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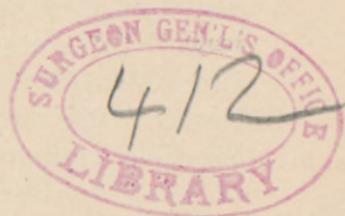
Some Remarks on my Hypothesis of the Self-Regulation of Respiration, and Dr. Cowl's Discussion of it.

BY
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SOME REMARKS ON MY HYPOTHESIS OF
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BY S. J. MELTZER, M. D.

IN No. 614 of this Journal, for September 6, 1890, Dr. W. Y. Cowl published an article entitled *The Factors of the Respiratory Rhythm and the Regulation of Respiration*. In this paper the author criticises adversely my theory of the self-regulation of respiration, upon which criticism I wish to make the following remarks:

In my article * on *Self-regulation of Respiration* I mentioned the experience I had had while stimulating the vagi with strong electrical currents. During the stimulation the respiration was arrested in the expiratory phase, the inspiratory muscles being relaxed; but after interrupting the current, the arrest changed into an inspiratory phase, a tetanic contraction of the diaphragm. H. Head † reports a similar experience which he had had with prolonged insufflation of the lungs; after cessation of the insufflation, the expiratory standstill changes into an inspiratory tetanus.

* *The New York Medical Journal* for January 18, 1890.

† Head, *On the Regulation of Respiration*, *Journal of Physiology*, vol. x, 1889.

nus. This phenomenon is termed by Head "negative after-effect." Dr. Cowl asks for evidence to show that this inspiratory after-effect is not dyspnœa from non-aeration of the blood coursing through the respiratory center during the preceding expiratory standstill. This is the evidence I am able to furnish:

1. The intensity and duration of the inspiratory tetanus are proportionally increased with the intensity of the stimulation, and not with its duration, or with that of the expiratory standstill. This shows clearly that the inspiratory tetanus is a primary effect of the stimulation, and not a secondary result from dyspnœa.

2. Dyspnœa from the arrest of breathing in the expiratory phase never effects an inspiratory standstill. If an expiratory standstill is brought about by the stimulation of the superior laryngeal nerve, no inspiratory tetanus is ever observed to follow such a standstill. Furthermore, an expiratory standstill can be effected in some rabbits by stimulating the vagus trunk itself with moderate electrical currents; but here the expiratory effect rather outlasts the stimulation, with no inspiratory after-effect, no matter how long the standstill has lasted.

Dr. Cowl further objects to the inference I am supposed to have drawn from my experiments on the trunk of the nerve, that the lungs themselves are likewise provided with inspiratory nerve fibers, and that these fibers exercise their function in ordinary breathing. On this point Dr. Cowl is mistaken: I did not draw any such conclusion from my experiments. The logical connection between my experiments and my hypothesis is as follows:

My experiments put me in a position to confirm the hypothesis that the vagus trunk contains two kinds of respiratory afferent nerves, which are antagonistic to each other in a manner resembling that of the antagonistic

nerves of the heart-beat—*i. e.*, that it contains one kind of nerves which inhibit the inspiration, and another kind which incite and augment it. I could further demonstrate the parallelism between these nerve fibers and the cardiac nerves in some particulars. For instance, the stimulation of the inhibitors of inspiration has only a short after-effect, as is the case with the inhibitory nerves of the heart, while the inspiratory nerves show a long after-effect, similar to the known long after-effect of the *nervus accelerans cordis*. Further, when both cardiac nerves, *vagus* and accelerator, are stimulated at the same time, we see during the stimulation the inhibitory effects alone influencing the heart-beat, and this is the case also with the respiratory nerves; strong stimulation of the *vagus* trunk produces constantly merely inhibition of inspiration—expiratory standstill. Now, if, after cessation of the simultaneous stimulation of the cardiac nerves, the long after-effect of the accelerating nerve appears fully developed, we should expect that a similar phenomenon might occur after the simultaneous stimulation of the respiratory nerves. In fact, after interrupting the strong current, I have observed that the expiratory standstill soon changed to an inspiratory tetanus; and what could this mean but that the expected phenomenon had occurred—*i. e.*, that the inspiratory nerves had been likewise stimulated, that their impulses had been concealed but not destroyed, and that, therefore, after the short expiratory after-effect died out, the long inspiratory after-effect appeared unrestrained and produced the inspiratory tetanus? Thus, as I believe, I gave a satisfactory explanation of the phenomenon of the negative after-effect in my experiments on the *vagus* trunk; but with this the direct conclusion from my experiments ends. As regards Head's "negative after-effect" after long insufflation of the lungs, I have, of course, applied to it the same explanation

