THE PHYSIOLOGICAL BASIS OF MENTAL ACTIVITY

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Proceedings of a Symposium held in Mexico City, October 9 and 10, 1961

EDITED BY

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ELECTROENCEPHALOGRAPHY AND CLINICAL NEUROPHYSIOLOGY

SUPPLEMENT NO. 24

ELSEVIER PUBLISHING COMPANY

AMSTERDAM/LONDON/NEW YORK

Electroenceph. clin. Neurophysiol., **1963**, *Suppl. 24*

SOLE DISTRIBUTORS FOR THE UNITED STATES AND CANADA
AMERICAN ELSEVIER PUBLISHING COMPANY, INC.
52 VANDERBILT AVENUE, NEW YORK 17, N.Y.

SOLE DISTRIBUTORS FOR GREAT BRITAIN
ELSEVIER PUBLISHING COMPANY LIMITED
12B, RIPPLESIDE COMMERCIAL ESTATE
RIPPLE ROAD, BARKING, ESSEX

LIBRARY OF CONGRESS CATALOG CARD NUMBER 63–16082

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Preface

In the last few years, science has witnessed the expansion of the frontiers of neurophysiology in an eager attempt to understand the functional substrate of behavior and mental processes. Hopefully, the knowledge on the physiology of the brain has accumulated so rapidly that at the present time the day does not appear remote when the neurophysiological invasion into the fields of psychology and psychiatry would result in a unique science of brain functioning with a common language for scientists interested in their different aspects. The construction of the bridge to fill the gap notoriously existing between the realms of the brain and mind has been initiated and requires a multidisciplinary collaboration.

With these considerations in mind, when I was asked to organize a Symposium of Neurological Sciences to be held in connection with the 9th Latinamerican Congress of Neurosurgery and with the 5th Latinamerican Congress of Electroencephalography and Clinical Neurophysiology, it seemed appropriate to select a broad neurophysiological topic of common interest to clinicians dealing with the human brain. As a final decision after several consultations the title *The Physiological Basis of Mental Activity* was accepted. Originally, such a meeting was planned to be both international and multidisciplinary. However, financial restrictions permitted us only to reach the first goal.

Drs. Horace W. Magoun and John D. French accepted to act as Honorary Presidents and supported this endeavour from the beginning with their valuable encouragement, enthusiasm and suggestions. Special thanks are due to these outstanding figures in this Symposium.

Although a balanced representation for the ambitious topic to be discussed would have required the participation of a great number of scientists, the number was limited by the time available. Furthermore, it was regrettable that various circumstances prevented several distinguished investigators from attending the meeting.

The Symposium was held under the auspices of the Secretaría de Salubridad y Asistencia (Mexican Public Health Service) directed by Dr. José Alvarez Amézquita, whose sincere and sustained interest in this scientific event is gratefully acknowledged. The meetings took place at the Congress Building of the Medical Center in Mexico City belonging to the Instituto Mexicano del Seguro Social. It is a pleasure to acknowledge the Director, Lic. Benito Coquet, who generously provided the facilities at the Medical Center.

The formal sessions started on October 9, 1961, and continued morning and afternoon throughout October 10. A cordial atmosphere with maintained interest and active discussions were outstanding features of the meeting.

Of the pleasant social occasions which accompanied the Symposium, the reception

offered by the Rector of the University of Mexico, Dr. Ignacio Chávez, deserves special mention. His gracious hospitality left a pleasant souvenir of Mexico among the Symposium participants. The welcome reception given by Mr. R. Kolbe, manager of "Librería Internacional", is also acknowledged with thanks.

The Symposium was officially closed in a solemn ceremony presided by Lic. Adolfo López Mateos, President of Mexico, accompanied by outstanding members of his Cabinet Council, by Dr. Donald B. Lindsley who represented the International Brain Research Organization (IBRO), and by the Executive Secretary.

After a short address in which the importance of brain research for the humankind was emphasized and both the interest and support provided by the Mexican Government to scientific research and the important scientific contributions and goodwill of the Symposium participants were acknowledged, Lic. López Mateos handed with personal congratulations Diplomas with his signature to each participant. This internationally reaching act and pioneer among official ceremonies in the history of México, can be taken as a demonstration and example of the encouragement and support that Nations should provide to scientific research and interchange of ideas among scientists.

