A STUDY OF THE MECHANISMS MEDIATING THE VAGAL RESPIRATORY REFLEXES

A Thesis

Presented to

the University of Manitoba

In Partial Fulfillment

of the requirements for the Degree

Master of Science

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by

Edwin Frank Brachman, B.A.

May, 1949.

ACKNOWLEDGEMENT

I wish to express my appreciation to Dr. H.V. Rice, who directed this work, for his unfailing interest and for many valuable suggestions. I am also very much indebted to other members of the Department of Physiology for their kind co-operation at all times.

TABLE OF CONTENTS

CHAPTER PAGE

CHAPTER PAGE

LIST OF TABLES

LIST OF TABLES
(continued).

LIST OF FIGURES

CHAPTER I

INTRODUCTION.

A. Statement of Problem

This particular work centers around an attempt to relate different consistent respiratory effects that have been observed with different frequencies of stimulus applied to the central stump of the vagus nerve to a neurohumoral concept. Rice and Joy (1947) have postulated that the acceleratory or inhibitory effects obtained with appropriate stimuli may be attributable to the extent or degree of a central state dependent on one group of sensory fibres mediating afferent impulses directed centrally. In the light of the fact that different drugs, among which is acetylcholine, have been observed to have varying biological effects, stimulatory or depressor, depending upon their concentration, the possibility has been suggested by Rice and Joy in their concentration hypothesis that the central picture may be one analagous to this phenomenon, the degree of the central state being comparable with, and moreover, conceivable directly based on a build-up, the extent of which may be related to the sum total effect of various frequencies of impinging stimuli.

B. Importance of the Study

The entire picture of respiratory control by the nervous system and the method by which this is facilitated has been investigated widely. Indications are that while the general mechanism leading to pulmonary aeration of the circulating blood and subsequent oxygenation of the tissue appears to be understood, the finer details, on the other hand, concerning the integration into the overall pattern of all the impulses originating in divergent parts of the body is far from being completely agreed upon. The areas in the central nervous system known to be connected with respiration, peripheral nerve endings in various parts of the body and the combination of the whole has been a study that has gained impetus with the classical experiments of Hering and Breuer around 1868 when the importance of the proprioceptive impulses was examined and explanations advanced.

CHAPTER II

REVIEW OF THE LITERATURE

A. Extent of the Review

An investigation of vagal respiratory reflexes must, of necessity, entail an examination of other respiratory controls, central and peripheral. Reasons for this are:

1. To get an overall view of generally accepted concepts.
2. In the light of these established views, to assess data concerning which there is considerable dispute and with regard to which new problems are continually springing up to demand an explanation. A great deal of the problem resolves itself around the proper placing of emphasis whether on chemical stimuli, originating as far as is known in the chemoreceptors of certain well defined areas of the vascular system; or on impulses from the stretch receptors in the lungs; or on an inherent automaticity that is claimed by many workers as being evident in connection with the respiratory centre.

In addition, the actual mechanism of nervous transmission is a factor that is intimately bound up in a consideration of the control of respiratory action.

B. The Respiratory System

1. The Central Mechanism

(a) Location and anatomical relationship of constituent Parts

Early workers have established the presence of a respiratory centre in the brain. The classical experiments of Markwald (1887) and Lumsden employing transsection (1923), form the basis of our knowledge of its location. Markwald reached the following conclusions as a result of his numerous observations:

(1) That the centres of respiration are situated in the medulla oblongata and are in close connection with the origins of the vagi,

(2) The respiratory centres in the medulla oblongata are automatically active as well as excitable by reflex action,

(3) The automatically active centre can only liberate respiratory spasms, but no regular rhythmic respiratory movements,

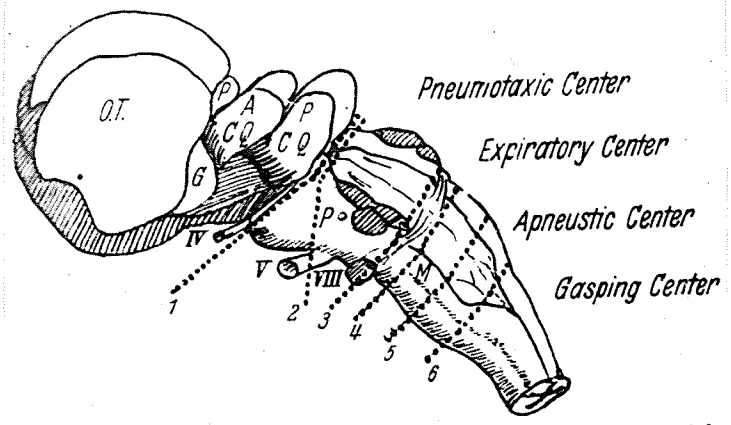
(4) Normal rhythmic respiration is a reflex act, mainly liberated by the vagi.

(5) The vagi constantly stimulate; they possess tonus and are sufficient to serve as the only active regulators of respiration. During absolute rest of the animal organism, they probably act alone.

(6) Next to the vagi, the upper brain tracts are of great importance for the liberation of regular rhythmic respiration. They are capable of replacing the non-activity of the vagi. During sleep, during hibernation, or after certain narcotics, the reflexes from the upper tracts on the respiratory centre often remain alive. The great difference between the individual tracts, lies in this -- that while the vagi are in constant stimulation and act continuously on the respiratory centre possessing tonus, the upper tracts have only a secondary influence on respiration. From the brain flow all voluntary impulses of respiration, all emotional responses, all activity resulting from sensory impressions, and stimuli which are the result of mental actions. These all modify respiration.

(7) There are no true respiratory centres above the primary centres in the medulla nor are there true respiratory centres in the cord.