which I have given of the similar phenomenon in my experiments. The question: Are the lungs provided with both kinds of nerves as they are found in the vagus trunk? I did not discuss at all. On this point I simply took the same view which Head himself holds, and which is shared by such eminent physiologists as Hering and many others.*

What I added is this: If the lungs are provided with two sets of nerves as they are found in the vagus trunk, which I have no reason to deny, then the same relations ought to prevail between the nerves of the lungs that are found in the vagus trunk, and consequently the negative after-effect following insufflation of the lungs may have the same meaning as that given to the similar phenomenon in the experiments with the trunk. I hold the same position in my hypothesis. I accepted the premises as given by Hering and Breuer, that the lungs are provided with two kinds of nerves, both of which are taking part in the reflex mechanism of the respiration; but, while Hering and Breuer assume that nerves of one kind are stimulated by expansion, and those of the other by the collapse of the lungs, I am of opinion that it is far more rational to assume that both kinds of nerves are always stimulated simultaneously by the same stimulus--the expansion of the lungs--and that the sequence of expiration and inspiration is due to the peculiar mutual relations of the antagonistic nerves (relations which are known to exist in the antagonistic system of the cardiac nerves and which have been found to exist among the antagonistic respiratory nerve fibers of the

* I may quote here an acknowledged authority, Foster, who says, in the latest (5th) edition of his standard text-book, p. 595: "And, assuming on the strength of analogy the existence in the vagus of two sets of fibers, we may say that expansion stimulates the endings of the fibers which inhibit inspiration and concurrently tend to augment expiration, while collapse stimulates the fibers which inhibit expiration and augment inspiration."

vagus trunk). In other words, when both kinds of nerves are stimulated simultaneously, the inhibitory effect prevails during the stimulation, but after its cessation the long inspiratory after-effect comes into play.

It is obvious that whoever undertakes to criticise my theory of self-regulation, whether adversely or favorably, is bound to discuss my share in it—*i. e.*, the tenableness of the application of the relations existing between the cardiac nerves to the antagonism of the respiratory nerves. I am sorry that Dr. Cowl has not even touched this point, and yet he says sharply that my new theory of respiratory rhythm deserves further attention, “chiefly because of a disregard therein of a mass of facts that show a central origin for inspiration.” As I have to share this reproach with quite a number of physiological writers, it will be easier to bear it. There are some very prominent physiologists who consider it a disregard of facts to maintain that the inhibition of the inspiration is not of a central origin, still on this point I have the pleasure to be on the same side with my critic, who declares himself to be in favor of Gad’s theory of respiration. But let us see the “mass of facts” which, according to Dr. Cowl, I (with many others) have disregarded. Two points are enumerated against my theory in Dr. Cowl’s paper—the relation of the blood to respiration, and Gad’s experiment upon which his theory of respiration is based. Concerning the first point, Dr. Cowl cites a number of authors who have experimentally demonstrated the high sensitiveness of the respiratory center to changes of the constituents of the blood. While I admit the perfect correctness of these facts, I do not see how they could affect my theory. Does Dr. Cowl know of any experiment which shows that the blood, and that alone, is the exciting cause of respiration? On the contrary, there are authors who, while not denying the influence of the blood on respira-