It is a pleasure to thank Dr. Charles E. Henry who as Consultant for Supplements of *Electroencephalography and clinical Neurophysiology*, dedicated much of his valuable time to revising the manuscripts submitted for publication. The Executive Secretary and Editor is indebted to his colleague, Dr. Truett Allison, who assisted considerably in the editorial task. Finally, he wishes to express his personal gratitude to Miss Edith Peraza Ojeda whose indefatigable work and maintained enthusiasm made possible the completion of the manuscripts for the publisher.

Mexico City, July 1963 RAÚL HERNÁNDEZ PEÓN

Solemn Closing Ceremony of the Mexico City Symposium, presided by Lic. Adolfo López Mateos, President of Mexico. From left to right: Dr. José Alvarez Amézquita, Secretary of the Mexican Public Health Service; Donald B. Lindsley, Professor of Psychology at the University of California at Los Angeles and representative of IBRO in this Meeting; Lic. Adolfo López Mateos, President of Mexico; Dr. Raúl Hernández Peón, Executive Secretary of the Symposium; Dr. Jaime Torres Bodet, Secretary of the Mexican Education Department; Ing. Eugenio Méndez Docurro, Director of the Polytechnical Institute; and Dr. Guillermo Haro, President of the Academy of Scientific Research.

Officers of the Symposium

Honorary Presidents
DR. H. W. MAGOUN
DR. J. D. FRENCH

Executive Secretary
DR. R. HERNÁNDEZ PEÓN

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Central Sensory Mechanisms

Contents

Specific and Unspecific Influences on the Olfactory Bulb

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INFLUENCE OF OLFACTORY STIMULI

The study of the specific patterns of response evoked in the olfactory system by an olfactory stimulus practically started when Adrian and Ludwig (1938) showed that a drop of stimulating fluid placed in the olfactory sac induced a train of discharges in the olfactory stalk of various fishes. Later, Adrian (1942, 1950a) reported that similar oscillations of potential were recorded from mammalian olfactory bulbs. He distinguished between *intrinsic waves* due to the persistent activity of bulbar cells and *induced waves* produced at a frequency of 30–40/sec when an osmotic stimulus was applied to the nose. Further investigations (Adrian 1950b, 1951a) convinced him that a differential sensitivity for different odors existed along the antero-posterior axis of the olfactory bulb. This spatial differentiation was present for two classes of substances: esters evoked synchronous discharges from the more rostral part whereas hydrocarbons and oily substances were effective in the caudal regions of the bulb. Adrian's results promoted a series of investigations on the histological basis of this differentiation. Le Gros Clark (1951) examining serial sections of the whole nasal cavity after partial lesions of the bulb found that the upper and posterior areas of the olfactory epithelium projected predominantly or exclusively to the upper surface of the bulb and saw that such a topical localization was rather precise.

Besides a spatial differentiation, Adrian (1950b, 1951a) noted that a temporal differentiation of the responses could also be detected from the bulb. Esters and oily substances, if presented at high concentration, stimulated both regions of the bulb, but still a difference of latency and duration of the discharges was present. Esters quickly produced a response which was soon over while oils gave longer-lasting discharges.

The problem of differential activation of the bulb has been reinvestigated by Mozell and Pfaffman (1954) and Mozell (1958). These authors recorded the integrated response from different regions of the bulb to stimuli of specific odors. They showed that as the recording electrode moved from the more rostral to the more caudal part of the bulb the responses to amyl acetate stimulation decreased relative to heptane. They also observed a difference in time course of the responses when the concentration of the two substances was regulated in such a way as to give comparable responses.

