EXPERIMENTAL CATATONIA

A General Reaction-Form of the Central Nervous System and its Implications for Human Pathology

By

HERMAN HOLLAND DE JONG, M.D.

Associate Professor of Neuro-Psychiatry, Duke University Medical School, Durham, North Carolina. Former Director of the Neurophysiological Institute, Amsterdam University, Holland

BALTIMORE
THE WILLIAMS & WILKINS COMPANY
1945

Made in the United States of America

Published September, 1945

COMPOSED AND PRINTED AT THE
WAVERLY PRESS, INC.
for
THE WILLIAMS & WILKINS COMPANY
BALTIMORE, MD., U. S. A.

EXPERIMENTAL CATATONIA

FOREWORD

By NOLAN D. C. LEWIS

Director of New York State Psychiatric Institute and Hospital

Professor of Psychiatry, Columbia University

The clinical condition known as "catatonia" in man represents a biological phenomenon that has manifested itself in various ways and degrees in the animal kingdom probably from the early stages of evolutionary development. As far as man is concerned, from the comments scattered here and there through the ancient medical and theological manuscripts, one may infer that catatonic states must have been fairly common in our early civilizations. Like other conditions it has a long history of attempts to explain it in terms of numerous concepts ranging from demonological ruminations to more comprehensive and accurate clinical ideas of it as a special disorder. The consideration of catatonia in the scientific sense is a relatively recent development.

The clinical picture of catatonia in mental patients is usually not difficult to recognize. The stuporous reactions, the negativism, cerea flexibilitas, perseverational behavior and characteristic excitements appear in different combinations and degrees. The condition has been variously attributed to histopathological changes in the cerebral cortex, to endocrine imbalance, to endogenous toxic conditions, to circulatory disturbances, and to psychological regression.

These catatonic symptoms may occur in patients with organic brain diseases such as paretic neurosyphilis, alcoholic encephalopathies, head traumas, brain tumors, epidemic encephalitis, carbon monoxide poisoning, acetylsalicylic acid intoxication, and in post-convulsive states. Its most classical expressions appear in schizophrenic states and some of its symptoms (never the complete syndrome) can also be produced by suggestion in the hypnotic state.

In Amsterdam, nearly twenty-five years ago, the author of the present volume made some plethysmographic experiments on catatonic patients. The type of vascular response found seemed to indicate the possibility of an organic toxic component in the condition, which suggested the procedure of utilizing some toxic substance that would produce a catatonic state artificially in animals. Among the drugs selected for this purpose was bulbocapnine and thus the systematic investigation of experimental catatonia in animals was initiated.

From time to time during the years other students of the subject have

collaborated with de Jong. Among these Baruk may be mentioned particularly, as the work of this team has been reported in numerous publications which have directed attention to the spontaneous one observed in the clinic. It was found that practically all of the motor phenomena seen in human catatonia could be duplicated in the higher animals by means of the bulbocapnine method. The extent to which catatonic manifestations could be produced seemed to be related directly to the degree of development of the nervous system.

Catatonic motor responses may also be produced experimentally in the higher animals by the administration of a number of different chemical substances other than bulbocapnine. These substances (including bulbocapnine) apparently effect a loss of certain functions of the cerebral cortex allowing the action of the lower centers to become dominant. The author has also shown that catatonia can be produced experimentally by a variety of other procedures including asphyxiation, normal and pathological metabolic substances, by brain lesions and by other mechanical means. Therefore the neurophysiologic mechanisms whatever they are fundamentally can be released by more than one type of "trigger" and it is possible in certain humans that they may be precipitated by psychologic factors. While the relative importance of psychologic factors in the production of catatonia in schizophrenia and some other human behavior disorders is not yet firmly established scientifically, the production of catatonia experimentally may indicate that toxic elements and psychogenic factors combine to form the clinical picture.

The author of the present book which presents comprehensively in its different sections the whole field of experimental catatonia, is now Associate Professor of Neuropsychiatry at Duke University, Durham, North Carolina. On May 14th, 1940 he escaped from Holland, where he had been Director of the Neurophysiological Institute and Head of the Out Patient Department of the Amsterdam University Neurological Clinic. *The discovery of experimental catatonia, which Professor Foerster called one of the greastest discoveries of modern medicine, gave Professor de Jong an international reputation.* His researches were supported in Amsterdam by the Rockefeller Foundation from 1932 to 1938 and later for two years at the Psychiatric Institute and Hospital, Columbia University Medical Center in New York. In Holland he was awarded the Ramaer Medal for the most outstanding contribution to neuropsychiatry over a five year period and Babinski and Pavlov showed a special interest in his work. He is also a Laureate of the Academy of Medicine in Paris.

