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Respiratory Neurones Discharge Patterns During the Times of Phase Transition

Maaike De Vries*

Department of Epidemiology, University Medical Center Groningen, University of Groningen,Germany

Abstract

The mechanisms of the transitions between the respiratory phases have been investigated by applying electrical stimulation to sites in the rostral lateral pons. This general region is considered to contain the pneumotaxic centre, since lesions in the region produce apneustic respiration. Further support for this hypothesis was provided by the observation that respiration- synchronous neurones are found in the region.

Keywords: Stimulus-evoked; Respiratory periodicity; Powerful effects; Phrenic discharge; Inspiratory-inhibitory; Pontine region

Introduction

When inspiratory-facilitator points were stimulated during the inspiratory phase, there resulted an increase of phrenic discharge, with waves of increased activity locked to the individual stimuli. The magnitude of these evoked responses was dependent on time of stimulus delivery which compares the summed phrenic responses to stimulus trains delivered at different times during the inspiratory phase. It can be seen that the later the stimulus train was applied, the larger was the evoked increase of phrenic discharge, as shown by the increased amplitude of the individual stimulus-evoked waves [1]. Thus, as inspiration progresses it is easier to excite inspiratory neurones, an effect which is presumably related to the gradual increase of spontaneous discharge level. A comparable phenomenon is observed for expiratory facilitation, as the expiratory phase progresses, stimulation at expiratory-facilitator points becomes more effective in lengthening the phase [2]. The importance of the region for respiratory periodicity was further confirmed in the present study by the finding that electrical stimulation produced powerful respiratory effects, such as short-latency depression and excitation of phrenic discharge, as well as switching from one respiratory phase to the other.

Methodology

Two major constellations of effects, elicited at different sites, were, inspiratory-facilitator, increase of phrenic discharge, switching from the expiratory to the inspiratory phase; and expiratory-facilitator, reduction of phrenic discharge, switching from the inspiratory to the expiratory phase [3]. The existence of intimate relations between rostral lateral pontine systems and more caudal systems is shown by the fact that stimulation in these regions during the inspiratory phase produces a short-latency depression of phrenic discharge. Thus, there are paucisynaptic descending inhibitory pathways to medullary and/or spinal inspiratory neurones. However, it is unlikely that this response is simply due to stimulation of descending fibres, since it was obtained from many sites in the lateral pons. In particular, it was obtained from both inspiratory-facilitator and inspiratory-inhibitory sites, i.e. from sites where continued stimulation led either to continued augmentation of phrenic discharge, or to complete cessation of phrenic discharge and switching to the expiratory phase. Therefore, it is reasonable to suppose that stimulation in these regions is activating portions of a complex network which has a fast outflow pathway [4]. Further support for the idea that the pneumotaxic centre is a complex integrating system is provided by the observations [5]. The phrenic response to a stimulus train delivered during the inspiratory phase consisted of complex alternations of excitation and depression. The form of these complex responses was similar for stimulation at both inspiratory-excitatory and inspiratory-inhibitory points as shown in (Figure 1). The long-term nature of the response only became apparent after many stimuli in a train had been delivered, and moreover was related to anatomical locus. Thus, temporal summation is important in the long-term response to stimulation. These observations suggest that the active regions contain complex networks whose functions cannot be specified as simply inspiratory-facilitatory or inspiratory-inhibitory [6]. Therefore, one should not expect any simple concordance between effects of lesions and of stimulation; for example, the apparent contradiction that lesions in the dorsolateral rostral pontine region produce apneustic respiration, while stimulation in the same region may produce maintained inspiration, only means that we are not

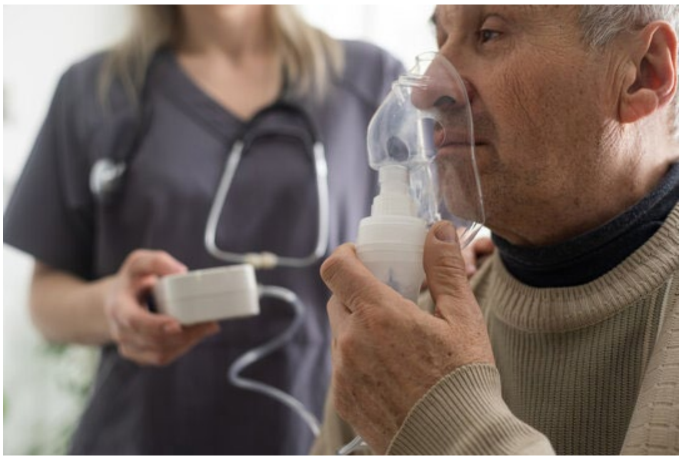

Figure 1: Complex responses at both inspiratory-excitatory and inspiratory-inhibitory points.

***Corresponding author:** Maaike De Vries, Department of Epidemiology, University Medical Center Groningen, University of Groningen, the Netherlands, Germany, E-mail: Maaike@gmail.com

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dealing with a simple efferent system. The most important observations in the present study concern the ability to produce switching from one respiratory phase to the other by use of relatively short stimulus trains.

