

## **Barry Blackwell: Pioneers and Controversies in Psychopharmacology**

### **Chapter Six: Jean Delay**

#### **Preamble**

Jean Delay is perhaps best remembered for the discovery of Chlorpromazine, the first effective drug for the treatment resistant psychotic men and women who filled the world's asylums in the mid twentieth century. Compared to Delay's other scientific and literary accomplishments, as told in Driss Moussai's biography, his role in this discovery was largely conceptual and clinically modest, but as was customary in hierarchical French academia, Delay's name came first on scientific publications.

The clinical work was conducted by Pierre Deniker and an intern in his department, J.M. Harl, who died prematurely in a mountain climbing accident. Deniker described the early work in detail (Deniker, 1970) when he received the Taylor Manor Award for the discovery and presented his paper, *"Introduction of Neuroleptic Chemotherapy."*

"Logically a new drug was tried in cases resistant to all existing therapies. We had scarcely treated 10 patients - with all due respect to fervent adherents of statistics - when our conviction proved correct. It was supported by the sudden, great interest of nursing personnel, who had always been reserved about innovations."

When the first paper was presented to the French Medico-Psychological Society at a meeting on shock or sleep therapy the effect was described as "neuroleptic" – effecting the neuron - in cases of "manic excitation, and more generally, psychotic patients who were often resistant to shock or sleep therapy." The specific effects were noted on "agitation, aggressiveness and delusive conditions of schizophrenia which improved. Contact with patients could be re-established, but deficiency symptoms did not change markedly."

When six definitive papers were published between May and June 1952 these observations had been made on only 38 patients without any attempt at controlled design (Delay, Deniker and Harl 1952). The first controlled trials were by Joel Elkes in England (Chapter 3) and Heinz

Lehmann in Canada (Chapter 7). Within five years the drug was in use worldwide with the exception of America, where psychoanalysis still held sway. The phenomenon of “deinstitutionalization” had not yet taken place, but its relative failure might have been predicted by Deniker’s prescient observation that these drugs “failed to benefit deficiency symptoms,” those most necessary for survival in community.

**References:**

Delay P, Deniker P, Harl JM., Utilization en therapeutique d’une phenothiazine d’action central selective. *Annals Medico-Psychologiques*, 1952; 110, 112- 117.

Deniker. In (eds. Ayd FJ, Blackwell B.) *Discoveries in Biological Psychiatry*. Philadelphia, JB Lippincott, 1970.

**A Biography of Jean Delay**

**by**

**Driss Moussaoui**

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**Reviewed by Barry Blackwell**

This short volume of 112 pages plus references, eight illustrations and index is high in impact and contemporary relevance. It was authored by Driss Moussaoui, Chairman of the Rushd University Centre in Casablanca, Morocco, whilst he was Secretary for Meetings of the World Psychiatric Association (WPA) from 1996 to 2002. Its stated purpose is threefold: first, to eulogize outstanding pioneers of the WPA, this is the initial volume in a proposed series; secondly, to pay tribute to the man who for 27 years was in charge of Psychiatry at the University of Paris, a close collaborator of Pierre Pichot and Pierre Deniker who mentored Driss as a young foreign medical graduate studying psychiatry in France; and finally, as a tribute to Jean Delay’s unique contribution in founding a world renowned academic program that played a leading role in French and

international psychiatry and initiated a worldwide neuropsychopharmacology revolution with the discovery of chlorpromazine in 1952. Dr. Moussaoui's devotion to this task is further illustrated by his initiation of the Jean Delay Prize (the largest in psychiatry) for work that "best helps to bridge the gap between biological and psychosocial aspects of psychiatry," a goal that reflects its namesake's devotion to integrating all aspects of our field.

From this reviewer's perspective, an added virtue of this biography is that describing the persona, life challenges and career accomplishments of this remarkable man may serve as an inspiring role model for neuroscientists of all disciplines and cultures, at a difficult time in the evolution of neuropsychopharmacology.

This book has a novel and creative format; its nine chapters are thematic rather than strictly chronological. They portray the professional and personal man with his associations and accomplishments in both the medical and literary domains, including his family, friends, and colleagues, other sectors of psychiatry, as well as major societies and organizations. This mosaic creates a cohesive whole, which the author describes as "a rambling harvest" and, while there are occasional repetitions, these are never redundant.

An overarching metaphor, presented by Delay in the book's prefatory quotation and limned by Juan Jose Lopez-Ibor (President of the WPA) in a preamble, is the mythological two-faced image of Janus; integrating science and literature across a palate that blends the social, psychological and biological components of psychiatry, in both its academic and community settings.

