treatment with Largactil has once again resulted in improvement; hence her release was envisaged and discussed with her—perhaps prematurely, for her condition soon deteriorated again, for the third time. It was after this second relapse that a low-dose insulin treatment was initiated 15 days ago.'⁶²

Although both insulin therapy and Largactil were regularly administered at the same time, electroconvulsive therapy (ECT) was rarely induced concurrently with Largactil. Yet ECT was frequently given prior to Largactil being administered. In this respect, Anne S.'s treatment was standard. During her second stay at Sainte-Anne for 'depression', she was initially subjected to six sessions of ECT; given the lack of any improvement, the psychiatrist initiated Largactil treatment.⁶³ In this instance, it was Largactil rather than shock therapy that was seen as the last resort. Moreover, there are patient records that do not seem to conform to any rationale. Eric C., interned following a 'delirious outburst', is a good example of the prevalence of 'therapeutic tinkering' at the time (Table 4). Indeed, many psychiatrists nowadays often yearn for such a makeshift approach, faced as they are with a restrictive regulatory framework that curbs the administration of therapies.⁶⁴

During the early years, psychiatrists nevertheless remained sceptical about Largactil's calming and therapeutic effects. Several days after starting Largactil treatment on a patient, the doctor noted: 'Calmer as a result of Largactil (?) but mystical ideas.'⁶⁵

⁶⁰ASA, sector 16, no. 332602, letter from Wiart (intern) at Ainay-le-Château (13 April 1959).

⁶¹ASA, third district, no. 357178, medical note (not dated, probably beginning March 1958).

⁶²ASA, CMME, SS116582, medical note (not dated, probably June 1956).

⁶³ASA, third district, no. 352447. Anne S. was at Sainte-Anne from June 1958 to January 1959.

⁶⁴ASA, sector 16, no. 334859. Eric C. was at Sainte-Anne from July 1955 to November 1955; Tansey and Christie, 'Drugs in Psychiatric Practice', 131–205.

⁶⁵ASA, 3rd. district, no. 358554, medical note (20 March 1955).

Table 4. Eric C’s therapeutic table

Date	Therapies
11 July 1955 (date of admission)	Largactil
18 July–23 September 1955	57 insulin injections
28 July–5 August 1955	5 ECT
5 September–29 October 1955	Largactil

Source: See footnote 64.

While neuroleptics seem to cater more specifically to psychosis, as reflected in their classification as ‘antipsychotics’, clinical practice at Sainte-Anne demonstrates widespread use and covered a broad spectrum. This fact was also emphasised in publications by Delay and Deniker: in a 1955 article published in English, they asserted that chlorpromazine could cure the whole spectrum of psychiatric conditions: ‘manic states’, ‘schizophrenia’, ‘alcoholism’, ‘anxiety’ and ‘depression’.⁶⁶

This wide-ranging effectiveness suited Rhône-Poulenc, the pharmaceutical firm, which chose to give chlorpromazine the name ‘Largactil’ (from the Latin *larga actio*, or wide-ranging activity) when marketing the medication in the French-speaking world.⁶⁷

Even in the late 1950s, this therapeutic heterogeneity prevailed (Table 5). Catherine L., a 39-year-old woman, was interned a second time in September 1959 due to ‘melancholic bouts’. Despite medical publications already stressing the fact that Largactil was probably not suitable for this type of diagnosis, she was nonetheless administered chlorpromazine. A physician was surprised by the difficulty he had in establishing contact with Emmanuelle R., who had ‘just had a Largactil injection. Calm. Even sleepy, somewhat difficult to understand. Contact established with difficulty and precarious but appropriate.’ Eleven days later he noted: ‘relative insomnia despite Gardénal + Largactil drps. Rather depressed.’⁶⁸

The difficult process of stabilising medication with respect to diagnosis in psychiatric practice was also evident in the standards established for dosage. While the 1955 Paris conference had sought to establish a consensus based on a dosage of 300–400mg, considerable differences can be observed at Sainte-Anne, not just between patients but also between the doses given to a single patient. In general, doses tended to increase from one year to the next. For example, Henri P., admitted for ‘depression’ in 1954, was administered 25mg per day, significantly less than the standard dose.⁶⁹ For a patient, such alterations could be quite substantial from one day to the next, as was the case with 35-year-old Christian D., admitted to Sainte-Anne in October 1958 for schizophrenia. This bookkeeper was initially given insulin treatment, but this was discontinued after 53 injections—which in itself was an extensive use of insulin therapy, as this was often limited to 20 injections. Following the failure of insulin therapy, Christian D. was then administered 400mg of Largactil per day. Three months later, and with no discernible grounds for such

⁶⁶Jean Delay and Pierre Deniker, ‘Neuroleptic Effects of Chlorpromazine in Therapeutics of Neuropsychiatry’, *International Record of Medicine and General Practice Clinics*, 1955, 168, 318–26.