Doubtless, although of the greatest interest to the physiological mechanism of odor discrimination, the differential responses recorded with gross electrodes from the

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olfactory bulb do not give any information whatsoever of how second order neurons behave in response to various stimuli and how they can transmit information to the olfactory centers of the brain. Adrian (1951c, 1953) was the first to record with fine electrodes from the depth of the bulb. Although he could not identify the recorded neurons, he believed that he was recording the activity of mitral cells. This author reported that different smells were effective in evoking the discharges of different neurons provided that the concentration was kept low enough. Likewise, Walsh (1956) found that some cells responded to stimulation by some odors and not by others. Mancia *et al.* (1962) have recorded with fine microelectrodes from the external plexiform, mitral and granule layers of the olfactory bulb. They payed particular attention to the physiological and histological identification of the cells recorded and studied: (a) the effect of the same olfactory stimulus on different cells; (b) the differential effect of various olfactory stimuli on the same neurons and (c) the differential effect on the same neurons of independent stimulation of the two olfactory mucosae. These authors used *cerveau isolé*, *encéphale isolé* and curarized rabbits in addition to some animals anaesthetized with urethane. In order to identify the cells studied and the layers from which the micro-electrode was recording, the lateral olfactory tract was stimulated antidromically. The criteria used for identification of the cells (Von Baumgarten *et al.* 1961; Green *et al.* 1962) and of the layers (Von Baumgarten *et al.* 1962b) have been discussed and will not be repeated here.

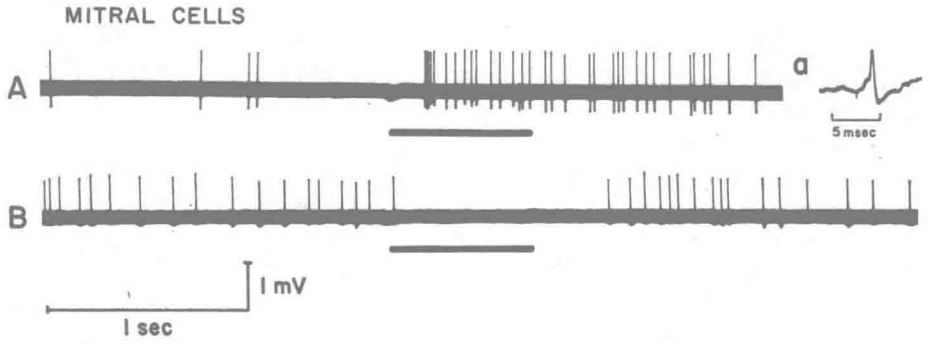

Fig. 1

Effect on two different mitral cells of the same olfactory stimulation (amyl acetate). Rabbit under urethane. Black signals indicate the olfactory stimulation delivered through the ipsilateral nostril. *A*: *mitral* cell (antidromically activated by lateral olfactory tract stimulation shown at *a*, stimulus artifact retouched), strongly facilitated by the olfactory stimulation. *B*: same experiment. Another mitral cell also activated antidromically by lateral olfactory tract stimulation and inhibited by the same olfactory stimulus. (This and Fig. 2, 3 and 4 from work of Mancia *et al.* 1962).

The patterns of response of different cells (mitral, tufted, granule) to an olfactory stimulus (amyl acetate, clove oil, creosote, ether, tobacco, room air and air purified through charcoal) were always complex and sometimes dependent on the background activity which preceded the stimulus. The cells were influenced at the beginning of the stimulus ("on" responses) but most of them also responded to the end of the puff ("off" response). Facilitation and inhibition were equally observed, and similar cells

could respond in an opposite way to the same stimulus. Fig. 1 presents a typical case; the cells recorded were mitral cells only a few microns apart. Both were activated antidromically by lateral olfactory tract stimulation. However, they responded to the same stimulus in an opposite way. The same behavior was common to cells recorded in other layers (external plexiform and granule).