tion, do not consider the blood a necessary factor for the continuance of respiration. A. W. Volkmann* observed the continuance of respiration in a kitten forty minutes after excluding the circulation, and M. Marckwald† puts it up as a thesis (the 17th) that the normal excitation of the respiratory center is independent of the incentives of the blood. As to myself, I am not a party to either side in this question, at least so far as my hypothesis is concerned, the necessary premise to my theory being only the generally admitted assumption that the afferent nerves coming from the lungs normally affect the respiration; and I attempted to establish a hypothesis on the mode of their peripheral stimulations, leaving it an open question whether there were indeed any other causes for the respiration besides the reflex acts. But, aside from my hypothesis, I may say this: In all the discussions on the subject in question I miss the distinction between the significance of the blood as a *cause* and only as a favorable *condition* of respiration—a distinction which is sharply made in the relation of the blood to the heart-beat. There was a time when some physiologists—Haller, for instance—entertained the opinion that the venous blood was the cause of the rhythmic motion of the heart, and although in our days the importance of the blood and its constituents for the heart-beat has been studied and demonstrated (by C. Ludwig, H. Kroenecker, and their pupils), at all events more convincingly than in the experiments on the respiration, still at present the opinion is generally accepted that the blood is significant in the contraction of the heart only as an important condition and not as a cause. I do not mean to say that

* A. W. Volkmann, Ueber die Bewegung des Athmens. Müller's *Archiv*, 1841.

† Max Marckwald, Die Athembewegung und deren Innervation beim Kaninchen. *Zeitschrift für Biologie*, 1886, pp. 1-120.

this view should be adopted also in the doctrine of the respiratory mechanism, in which I admit the possibility that the blood, and more especially its carbonic-acid gas, may be one of the causes of the respiratory movements, but I wish to point out that such an assumption should not be made without good proof, the more so because the blood is of importance to the integrity and function of every organ in the body. This fact seems to demonstrate the value of the blood as a general nutritive rather than as a common stimulus for manifold different functions.

Concerning the experiments of Gad, Dr. Cowl says that they involve facts which are acknowledged to show the pulmonic incitation of inspiration. Gad observed that after dividing the vagi without stimulating them (Gad's freezing method) the inspirations become more predominant. This certainly shows that an inhibitory tonus is removed by cutting the vagi. Gad goes still further. He concludes that the vagi contain only inhibitory nerves, and that inspiration is of central origin exclusively. But this part of Gad's conclusions consists of mere admissible assumptions, not necessarily inferences following from his experiments. I could even use the experiment cited as a proof of my theory thus: On stimulating the inspiratory and inhibitory nerves simultaneously, the inhibitory effect prevails; consequently if there is any tonus from the nerves of the lungs it must be of an inhibitory nature; therefore we see a certain inhibitory influence disappearing after dividing the vagi. My explanation of the said experiment finds a perfect analogy in the cardiac nerves of the frog. According to some authors,* the frequency of the heart-beat is increased after division of the vagi. Should we with Gad conclude that

* Funke, Bidder, Rosenthal, and others. See Hermann's *Handbuch d. Physiol.*, Bd. iv, 1. Theil, p. 378.

the vagi contain only inhibitory nerves? We know now* that the vagi of the frog contain also augmenting nerve fibers. Every one explains the said increase by the well-established fact that the inhibitory tonus is the predominating one, just as I would explain the increase of the inspiration after dividing the vagi. But even leaving aside my explanation, why must it follow that the inspiration is of a central origin? We could assume, for instance, that the inspirations and expirations were generated in the respiratory center only by reflex acts from the lungs and from all other parts of the body; but while in the reflexes from the lungs the impulses for expiration are at least not overshadowed by the inspiratory impulses, the latter are predominating in the reflexes from the other parts of the body, or at least in some of them; therefore the predominance of the inspiration after cutting the vagi. I do not mean to defend this theory as my own; I merely wish to demonstrate that Gad's experiments admit of many other explanations than the one given by him; and Dr. Cowl certainly goes too far in considering the experiment in question as a fact against the assumption that the lungs are provided with inspiratory nerves. On the other hand, if we have no sure proof that inspiratory fibers are absent in the lungs, we may assume, with some degree of probability, that such nerves exist there in view of the positive fact that inspiratory nerve fibers are contained in the trunk of the vagus. For what other purpose could these inspiratory nerves be contained in the trunk? As to the expiratory nerves, we might believe that they were for the act of vomiting; but of what use could the inspiratory nerves be if not to supply the lungs?