As a leading investigator in his field Prof. de Jong has stimulated a great deal of research in many world centers where psychiatry and neurology are studied. His book will be a valuable source of information for many years to come.

FOREWORD

By DAVID T. SMITH

Associate Professor of Medicine, Duke University School of Medicine

In a series of ingenious experiments extending over a period of more than twenty years, Herman de Jong and his associates have moved the syndrome of catatonia from the realm of armchair philosophy to the laboratory.

These investigations have shown that experimental catatonia is a general reaction form of the central nervous system. It could be produced in a great variety of ways: by drugs, by anoxemia, by centrifugation and by limiting the blood supply to the liver. The common denominator in all these experiments is obviously a derangement in the metabolism of the central nervous system. The more prolonged states of catatonia were induced by alteration in either the liver or the intestine. This suggests the intriguing theory that abnormal metabolism in the liver results in the development of toxic products, either directly or by the failure of the liver to detoxify certain substances, and that these toxic materials in turn affect the central nervous system and thus induce catatonia.

de Jong has found that patients with schizophrenic catatonia and also some other schizophrenics do have an alteration of liver function, as shown by the cephalin-flocculation test. One should bear in mind however, as the author emphasizes, both human and animal catatonia can be elicited in different ways and therefore all possible etiologies should be studied intensively. The probability of a specific liver damage as a cause of schizophrenic catatonia and certain other types of schizophrenia is such a promising lead that it should be followed and studied exhaustively. In my opinion, Professor de Jong and his associates are the best qualified research group to investigate this specific metabolic disturbance of the liver.

INTRODUCTION

Experimental catatonia was first described by the author and H. Baruk in the book, "La Catatonie Expérimentale par la Bulbocapnine", published in Paris in 1930 by Masson and Company. In this work only the experimental production of catatonic symptoms by means of bulbocapnine was described. The present writing, however, deals chiefly with the production of catatonic signs by many substances other than bulbocapnine and by certain non-chemical means, as well as with the applications of some of the results thus obtained to the study of human catatonia and schizophrenia.

Some facts from the history of bulbocapnine catatonia may be recalled here. The idea of experimentally producing catatonic symptoms came to the author first in 1921 after plethysmographic studies of normal and pathological individuals in which catatonics showed a special reaction-type.

Finally, a drug, bulbocapnine, was found in the pharmacological literature which, it was thought, might be capable of producing a series of signs in animals comparable to motor phenomena present in human catatonia. At first it appeared uncertain whether one was dealing with exactly the same signs in both categories. Therefore a series of comparative studies on bulbocapnine animals and catatonic patients was undertaken in collaboration with H. Baruk of Paris. As a result of these studies we finally became convinced that, in the case of bulbocapnine intoxication in different animals, we were really dealing with motor phenomena deserving the designation "Experimental Catatonia". The similarity between the motor signs of the human catatonic syndrome[1] and the picture obtained by intoxicating different animals with bulbocapnine was strikingly evident. In our experiments, the drug was injected in the entire animal series from snakes to monkeys, and we simultaneously compared the signs thus obtained with motor phenomena of human catatonics.

Many authors in different countries repeated our work, inspired by the possibility of experimental reproduction of motor symptoms predominantly connected with a psychiatric clinical picture. The way to a deeper penetration into the biological basis of certain psychotic conditions seemed to be opened. Extremes of praise and of disapproval were the reactions in psy-

[1] It should be emphasized that human catatonia is a syndrome and not a clinical entity as was thought by Kahlbaum in 1874. Although the syndrome, "catatonia", is most often seen in schizophrenia, it is erroneous to *identify* catatonia completely with dementia praecox, since the syndrome occasionally occurs in the course of a multitude of conditions such as encephalitis, malaria, typhoid fever, general paresis, brain tumor, coli bacillosis, carbon monoxide intoxication, etc.