Differential responses to different olfactory stimuli were present in some cells. Mitral and granule as well as cells in the external plexiform layer could have specific patterns of response to various stimuli. Fig. 2 shows two cells recorded simultaneously in the external plexiform layer just above the mitral region. Amyl acetate and clove

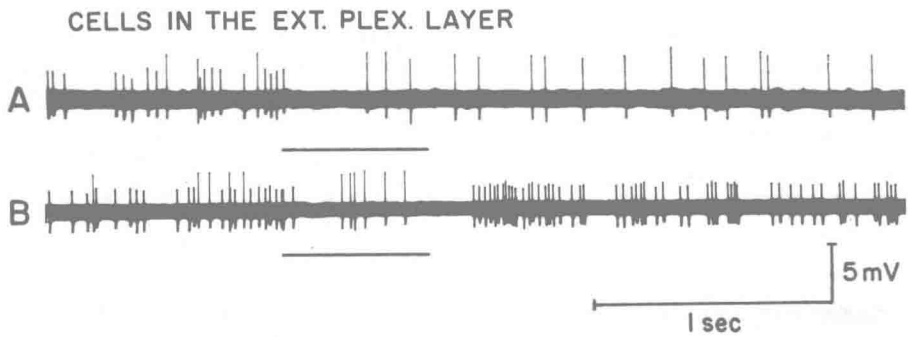

Fig. 2

Opposite effects by two different odors on the same cells recorded in the external plexiform layer. Rabbit under urethane. Black signals indicate the olfactory stimulation applied through the ipsilateral nostril. Two cells of different amplitude recorded simultaneously. *A*: olfactory stimulation with *amyl acetate* inhibits completely the small unit and facilitates the large one. *B*: olfactory stimulation with *clove oil* briefly facilitates and subsequently inhibits for a long period the large unit. The small one instead is inhibited during the stimulation and facilitated afterwards.

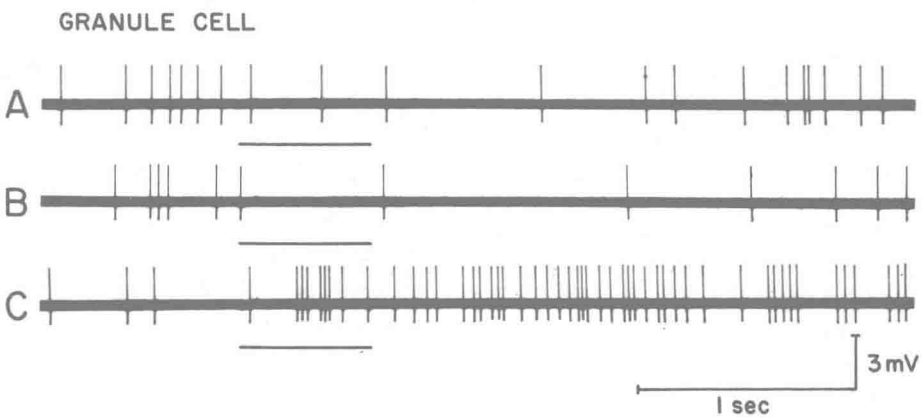

Fig. 3

Response of the same granule cell to different olfactory stimuli. Rabbit under urethane. Black signals indicate the olfactory stimulation applied through the ipsilateral nostril. *A*: filtered room air slightly inhibits the spontaneous discharge of the unit. *B*: amyl acetate produces a stronger inhibition. *C*: creosote facilitates the same cell.

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oil stimulation influence differentially the two cells. While amyl acetate inhibits completely the small cell and for a long period, the larger one is instead facilitated after a short inhibition. Fig. 3 shows a granule cell slightly inhibited by filtered air and amyl acetate but strongly facilitated by a creosote stimulus. In these experiments the olfactory stimulus was delivered only to the nostril ipsilateral to the bulb recorded.

Stimulation of the contralateral nostril, when the ipsilateral one was blocked and/or the mucosa destroyed also sometimes influenced olfactory neurons. The effect was usually inhibition and disappeared after transection of the anterior commissure, indicating that it was mediated through this pathway. Kerr (1960) also noted a depressing effect on the gross activity of the opposite bulb when one nostril was stimulated. Thus, it is not surprising that the physiological stimulation of one mucosa has an inhibitory influence on bulbar neurons of the opposite side. What is surprising is that Mancia *et al.* (1962) found almost a "mirror image" response when the two olfactory mucosae were stimulated independently. In these cases, simultaneous stimulation of the two mucosae resulted in a more complex effect which had characteristics in common to the response to either type of stimulus. Fig. 4 shows this