The text begins by describing Delay's origins in the medieval Basque city of Bayonne, born of a father who was a successful surgeon, and who, eager for the son to follow in his footsteps, disparaged Jean's fledgling literary talents and ignored his innate clumsiness. Delay's mother, on the other hand, was a nurturing, sensitive, and affirmative influence on her only child.

All Jean's early pursuits and games were intellectual; he had an exceptional memory, was academically precocious and gained a baccalaureate in philosophy at age 14 with a thesis on "The relationship between the physical and moral." The following year, he entered the faculty of medicine in Paris and aced the competitive exam to become a hospital clerk, at age 18. His choice of psychiatry as a specialty deviated from the norm among top interns (as it does today), while his

rejection of surgery (reinforced by hating the sight of blood) upset his father. Instead, leaning to the distaff side of his heritage, he also chose to study aesthetics at the Sorbonne along with his medical, neurological and psychiatric programs. When he graduated with the highest grade in philosophy, his thesis supervisor advised him to “leave medicine and devote yourself to aesthetics.” Rejecting this advice, he nevertheless, began to write and publish short stories at the age of 20, while an intern at the Salpêtrière hospital, under the pseudonym Jean Faurel, a decision based on advice that being recognized as a writer might diminish his reputation as a scientist. But in his personal diary Jean wrote: “My true life, literature; my profession, psychiatry.”

At age 31, Jean Delay obtained a Professorship of General Medicine at the Paris faculty and developed an interest in the new field of the EEG. Soon after, in the middle of World War II, he obtained a doctorate in literature, with a thesis on “The Dissolutions of Memory,” which Pierre Janet lauded as “a work that reconciles psychiatry and medicine.”

In 1942 Jean made his final professional move to become Professor of Medicine (the youngest in France) at the Saint-Anne Hospital and joined the Clinic of Mental Illness and the Brain (CMME). He became Chair in 1946 (age 39) and remained until his retirement from medicine in 1970, at age 63. This was the environment in which he created his major accomplishments, beginning with a hospital which was still a virtual asylum, and turning it, over the next 24 years, into a multi-disciplinary academic team and program with laboratories in all the disciplines related to psychiatry, unique and exceptional in France. The CMME became a magnet for the best young doctors from around the world (foreign assistants) many of whom (like Driss Moussaoui) went on to found academic departments in their home countries.

Delay’s major colleagues during this period were Pierre Pichot, Pierre Deniker, Raymond Sadoun and Therese Lemperiere. Pichot had dual training in mathematics and psychology, pioneering quantitative psychopathology and behavioral psychotherapy, while co-editing two text books with Jean Delay on Psychology and Psychometric Tests. Pierre Deniker did Trojan work during the war with the French Red Cross, eventually joining the Free French fighting forces and receiving the Croix de Guerre. Subsequently, he participated in the discovery of chlorpromazine and co-edited a textbook with Delay on New Medications in Psychiatry. Therese Lemperiere was the woman on Delay’s team, devoting most of her time on a women’s unit and her special interest

in hysteria. Raymond Sadoun was a prominent member of the team in the mid and later years, an expert in epidemiology, who worked closely with WHO.

During his scientific career, Jean Delay published more than 40 books, as well as more than 700 medical articles on every aspect of psychiatry, distributed across national and international journals. Confronted with this massive oeuvre, Driss acknowledges the impossibility of an in-depth review and opts instead to identify Jean Delay's most outstanding contributions.

The first, chronologically, is the First World Congress of Psychiatry in Paris on September 19, 1950. This event is placed in the context of earlier international congresses, dating from 1850, as well as the devastation following the end of the war in 1945. Its multi-national nature is emphasized, with 52 different countries and 35 societies involved, including a planning process that took three years.

Second, in time, but prime in scientific and humanitarian impact, was the discovery of chlorpromazine with Pierre Deniker and J-M Harl, announced to the world in May 1952. The biography presents a compelling portrait of the clinical principles underlying the team's use of the drug and identification of its properties. It was not to potentiate other sedatives for "hibernation," but used alone, it modified cognition, affect and behavior in unique ways when given continuously by mouth or injection, to produce a prolonged action in individually variable amounts (as low as 75 mgs daily) that took several weeks to secure full benefit. The dramatic changes the drug produced in asylum care are elegantly portrayed; from a lifetime of often bedridden squalor, including strait jackets, forced feeding, violent and frequently ineffective "treatments," to the possibility of returning to life in the community. The international network of psychiatrists assembled for the First World Congress (1950) ensured swift dissemination of chlorpromazine's promise and potential to other countries by the time of the Second World Congress (1957), with the notable exception of America, where psychoanalytic hegemony over academic psychiatry still considered drugs as mere adjuncts to psychodynamic therapy.