chiatric, neurological, and physiological circles. We were proud that among those who strongly approved were Pavlov, Babinski, and Foerster; however, we were well aware of the fact that some workers in their reaction of approval or of disapproval were guided more by their own direction of thought (organicists versus psychogenists) than by the consideration of the experiments themselves. In this regard it should be emphasized that the goal has not been to contribute to any particular trend of thought, but only to seek the truth. Both concepts, organic and psychogenetic, should have equal consideration. Furthermore, some of our critics were either psychogenists who had never done experimental work on animals, or physiologists who had never seen a catatonic patient. However, critical remarks from sincere workers have been given utmost consideration and have modified our original conceptions in more than one instance.

After the publication of the above-mentioned book on bulbocapnine catatonia, it became clear to the author that experimental catatonia could also be produced by other chemical, biochemical, and physical means. It then became desirable to extend the work on the subject more and more. This was made possible by generous grants from the Rockefeller Foundation over a six-year period (1932–1938). The small neurophysiological laboratory at the Neurological Department of the Amsterdam University Hospital was extended and was made the Institute for Physio-pathology of the Nervous System. In the following pages will be described the results of the work of this institute and its continuation, carried out in this country after 1940: from 1940–1942 at the Psychiatric Institute and Hospital, Columbia University Medical Center in New York (likewise supported by the Rockefeller Foundation) and from 1942 until the present at the Department of Neuropsychiatry, Duke University, Durham, North Carolina.

In the first part of the present book purely physiological studies in animals are described, beginning with experiments with bulbocapnine performed after the publication of "La Catatonie Expérimentale par la Bulbocapnine" and followed thereafter by a description of results produced by the injection of chemical and biochemical substances other than bulbocapnine. The number of substances capable of producing experimental catatonia was found to be very large. During the course of these experiments the main object was to try to discover a "chemical catatonizing nucleus." In experimenting with more and more simplified chemical substances it was found that even an element like nitrogen proved to be capable of producing catatonic symptoms. Experiments with CO_2 and other gases proved that a biological element rather than a chemical nucleus ("cellular asphyxiation") must be held responsible for the production of catatonic phenomena. Further experimentation dealt with catatonic symptoms produced by non-

chemical means, such as by neurosurgical procedures, centrifugation, bilateral ligation of the carotid artery, electricity, audiogenic stimulation, "animal hypnosis", etc. The variety of chemical and non-chemical means for producing experimental catatonia led to the conclusion that this syndrome represents a general reaction-form of the central nervous system.

In the second part of the book application of animal experimentation to human pathology is given. A "rotation test" characteristic of physiological negativism and catalepsy in catatonics is described. A series of extensive experiments deals with the search for a specific toxic substance in the urine of schizophrenics, so far with negative results. In the study of histamine content of schizophrenics and normal individuals no difference was found.

Experimental catatonia was found to be a general reaction-form of the central nervous system. In one field, however, a certain specificity was discovered, namely, that of alteration of metabolic function. Here it was found that **only the alteration of the function of either the liver or the intestine produced signs of experimental catatonia.** This led to re-investigation of the old problem of liver function in schizophrenics by more recent methods. Positive reactions with the cephalin-flocculation test were obtained in a relatively high percentage of catatonic schizophrenics and other dementia praecox patients in contrast to control groups. These positive results, together with findings in the animal experiments on alteration of metabolic function points to the **possibility** of a primary liver damage in those patients. The flocculation method also offers, to a certain degree, a practical qualitative blood test for the diagnosis of some catatonic and non-catatonic schizophrenia cases.

The author takes this opportunity to thank all those research workers who collaborated with him for their sincere and fruitful contributions. Collaborators during the first period of the work carried out in the Netherlands were the author's assistants, Dr. F. J. Nieuwenhuyzen (biochemist), Dr. D. J. Kok (veterinary surgeon), Dr. A. Geesink (surgeon), Dr. W. A. den Hartog Jager, and Miss E. Rietmeyer. Among other collaborators of the Amsterdam Institute we mention Dr. George W. Henry, New York City (U. S. A.), Dr. Alfred Gallinek, New York City (U. S. A.), Dr. O. Sager, Bucharest (Rumania), Dr. L. Noteboom, Amsterdam (Holland), Dr. J. Keller, Leipzig (Germany), and Dr. Franz Krause, Heidelberg (Germany). In this country co-workers were Miss Ethel Chase at the New York State Psychiatric Institute and Hospital, New York City, Dr. Edwin Stainbrook, Dr. William Brooks, Dr. Robert Heimburger, Dr. J. Harold St. John, and Miss Louise Sullivan of Duke University Medical School.