⁶⁷Swazey, *Chlorpromazine*, 140.

⁶⁸ASA, 3rd district, no. 361220, medical notes (5 September 1959 and 16 September 1959).

⁶⁹ASA, sector 16, no. 329571. Henri P. was at Sainte-Anne in the summer of 1954.

Table 5. Dispensing Largactil by diagnosis (1953–1959)

Depression	Schizophrenia	Delusional state	Alcohol
36%	55%	36%	21%

Note: Of the 360 hospitalisations, 205 dossiers clearly identify the diagnostic and therapies applied. During a single period of hospitalisation, a patient could be administered several therapies.

a change in dosage to be seen in his medical records, his daily dose was increased to 700mg.⁷⁰ The side effects of Largactil began to be noted in medical records from 1953 onwards. For example Nordin F., who was admitted to Sainte-Anne in September 1953, was subjected to the extensive array of biological therapies available to psychiatrists at that time: insulin, ECT as well as Largactil, although use of Largactil soon had to be discontinued. 'Patient feeling unwell after 2 injections of Largactil at 12-hourly intervals with drop in blood pressure from 12 to 8.'⁷¹ Other undesirable 'side effects' are also recorded in the files: dizziness, ringing in the ears, etc.⁷²

The patients' own accounts rarely appeared; nurses' notes, which often allow us to trace the patients' medical trajectories and individual experiences, have been removed from historical records at the Centre psychiatrique Sainte-Anne.⁷³ A few letters written by patients after their hospitalisation and kept in their medical records give us an idea of how they responded to antipsychotic medication. It is noteworthy that all these former patients wrote the name of the medication correctly. Admittedly, we can assume that those who wrote had a certain level of education. Nevertheless, this would also suggest that patients were informed about the medications they were prescribed, and that Largactil soon became part of the patients' first-hand psychiatric knowledge. Moreover, when patients discussed a treatment in their letters, they usually referred to Largactil. The medication seems to have been seen as a significant new development, at least from the perspective of some patients, for it was the only drug that was explicitly named. Being administered a medication—as in this case with Largactil—proved to patients that they were being cared for and looked after. Judith R. thus wrote to her mother following a three-month stay at Sainte-Anne: 'A nurse did tell me the name of my pills, but I've completely forgotten it. One of my colleagues takes 3 Largactil tablets a day. . . . You see, Mum, if they are starting to treat us with Largactil, that must mean that it works, don't you think?'⁷⁴ Patients' descriptions of the effects of chlorpromazine also enable us to highlight a singular aspect in the history of neuroleptics. Unlike in other medical specialisms, psychiatrists partly depend upon a patient's spoken responses to identify a particular medication's diverse effects, not all of which may be measurable. Simone M., a married woman of 36, was interned for 'inactive mania' in February 1959. During her two months of hospitalisation, she was given Largactil. In a letter to her psychiatrist, she

⁷⁰ASA, sector 16, no. 354778. Christian D. was at Sainte-Anne from October 1958 to January 1959.

⁷¹ASA, sector 16, no. 325038, medical report (20 September 1953).

⁷²ASA, sector 16, no. 355926. Charles R. was at Saint-Anne from December 1958 to January 1959.

⁷³Benoît Majerus, 'Making Sense of the "Chemical Revolution". Patients' Voices on the Introduction of Neuroleptics in the 1950s', *Medical History*, 2016, 60, 54–66.

⁷⁴ASA, 3rd district, no. 358128, letter from a patient to her mother (21 July 1959).

later described one of its side effects: repeatedly waking up during the night and experiencing difficulty falling back to sleep afterwards.⁷⁵

Finally, patients' letters shed light on an aspect that has not yet been addressed by historiography, albeit one which is difficult to trace: for the first decade in which neuroleptics were administered, Largactil was also used outside the standard psychiatric sphere, through the practice of private consultations and family doctors:

Our GP. He gave me Largactil and Sarpagan, which I've taken regularly for a week. ... I've had some rough days. I slept just 4 or 5 hours a night. I was dizzy, my ears ringing ... I was swinging between a state of excitement and depression, and the latter stopped me from sleeping. ... I consulted another doctor ... who told me that my disturbances were due (partially no doubt) to Largactil, and wrote me a prescription for Equanyl. I took this medication regularly (...) and the disturbances I was feeling have nearly disappeared.⁷⁶

Glimpses from a Black Box

The history of the introduction of chlorpromazine sketched out in this paper goes beyond the basic question of 'who discovered the first neuroleptic' and reveals a more complex picture than the one suggested by the opening quotation from Shorter and Healy that has been used to describe developments at the Centre psychiatrique Sainte-Anne in the 1950s. The sources explored—from the systematic analysis of publications by Sainte-Anne psychiatrists to patient records—enable us to go beyond overused labels such as 'discovery', 'revolution' and 'invention' and glimpse inside the black boxes that these terms actually conceal. What emerges is a much more intricate, unpredictable narrative: only as we uncover the details of how chlorpromazine was used in practice can we begin to grasp the complexities surrounding the introduction of this drug and its impact on the field of psychiatry.