Jean Delay's third important and most pervasive influence was his conceptual and integrative way of thinking and problem solving that included a bio-psychosocial approach combining all the available knowledge into one paradigm – long before George Engel introduced the model in America.

In summing up Jean Delay's scientific accomplishments, Driss Moussaoui engages in intriguing speculation about why Jean never received the Nobel Prize or Lasker Award for his seminal discovery. True, Deniker, a member of Delay's team did receive the Lasker Award in 1957, shared with Laborit, the French military surgeon who first recognized the unique properties of 4560 RP in pre-operative sedation, ("lytic cocktails") and Heinz Lehmann who introduced chlorpromazine into Canada after his wife translated the French articles. In the 1980s, Driss asked Deniker which team member was most responsible for the discovery; without hesitation he named Delay.

The Nobel Committee's rationale for failure to award the prize was an alleged lack of an underlying hypothesis to support the mechanism of action of the discovery. However, the Delay team had already postulated that a chemical substance could therapeutically benefit a mental illness with earlier work on isoniazid (INH) and depression, five years before Nathan Kline demonstrated that iproniazid benefited depression through a postulated action on monoamine oxidase – for which he also receive a Lasker Award. Furthermore, Delay's decade long work on the therapeutic action of chemical "shocks" to the diencephalon-hypophyseal system with drugs, including insulin and cardiazole, contrasted with the limited effects of lesser sedative drugs on psychotic patients, supporting Laborit's claim that chlorpromazine was doing something unique and beneficial. Interestingly, Delay spoke of this as not so much a "discovery", but as a "find" -- a nuanced distinction between serendipity (looking for one thing but finding another, as with Cade and lithium), compared to recognizing what is needed and anticipated (as in Pasteur's aphorism; "chance favors the prepared mind").

Moussaoui speculates that the Nobel Committee's real reluctance was due to the "problem of paternity." Too many potential conflicting squabbles for priority, of the kind well- documented in the literature and demonstrated by controversy over Kline's Lasker award for the MAOI discovery.

Due to the success of Jean Delay's entire program during its "Camelot" years, Driss comments: "He reigned supreme over the academic sector in France... his slightest gestures were observed, analyzed, dissected, and interpreted." Undoubtedly, this was facilitated by Jean's multidisciplinary interests and the relationships he developed with key figures in other fields and related programs.

Prime among these was collaboration with the public sector and its uncontested leader, Henry Ey, who never held an academic position, but was head doctor of the Bonneval asylum from 1933 until retirement 37 years later, in 1970. The relationship between these two men was a model of academic-public sector collaboration, each of them prominent and productive in their own domain, both authors of influential textbooks and adherents to a bio-psycho-social model. This collaboration was still remarkable, given their contrasting personalities. Ey was an extrovert, “go-ahead rarely bothering about protocol,” while Delay was an introverted diplomat, “an aristocrat who kissed ladies’ hands.” But what they also shared was an insatiable desire to serve psychiatry, demonstrated by their crowning accomplishment as joint organizers of the First World Congress of Psychiatry, and subsequently, the World Psychiatric Association.

Delay’s relationship with psychoanalysis was more ambiguous and nuanced, “he handled the concepts with great dexterity but he refused all dogmatic excesses and said so in plain language.” He included psychoanalysts in his team, but selected those “he knew would serve the patients well.” Jacques Lacan was a seminal example. Jean’s attempts to synthesize the organic with the dynamic inevitably elicited complaints from both sides of the fence, but he remained determined to integrate complex theoretical positions and take the best from each, remaining undeterred.

Also contributing to Jean Delay’s place in the scientific and public limelight was his involvement in various scientific societies. He was the first person to serve twice as president of the WPA (1950, 1957). Other organizations he served as President were the French language Congress of Neurology and Psychiatry (1954), the Societie Medico-Psychologique (1960) and the International Congress of Psychosomatic Medicine (1960). Delay was a founding member of the Collegium Internationale Neuro-Psychopharmacologicum (CINP) and later served as its president (1966). In 1955, he was elected to the National Academy of Medicine at the unusually young age of 48. He attended all its sessions, until 1968, but after turmoil terminated his scientific career, his allegiance shifted to his first love, the *Academie francaise*.