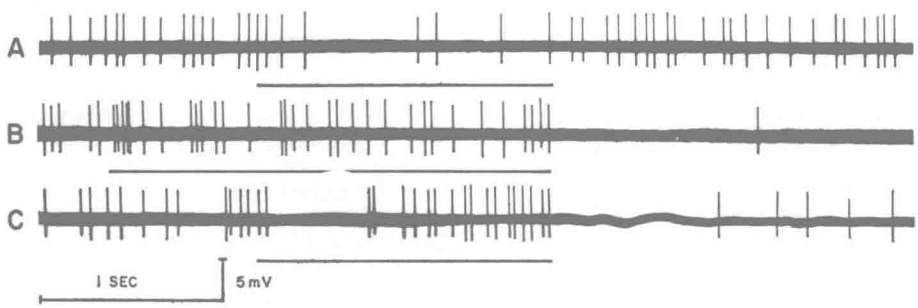

Fig. 4

Responses of the same cell in the external plexiform layer to ipsi-, contra-, and bilateral olfactory stimulation (tobacco smoke). *A*: stimulus applied through the contralateral nostril inhibits the spontaneous activity of the cell. *B*: stimulus applied through the opposite nostril produces a facilitation followed by an inhibition when the stimulus ceases. *C*: simultaneous stimulation through both nostrils produces a slight inhibition both at the beginning and the end of the stimulus (some spikes retouched in *C*).

phenomenon. The cell in *A* is inhibited by a stimulus applied through the contralateral nostril and *B* is slightly facilitated during and inhibited at the end of a similar stimulus delivered through the ipsilateral nostril. Simultaneous stimulation of the two nostrils in *C* produced an effect which has characteristics in common with either records (compare *C* with *A* and *B*).

Anatomists (Allison 1953; Cajal 1911; Le Gros Clark 1951, 1957) have shown that receptors are connected with dendrites of second order neurons (mitral and tufted cells) through the glomeruli. These structures are very complicated synapses and are interconnected by short axon cells and external granules. Quantitative studies (Allison

and Warwick 1949) have reported that 50,000,000 bipolar cells are connected to 45,000 mitral and 130,000 tufted cells. Thus, the glomeruli receive impulses from about 26,000 receptors and relay them to 24 mitral and 68 tufted cells. Therefore, the glomeruli appear to be the centers where information coming from many receptors is coded and transmitted to the second order neurons. Le Gros Clark (1957) found that in addition to a certain degree of topical localization between receptors and olfactory bulb, "fibres derived from receptors of different physiological significance are predominantly concentrated on correspondingly different glomeruli". However, this does not mean that impulses coming from one group of receptors are necessarily connected only with particular mitral or tufted cells. Anatomical (Allison 1953; Cajal 1911) studies suggest that a great deal of overlapping and randomization occur at the glomerular level accounting for the complex pattern of response observed. In addition we have to consider other mechanisms which may constitute the patterning of discharge of olfactory second order neurons: (a) interconnections between different glomeruli (external granule and short axon cells, Cajal 1911), (b) close functional connections between second order neurons on one hand and granule and short axon cells on the other, (c) a powerful system of "recurrent inhibition" which has a widespread inhibitory influence on a large majority of olfactory bulb neurons (Green *et al.* 1962), (d) centrifugal feedback paths originating from the opposite bulb (Allison 1953; Cajal 1911; Kerr 1960; Mancia *et al.* 1962) olfactory areas of the brain (Angeleri and Carreras 1956; Angeleri *et al.* 1956; Carreras and Angeleri 1956; Carreras *et al.* 1954), intralaminar thalamus (Arduini and Moruzzi 1953) and mesencephalic reticular formation (Hernández-Peón *et al.* 1960; Mancia *et al.* 1962).