From the viewpoint of the hospital's administrative management, the annual reports indicate both a high degree of satisfaction with existing therapies and an extremely sluggish realisation that neuroleptics were a source of innovation. In terms of scientific publications, neuroleptics did not feature among the preferred topics of physicians at Sainte-Anne in the 1950s. Except for the CMME, no other team at the hospital focused its research on neuroleptics. And although the CMME, the most renowned unit at Sainte-Anne due to its long-standing involvement in training doctors, was heavily committed to the issue of neuroleptics, the unit also conducted research in other areas of interest. If we make a simple quantitative appraisal of the articles published by psychiatrists at Sainte-Anne between 1952 and 1958, it would appear that insulin treatment was given most attention.

Although chlorpromazine was introduced without undue delay (in 1952), its use in therapeutic practice at Sainte-Anne developed slowly. In fact, up until 1956 other therapies remained more prominent within the institution. Compared with other psychiatric institutions throughout Europe, Sainte-Anne even lagged behind. If psychiatric therapy

⁷⁵ASA, sector 16, no. 357200, letter from Germaine D. to her physician (9 March 1959).

⁷⁶ASA, sector 16, no. 355926, letter from Dubois to the head physician (21 July 1957).

underwent a revolution in the 1950s, rue Cabanis in Paris was certainly not at its forefront. Despite the emergence of randomised controlled trials during this decade, they played no role for the Parisian physicians trying to establish the therapeutic value of chlorpromazine. Their basic model was drug-centred, hence the name neuroleptic—this term comes from the ancient Greek *lepsis*, meaning to take hold of the nerve.⁷⁷ It was only after the 1960s that psychiatrists switched to a disease-centred paradigm, hence the name antipsychotic.

While from today's perspective the use of chlorpromazine might appear to be a radical break with past practices for psychiatrists and historians alike, the evidence from Sainte-Anne reveals the extent to which therapeutic context and contemporary research needs to be comprehensively taken into account. Shock therapy was considered 'modern' in the early 1950s. Largactil was regarded as a complementary therapy, but not exclusively so. An analysis of the use of therapeutic tools reveals the level of 'tinkering' that occurred in medical practice. At that juncture psychiatric therapy was much less standardised than it is today. While the therapeutic arsenal was unquestionably diverse at the beginning of the 1950s, it was even more so by the end of the decade.

This brings me to the third and final point of these findings. Recently, several historians have suggested using the Seige cycle to describe the trajectory of neuroleptics. The cycle comprises three stages: 'first, an expanding use of the drugs, accompanied by high expectations; then, rising criticism and disappointment; and finally contracting use and limited application.'⁷⁸ Depicted as an ideal paradigm, this cycle is said to be applicable to all medications, with variations over time. Taking the example of the use of Largactil at the Centre psychiatrique Sainte-Anne, the validity of this model can be called into question. Indeed, chlorpromazine does not appear to have experienced this initial phase of enthusiasm. From the outset, criticism was voiced; Largactil's expansion did not come about at the expense of other therapies. Those involved in the field were more concerned with other issues. Although chlorpromazine was accepted in the 1950s, this was because it was part of a broader generation of biological and physical therapies. If today we still hail its emergence as a break with past practices, it is because drugs are the sole survivor of those heroic times, given that insulin coma therapy, ECT and malaria therapy have been largely abandoned or discredited.

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⁷⁷Caroline King and Lakshmi N. P. Voruganti, 'What's in a Name? The Evolution of the Nomenclature of Antipsychotic Drugs', *Journal of Psychiatry & Neuroscience*, 2002, 27, 168–75; Joanna Moncrieff, 'Magic Bullets for Mental Disorders: The Emergence of the Concept of an "Antipsychotic" Drug', *Journal*

of the History of the Neurosciences, 2013, 22, 30–46; Alan A. Baumeister, 'The Chlorpromazine Enigma', *Journal of the History of the Neurosciences*, 2013, 22, 14–29.

⁷⁸Snelders, Kaplan and Pieters, 'On Cannabis, Chloral Hydrate, and Career Cycles', 97.