It was in May 1968 that dramatic events occurred, “a sudden thunderstorm in a clouded sky,” ushering in the end of Jean Delay’s brilliant career as a clinician, scientist and educator, and with it, the golden era he had created. A national Trotskyist movement erupted, paralyzing France with widespread strikes, student protests, and blocked public transport. Its ideology was anti-

authoritarian and profoundly anti-psychiatric. Psychotic and delusional patients were not mentally ill but only “victims of the system,” an echo of contemporary Scientology sentiment and radical libertarian ideology. Delay became the prototype of an alleged “contemptible order of mandarins” and 500 people invaded his department, occupied his office and lecture hall, ridiculing his teaching. The students demanded the separation of psychiatry from medicine and its complete removal from the medical field. Within two years, some of these changes had been implemented and Delay decided to retire, due partly to ill health, but driven by a deep desire to devote himself entirely to his first love, literature.

Whatever relief removal of the scientific burden offered, it should not detract from Jean Delay’s remarkable literary accomplishments before, as well as after his retirement. He became a member of the elite *Academie francaise* in 1959, at the age of 52, when his scientific endeavors were at their peak. The *Academie* is composed of only 40 “immortals,” so named as they serve until death. It was founded in 1635 by King Louis XIII and out of 700 members elected since its creation, Jean Delay was the first, and only, psychiatrist to be admitted, but only after an arduous induction ritual, in which each potential candidate must defend his right to fill the vacant seat created by death of the owner, before the surviving 39 members, who take a secret vote based on the humanitarian, personal, and literary talents of the candidate. On election, Jean took the seat once occupied by Louis Pasteur and, upon his own death, it was taken by Jacques Yves Cousteau who, in his acceptance speech, talked of replacing someone who seemed to have been “a phenomenon somewhat like Leonardo da Vinci.” By the time Delay was admitted to the *Academie*, he had relinquished his pen name, comfortable that his considerable literary works would not detract from his scientific reputation.

In the biography, Driss Moussaoui offers a detailed dissection of Jean Delay’s entire scientific and literary oeuvre (Chapter VII). The two scientific works he highlights are “*Les dereglements de l’humeur*” (Mood Disturbances) and “*Introduction a la medicine psychosomatique* (Introduction to Psychosomatic Medicine). The literary work most contributory to election into the *Academie* was probably his psycho-biography of Andre Gide, “*La jeunesse d’Andre Gide*.” Out of his total 14 literary books, perhaps the major work, written after his retirement, was “*Avant Memoire*,” a socio-biography of nine generations of a Parisian family, which included his mother, covering three centuries of French society.



Apart from charting Jean Delay's scientific career, Driss also creates a portrait of the person within, reading between the lines of what he wrote, cataloging his considerable literary output, talking with colleagues, family, and friends.

What emerges is a man who created his own success the hard way, in a well-ordered manner, rising at 4 am every day ("20% inspiration, 80% perspiration"). Jean was a humanist, eager to care for and cure his patients, who viewed medicine as both science and art. He possessed a remarkable power of observation, with integrative thinking far ahead of his time and dedicated to bridge-building between people and organizations. Those who knew him best, sensed an inner fragility, reserved, anxious and timid, at times, traits partially tamed by an addiction to nicotine and concealed beneath a majestic appearance; haughty on occasion, but devoid of exhibitionism. Jean was also discrete, secretive and uncritical of others in public; a good listener and accomplished communicator, with well-chosen spoken and written words, "A sentence sculptor, he was also a purist who sought perfection in everything." Finally, Jean disliked confrontation, crowds, noise and agitation, as well as driving a car. His cardinal features were a search for synthesis and balance, of justice and service to others.

Those who counted most in Jean Delay's life were four women: his mother, spouse and two daughters, one a psychoanalyst and author, the other with a brilliant career in literature, the first woman in history to follow her father as a member of the *Academie francaise*.

Apart from family, Delay had many admirers, but few close friends, all carefully chosen and cherished. Most were older and all, even the physicians, had a strong literary bent. His three closest literary friends were all Nobel Laureates in Literature: Roger Martin Du Gard (1937), Francois Mauriac (1952) and Andre Gide (1957). On the medical side, Pierre Janet was also a professor of philosophy (and 50 years older) and Jean Bernard was an essayist and poet, a member of both the Academy of Sciences and *Academie francaise*.

A reader on the threshold or early stages of a career in neuroscience might reflect on the personal qualities, scientific modus operandi, support systems and research philosophy of Jean Delay. Above all, on his capacity for hard work, integration and collaboration. On a sadder note, it is well to acknowledge the role that a sudden change in the social or scientific zeitgeist can play in shaping and terminating a brilliant career.

In placing all this before his readers in a brief, succinct and enjoyable manner, Driss Moussaoui provides a service to our field and a worthy acknowledgment to his mentors.

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