References to work on experimental catatonia done by investigators apart from the above-mentioned group will generally not be given here, since it

is beyond the line of thought guiding the whole gamut of experimental material described in this volume.[2] Part of the work here presented has been published as short contributions in different languages in periodicals hardly accessible in this country, such as the Proceedings of the Royal Academy of Sciences of Amsterdam, Archives Néerlandaises de Physiologie des Hommes et des Animaux, the Nederlandsch Tijdschrift voor Geneeskunde, etc. Some of the work done in this country has been published by the Journal of Nervous and Mental Diseases, the Journal of Comparative Psychology, etc. The author is indebted to the editors of these periodicals for their permission to reprint material derived from the above mentioned publications.

All in all, this book presents for the first time the fruit of many years' work as a unit and in its logical sequence.

The author also wants to express his appreciation for the work done by Miss Ethel Chase for her artistic illustrations and by Mrs. Frances Stebbins, Mrs. Rose Lemert, Mrs. Frances Christenson, Dr. Edwin Stainbrook, Mrs. Doris Peacock, and Mr. Cyril J. MacKinnon for their editorial and secretarial work, made possible by grants from the Department of Neuropsychiatry of the Duke University Medical School and the Duke University Research Council, for which gratitude is hereby expressed. Appreciation is also expressed to the Williams & Wilkins Company in Baltimore, Maryland, for their excellent publishing work.

[2] As to Baruk's work on experimental catatonia in inflammatory and infectious processes, reference is made to statements in his book "Psychiatrie Médicale Physiologique et Expérimentale", Paris; 1938; and for studies done in this country on bulbocapnine catatonia, we refer to the work of Ferraro and Barrera, and many others.

CONTENTS

PART I

EXPERIMENTAL STUDIES IN ANIMALS

Chapter I

DEFINITION AND DESCRIPTION OF EXPERIMENTAL CATATONIA

The term "Experimental Catatonia" was deliberately chosen because of the similarity of motor symptoms in human catatonia and those revealed in the systematic study of bulbocapnine intoxication in different kinds of animals.

It may be briefly recalled that psycho-motor symptoms of **human catatonia** can be divided into (A) **hypokinetic** and (B) **hyperkinetic** phenomena. [See "La Catatonie Expérimentale par la Bulbocapnine" (2).]

(A) **Hypokinetic phenomena** are as follows: (1) **Diminished motor initiative.** The impulse to movement and action is diminished. This may occur to such a degree that the patient will remain motionless in one spot, often in a drooping position, for many hours.

(2) **Catalepsy.** The patient assumes positions passively introduced by the examiner. However, it is not always possible to cause him to hold every imposed posture. The catatonic patient usually has some preferred position to which he almost always returns, and in which he will stay motionless for a considerable time. Catalepsy is not limited only to the extremities but is found in the whole body. Diminished motor initiative and catalepsy are related phenomena. There is a difference only in degree, catalepsy representing a complete loss of motor initiative.

(3) **Negativism.** The patient has a tendency to do the opposite of what he is asked, and in this case one is dealing with a purely psychological phenomenon. In other cases, however, negativism appears as a psychomotor symptom. For instance, a negativistic patient lies in bed in a certain position. If his hand is pulled this way or that, he will bring it back immediately to its original position. If we try to push the patient forward, he resists and can be moved only passively *en bloc* (**passive negativism**). Sometimes the patient moves a few steps backward, after being pushed forward (**active negativism**). Negativism is a sign that occurs more frequently than catalepsy in human catatonia.

(B) **Hyperkinetic phenomena.** In contrast to the former group, one is dealing here with an abundance of movement, i.e., hyperkinesis. The clinical hyperkineses are often very characteristic. In their simplest form they may consist of a tremor. In other cases they are more elaborate and assume the form of stereotyped movements, which the patient repeats continuously or automatically, that is, they take place without the conscious will of the patient. Again, the hyperkineses may be irregular and of great