Lastly, I would like to mention briefly the problem of the role played by a mechanical factor in olfactory stimulation. Adrian and Ludwig (1938) first believed that a mechanical stimulus could evoke discharges in the olfactory stalk of fishes. Adrian (1953) discussed a similar mechanism in the stimulation of the mammalian olfactory system and reported responses from the rabbit's accessory bulb to mechanical deformation of the organ of Jacobsen (Adrian 1954). Adrian (1951b) however, changed his opinion on the basis that purified air did not evoke any discharge from the olfactory bulb. Recently Walsh (1956) noted that there are cells in the olfactory bulb which may be influenced by odor-free gases. Ueki and Domino (1961) advanced evidence in favor of the presence of mechano-receptors in olfaction. Purified air, in their experiments could, in fact, still evoke discharge from certain parts of the bulb. Recording from single units, Mancia *et al.* (1962) could not decide whether or not a mechano-receptor was involved, being aware of the great difficulty in delivering stimuli positively odor-free. On the basis of "on" and "off" responses observed on single cells to puff of air bearing odors, Green, Mancia and Irarrazaval (in preparation) made the hypothesis that mechanical factors were involved. Turbulence and other physical changes at or near the olfactory mucous membrane at the beginning as well as at the end of a "puff" could produce a change in the concentration of the stimulus and stimulate the receptors differentially. This hypothesis would also explain the "on" and "off" responses recently reported in olfactory pathways from amphibia (Takagi and Shibuya 1960).

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CENTRIFUGAL INFLUENCES

The existence of centrifugal fibers to the olfactory bulb was first described by Cajal (1911) on preparations made with the Golgi technique. The precise origin of these fibers is still unknown. Allison (1953) and Angeleri *et al.* (1956) have confirmed with degeneration experiments the existence of this system of fibers showing that they come from the olfactory areas of the brain. They have been described as making synaptic contact with granule cells whereas some can be followed up to the external plexiform layer where they establish connections with the accessory dendrites of mitral and tufted cells. Whether or not a centrifugal innervation of the glomeruli and bipolar receptor cells exists is still an unsolved question. In this connection it is worthwhile to mention that Kolmer (1927) described free nerve terminals distributed in the olfactory epithelium and considered them of trigeminal origin. Larsell (1918) thought that they derived from the "nervus terminalis" (see Le Gros Clark 1957).

Physiological evidences for a centrifugal control of the olfactory bulb have been accumulated in the past few years. Carreras *et al.* (1954) and Kerr and Hagbarth (1955) found that electrical faradization of various rhinencephalic areas (prepiriform cortex, cortical amygdaloid nucleus and olfactory tubercle) as well as high frequency stimulation of the anterior commissure depressed the spontaneous and the induced activity in the olfactory bulb. The latter authors considered that this influence was mediated by the centrifugal fibers which run in the anterior commissure. Since transection of commissural fibers resulted in an increase in amplitude of the induced waves recorded in the bulb, they concluded that the centrifugal system has a tonic inhibitory influence on the bulb. Carreras and Angeleri (1956) also observed a reduction in the amplitude of the induced waves by faradization of the prepiriform cortex (the effect was predominantly in the bulb contralateral to the stimulated areas), whereas a destruction of the same cortex produced an increase in amplitude of the induced waves. Carreras and Angeleri (1956) and Angeleri and Carreras (1956), moreover, presented evidence for a functional connection between prepiriform cortex and olfactory bulb. Faradization of the prepiriform area caused an after-discharge in the olfactory bulb. Both bulbs were affected, although the effect was predominantly contralateral. Local application of strychnine and acetylcholine in the prepiriform cortex evoked also synchronized activity in the bulbs. Application of atropine, instead, blocking the activity of the prepiriform cortex produced a release phenomenon on the contralateral bulb where the induced waves increased by 50–60 %. The effect was present, although less evident, in the ipsilateral bulb. Some of the results obtained by electrical stimulation of rhinencephalic areas of the brain have to be revised on the basis of experimental evidence for a widespread process of "recurrent inhibition" found in the olfactory bulb by Green *et al.* (1962) and by Von Baumgarten *et al.* (1962a). Antidromic stimulation of mitral and tufted cell axons has been shown to inhibit the spontaneous discharge of the majority of olfactory bulb neurons. The same phenomenon could account for part of the results reported above. This mechanism, however, cannot be invoked for the experiments where drugs were topically applied nor for the cases in which an increase in amplitude of