Discussion

The two types of switching obtained from different stimulation sites premature initiation of the inspiratory phase by stimulation during the expiratory phase and premature initiation of the expiratory phase by stimulation during the inspiratory phase resembled each other in several features, thus suggesting that similar mechanisms are operative in each type of phase transition [7]. The nature of the evoked respiratory effect was a non-linear function of stimulus strength: a slight increase of stimulus efficacy altered the response from a relatively minor effect to the major effect of initiating a phase transition. This observation indicates the existence of critical levels of excitation and inhibition for switching of activity [8]. Under stimulus conditions which were near threshold for phase- switching, there was uncertainty of the response: some individual stimulus presentations produced phase-switching, while others did not. This response uncertainty is another expression of the discontinuity of the stimulus-response curve, since under near-threshold conditions small statistical variations in the system could have a major effect on the direction of the response [9]. The ease of phase-switching depended on time of stimulus delivery, as stimuli were delivered later in the expiratory or inspiratory phases; there was progressive reduction of the threshold for initiation of the inspiratory or expiratory phase, respectively. This observation indicates the existence of continuous excitability changes within each respiratory phase [10]. It is of interest that similar phase-switching phenomena can be produced by stimulation of afferent nerves, such as the vagus and the superior laryngeal. Apparently then, various types of input can act on the basic mechanisms of transition between the respiratory phases as shown in (Figure 2). The characteristics of the phenomenon of phase-switching by electrical stimulation can be explained in the context of a general hypothesis of the origin of respiratory periodicity [11]. Throughout the respiratory cycle, there is continuous change of activity in different populations of respiratory neurones, so that through excitatory and inhibitory connexions sequential activation and deactivation of different groups of neurones are produced. At critical levels of activity, triggering actions are exerted to produce mass inhibition of some groups, together with mass excitation of others, as in the transitions between the respiratory phases. Thus, the relative sharpness of threshold for phase-switching by stimulation is due to the necessity of raising activity in triggering systems to critical levels. Further, the reduction of threshold for phase switching as stimulation is applied later in the phase is due to the superposition of stimulus-evoked activity on the gradually increasing spontaneous activity of triggering systems, so that at later times in the phase less excitation is needed to reach critical triggering levels [12]. These ideas are now applied to analysis of the transition from the expiratory to the inspiratory phase. The progressive decrease in the threshold for switching to the inspiratory phase as stimulus trains are delivered later in the expiratory phase indicates that there is gradual change of activity in systems promoting the onset of the inspiratory phase. Further, there must be critical changes of such activity just before the onset of the phase. The existence of such inspiratory-initiatory processes in the late expiratory phase is supported by the following additional observations [13]. Depolarization of thoracic inspiratory moto-neurones, and hyperpolarization of thoracic expiratory moto-neurones, may start before the onset of diaphragmatic discharge. In the present study, the premature initiation of the inspiratory phase by stimulation could occur after a considerable delay from the end of a stimulus train, indicating the existence of intervening processes. Such intervening processes have been directly observed; in a recent paper it was reported that when the dorsolateral pontine inspiratory-facilitator region is stimulated, increased discharge of some lower pontine respiratory neurones occurs during the time between start of stimulation and onset of the prematurely elicited inspiratory phase. The observations in the present study on switching from the expiratory to the inspiratory phase, as well as the related observations cited above, tend to support the previous suggestion of the author that pontine expiratory-inspiratory neurones have inspiratory-initiatory functions [14]. The observed pattern of discharge of such neurones is consistent with such functions. In the light of these observations on inspiration-promoting processes which occur during the expiratory phase, another observation seems paradoxical: as the expiratory phase progresses, there is an increase of excitability in expiratory-facilitator systems, indicated by the fact that stimulus-evoked lengthening of expiratory phase duration is increased as stimulation is applied later in the phase. Moreover, there is additional evidence for the existence of such augmenting expiratory facilitation. The same relation between expiratory phase lengthening and stimulus timing has been observed for afferent stimulation. In thoracic expiratory moto-neurones, there is increasing depolarization as the expiratory phase progresses. As might be expected from the existence of the preceding phenomenon, thoracic and abdominal expiratory muscle units have a pattern of augmenting discharge. In addition, many medullary expiratory neurones have such augmenting discharge patterns. Therefore, the conclusion is inescapable that during the expiratory phase two opposing processes occur simultaneously, increasing inspiration-promoting facilitation and increasing expiratory facilitation. The balance between these processes may contribute to the sharpness of threshold for initiation of the inspiratory phase and help to determine the duration of the expiratory phase. Another important observation is that, in an inspiratory phase which has been prematurely initiated by pontine stimulation, the pattern of phrenic discharge resembles that in a normally occurring inspiratory phase, provided that no further stimulation is delivered.

Figure 2: Input on basic mechanisms between the respiratory phases.

Conclusion

Thus, the characteristics of the inspiratory burst seem to be rather rigidly set, indicating tight organization of connexions between inspiratory neurones. In contrast, the characteristics of the expiratory phase seem to be more flexibly programmed, as shown by the fact that expiratory phase duration is determined by the activity level of the preceding inspiratory discharge. The analysis of the processes promoting the transition from inspiratory to expiratory phase is similar to that already presented for the expiratory-inspiratory phase transition. The fact that it is easier to terminate the inspiratory phase as stimulation is applied later in the phase indicates that inspiratory-inhibitory processes are augmenting as inspiration progresses.

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Conflict of Interest

None

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