Markwald concluded, on the basis of his numerous observations, that the centres of respiration are to be found in the medulla oblongata, in close relation with the origin of the vagi. Results of Lumsden's work have been considered by some as identifying four distinct respiratory centres:



O.T.- optic thalamus
P - pineal body
G - geniculate body
ACQ - anterior corpora quadrigemina
PCQ - posterior corpora quadrigemina
P - pons
M - medulla

Figure 1

Fig. 99. LUMSDENS respiratory centers. [LUMSDEN: J. of Physiol. 58, 81 (1923).]

(a) a gasping centre -- situated just above the apex of the calamus scriptorius and believed to be a passive relic of primitive respiration,

(b) an apneustic centre -- at the level of the striae accousticae-which is regulated by a pneumotaxic and expiratory centres, absence of this control resulting in prolonged inspiratory spasms,

(c) a pneumotaxic centre -- located in the upper pons, functioning as a periodic interrupter of the apneustic centre to produce the frequency and depth of normal breathing,

(d) an expiratory centre, the location of which has been determined as lying between the gasping and apneustic centre. During the expiratory phase of respiration this centre is considered to be a weak partner to the pneumotaxic centre's interruption of apneusis by the initiation of expiration. Lumsden has viewed the function of the expiratory centre as being largely passive, apneustic interruption being primarily a function of the pneumotaxic centre. Criticism of this view, as to the relative functions of Lumsden's respiratory components has been directed by some research workers, notably Gesell, who consider this interpretation to be unnecessarily complex when a relatively simple concept of a balance between two interacting half centres, inspiratory and expiratory, would appear to account for observed respiratory phenomena.

Investigations conducted in recent years by Pitts, Magoun and Ranson (1939), Gesell (1940), Pitts (1942) and Wyss (1943), have confirmed earlier work. Respiration is not significantly altered by transection of the brain at any level anterior to the upper border of the pons. Cutting through the lower border of the medulla oblongata results in complete cessation of respiration. Between these two levels, sectioning results in various marked respiratory disorders due to the presence there of the respiratory centre.

More recent work appears to have established that this respiratory centre is a composite of, first, an inspiratory, and secondly, an expiratory centre: Pitts, Magoun and Ranson (1939) define the inspiratory portion in the cat as overlying the upper (cephalic) four-fifths of the inferior olive, the expiratory half being situated dorsally and slightly anterior to the cephalic end of the inspiratory centre. Finlay has, in a human patient, described a brain lesion at a position corresponding to the cat's inspiratory centre which resulted in respiratory failure, indicating the likelihood of analagous positions in cat and man. However, Wyss and Croisier (1943) in their studies involving destruction of the dorsal portions of the

medial and lateral reticular formations of one side of the medulla by thermocoagulation, found the "inspiratory" effect of low frequency stimulation of the vagus trunk was completely absent, while the "expiratory" effect (high frequency stimulation of the vagus trunk) remained unimpaired. These investigators interpreted this to indicate a localization of the inspiratory centre dorsal to the expiratory centre in the medulla, the reverse of that postulated by Pitts, Magoun and Ranson. Wyss and Croisier appear to have little support from other investigators. An explanation of their results may lie in a segregation of functionally similar intrabulbar vagus afferent pathways in such a way that inflicted lesions could conceivably destroy all of one type while leaving others wholly or partially intact. A third view is represented in the work of Gesell, Bricker, and Magee (1936) whose results appear to indicate diffuse intermixing of the expiratory and inspiratory neurones within the same region. Brookhart (1940), on the other hand, working on dogs, does not believe a special expiratory centre exists but says neurones connected to the antagonistic respiratory muscles are scattered throughout the reticular formation.

It has been suggested that the variety of responses obtained by different workers might be due to stimulation in one case directly upon the cell body and, in the other, by direct action upon either dendrites or axons. Extensive work has been done by Comroe (1943) employing both chemical and electrical stimuli in the localization of each half centre.

It appears as if one or all of the views may be partly correct. The extreme difficulty of a solution to this problem is to be emphasized. The very fact that sensory nerve stimulation results in either inspiration or expiration would seem to show the inadequacy of any arbitrary judgment resulting from equivalent responses on central stimulation. The possibility exists that while, say expiration for instance, is the result of central stimulation, nevertheless, inspiratory neurones may have been stimulated. Support for this may be obtained in the fact that expiration as a net result has been obtained with mixed expiratory and inspiratory stimulation of sensory nerves. The problem may resolve itself around a statement made by Markwald:

> "the centre can only be electrically stimulated in the same way as if the stimuli came from the centripetal nerves.".

About the anatomical relationship of the constituent portions of the respiratory centre, it can thus be seen that unanimity does not exist.

In summary, points about which there has been a general agreement among physiologists are:

1. That primary inspiratory and expiratory neurones are located in the medulla.
2. That they are scattered diffusely in the reticular formations parts of the medulla.
3. That they are confined within definite regions of the latter.

Beyond this, there are many aspects of the organization of the respiratory system concerning which viewpoints differ at the present time.

Aside from the respiratory centre proper, the brain stem inhibitory system (Lumsden's pneumotaxic centre) consists of a number of reflex connections, the function of which is to translate apneustic movements originating in the lower inspiratory (apneustic) centre into rhythmical respiration. Stella, using transection, and Pitts, electrolytic lesions, both found that it lies bilaterally in the ventral part of the tegmentum in the upper few millimetres of the pons near the midline on each side. Another problem is the relation of vagal function to pneumotaxic function as concerning the apneustic centre. Stella and Pitts, Magoun and Ranson, working separately found that, in contrast to Lumsden's