The main objection to an exclusive reflex theory of res-

* R. Heidenhain, Untersuchung über den Einfluss des Nv. Vagus auf die Herzthätigkeit. Pflüger's *Archiv f. d. ges. Physiologie*, 1882.

piration is that it ignores the fact that respiration continues after the division of the vagi. This objection has not yet been seriously discussed even by adherents of this theory. Though my own position is not affected by this objection, since my hypothesis does not necessarily exclude other factors for the regulation of respiration, I should like to introduce here briefly some points bearing upon the discussion of the above-mentioned objection. As I pointed out before, there are, besides the reflex from the lungs, many others from nearly all parts of the body, which exert an inspiratory as well as an expiratory influence on the respiratory center. No one denies that fact. Consequently, a vast source of respiratory impulses remains even after excluding the reflexes from the lungs. But while this latter reflex furnishes, in the expansion and collapse of the lungs, an explanatory factor for the alternation of inspiration and expiration, we lack a similar factor in the other respiratory reflexes from which we may expect that the impulses for inspiration and expiration are generated simultaneously. The question, therefore, is not as to where the impulses for respiration arise after the division of the vagi, but as to *what is the source of the alternation* of the respiratory movements? To this we could perhaps answer that the remainder of the reflexes might also possess certain qualitative differences between the inspiratory and expiratory afferent nerves, which could be construed in some way or other as explanatory factors for the continuance of the alternate breathing after dividing the vagi. For instance, smaller degrees of stimulation excite the inspiratory and stronger degrees the expiratory nerves (Langendorff*); or the inspiratory nerves become exhausted earlier than the

* S. Rosenthal, Hermann's *Handb. d. Physiol.*, Bd. iv, 2. Theil, p. 252.

expiratory nerves (Burkart*); and there are many other ways which still remain to be studied.

But I do not intend to follow out these vague speculations any further. I rather wish to bring forward another reflection which, it seems to me, deserves serious consideration. I mean the introduction into our discussion of the factors of *repetition* and *inheritance*. Suppose the respiratory center were not automatic and received impulses to its working by reflex channels from the whole body, especially from the lungs. The impulses coming from all parts of the body are uninterruptedly simultaneous for inspiration and expiration; but the reflexes from the lungs, by virtue of the steady sequence of the expansion and collapse of this organ, are not simultaneous, but alternately inspiratory and expiratory. May we not expect that such a center, after being life-long influenced by steadily acting reflexes to a prompt alternate working, will acquire, first, a high degree of sensitiveness so as to respond promptly and specifically to the smallest stimuli from whatever quarter they may come; second, a tendency to respond alternately with inspirations and expirations, even on simultaneously received impulses? (This would be the case still more if there were any qualitative differences between the two kinds of afferent nerves tending to their alternate working.) We may expect, furthermore, that such acquired qualities of the respiratory center would be transmitted to the descendants, and that in the course of many generations, by the prompt repetition during the whole life of each generation and by transmission from generation to generation, all the newly acquired fineness and promptness of the qualities mentioned ought to constitute an inseparable part of the respiratory center. In this sense we may speak of an automatism of the center. But we should un-

* Burkart, Pflüger's *Archiv f. d. ges. Physiol.*, Bd. xvi, p. 427,

derstand clearly that the center itself does not generate impulses; the impulses are always transmitted by some reflex from a peripheral point; the center supplies merely the high sensitiveness and the readiness to respond alternately to simultaneous excitation by inspiration and expiration. Now, we may try to answer the above-mentioned objection to the pure reflex theory of respiration in the following way: The impulses for inspiration and expiration are normally transmitted to the respiratory center by reflexes from all parts of the body; the alternation of inspiration and expiration is normally induced and maintained by the sequence of expansion and collapse of the lungs. But, by virtue of repetition and inheritance, the respiratory center possesses an automatic readiness to respond with alternation to simultaneous reflexes for inspiration and expiration which enables the center to continue a rhythmic breathing, even after exclusion of the main factor for the rhythmic respiration—the lungs.

In conclusion, I wish to add that I am glad to be in full accord with Dr. Cowl in the high appreciation of the invaluable services rendered to the physiology of respiration by Professor Gad, whose investigations served me partly as a basis for my hypothesis; but this latter should be judged on its own merit or demerit, and not by the fact that it differs from the opinion of acknowledged authorities.



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