

# Respiratory Responses Evoked by Switching Phases

## Nicolini Antonello\*

Department of Pulmonology, Physiotherapy School, University of Genoa, United Kingdom

## Abstract

Phrenic discharge was used as the indicator of the central respiratory cycle, with the inspiratory and expiratory phases, respectively, being specified as the times of phrenic activity and of phrenic silence. The effects of stimulation were labelled operationally as inspiratory-facilitator or expiratory-facilitator on the basis of changes elicited by stimulation during both the inspiratory and expiratory phases. An example of each type of effect, elicited by a relatively long train of high-frequency stimulation.

**Keywords:** Inspiratory phase; Phrenic signal; Phrenic waves; Expiratory-facilitator; Stimulus efficacy; Computer summation

# Introduction

The effects of stimulation at an inspiratory-facilitator point in the dorsolateral pons were, shortening of the expiratory phase during which the stimulus train was started, increased phrenic discharge in subsequent inspiratory phases, as shown by the increased slope and peak amplitude of the integrated phrenic signal and shortened expiratory phases throughout the period of stimulation. The sequence of effects was typical of the many electrode explorations made in the rostral lateral pons. With high-frequency stimulation and stimulus pulse durations of 0.1-0 3 m-sec, the threshold currents for switching of the respiratory phases were in the range 0 1-0 3 mA [1]. Prominent inspiratory-facilitator effects were obtained dorsally in the region of the nucleus Para brachialis, more ventrally, there was a zone of transition; and still more ventrally, prominent expiratory-facilitator effects were obtained from the region medial to the nucleus of the lateral lemniscuses [2]. In more medial electrode tracks at the same level of the pons, similar sequences of effects were obtained, but the effects were always of lesser magnitude than those obtained from the more lateral regions. A detailed analysis of the changes in phrenic discharge produced by stimulation during the inspiratory phase reveals the complexity of the responses [3]. A comparison is made of the responses to stimulus trains starting in the middle of the inspiratory phase and delivered at an inspiratory-facilitator point and an expiratory-facilitator point in the same cat. As seen in the traces of the integrated phrenic signal on a slow time base, stimulation at the dorsolateral inspiratoryfacilitator point caused an increase of phrenic discharge, followed by termination of the inspiratory phase at an earlier time than occurred without stimulation; while stimulation at the ventrolateral expiratoryfacilitator point produced a reduction of phrenic discharge and an even earlier termination of the phase. If the computer-summed responses from the two points are compared on faster time bases, the following effects are seen [4].

# Methodology

The earliest change of activity was a reduction of phrenic discharge with a latency of about 5 m-sec from the first shock. This latency was about the same for both sites of stimulation [5]. Thereafter, for the responses from both sites, there was a tendency to synchronization of the evoked phrenic waves with individual stimuli. The degree of synchronization was greatest when stimulus frequency was close to the frequency of spontaneous phrenic oscillation. In the response elicited from the inspiratory-facilitator point, the waves tended to augment with each successive stimulus. A highly interesting observation was the brief latency of the initial depression of phrenic discharge; in different cats, this latency varied from 4 to 7 msec [6]. Furthermore, in each cat similar latencies were obtained from stimulation at many points in the rostral lateral pons; in particular, the latency for the initial depression was about the same for both inspiratory-facilitator and inspiratoryinhibitory points [7]. The distinction between inspiratory-facilitator and expiratory-facilitator responses was defined operationally in terms of increase or decrease of phrenic discharge, as well as decrease or increase of expiratory phase duration, respectively as shown in (Figure 1). This distinction was less obvious when the initial portion of the phrenic response was examined [8]. In some cases, it was difficult to distinguish between inspiratory-facilitator and inspiratoryinhibitory points on the basis of the initial phrenic response; the difference only became clear during later portions of a stimulus train, when marked augmentation or reduction, respectively, of phrenic discharge occurred. However, in most cases the initial reduction of activity was more prominent on stimulation of expiratory-facilitator than of inspiratory-facilitator points [9]. When inspiratory-facilitator



Figure 1: Inspiratory and expiratory responses of phrenic discharge.

\*Corresponding author: Nicolini Antonello, Department of Pulmonology, Physiotherapy School, University of Genoa, United Kingdom, E-mail: Nicolini@ gmail.com

Received: 27-Jun-2023, Manuscript No. JRM-23-108411; Editor assigned: 30-Jun-2023, PreQC No. JRM-23-108411(PQ); Reviewed: 14-Jul-2023, QC No. JRM-23-108411; Revised: 19-Jul-2023, Manuscript No. JRM-23-108411 (R); Published: 26-Jul-2023, DOI: 10.4172/jrm.1000173

Citation: Antonello N (2023) Respiratory Responses Evoked by Switching Phases. J Respir Med 5: 173.

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Figure 2: Phrenic discharge maintained at a constant level.

points were stimulated, the increase of phrenic discharge was usually associated with shortening of the inspiratory phase, although the degree of shortening was less than that for inspiratory-inhibitory points.

#### Discussion

Less commonly, the initial increase of phrenic discharge was maintained at a constant level for times up to several hundred m-sec, so that the duration of the inspiratory phase was lengthened as shown in (Figure 2). The latter effect usually occurred in cats where the spontaneous inspiratory burst had an apneustic tendency, i.e. where there was maintained phrenic discharge following the initial period of augmenting discharge. The general experimental procedure used in this study was to locate points in the lateral pons where stimulation produced marked inspiratory-facilitator or expiratory-facilitator effects, and then to study the dependence of these phenomena on different parameters and patterns of stimulation [10]. Special attention was paid to the dependence of responses on time of stimulation in the respiratory cycle. When short stimulus trains of suitable properties were applied to inspiratory-facilitator points during the expiratory phase, the result was switching from the expiratory to the inspiratory phase, i.e. the onset of a complete inspiratory phase [11]. A striking feature of the switching response was its relatively sharp threshold as a function of stimulus conditions, stimulation produced either, a moderate shortening of the expiratory phase or a small phrenic burst, or with increased stimulus efficacy, a complete inspiratory burst similar to the normally occurring burst. Another interesting effect is that, at a particular current strength near threshold, some individual trains produced switching to the next phase while others produced only a moderate shortening of the phase. This effect is shown more systematically in a series from another cat, where test trains were delivered at each of several current strengths, and starting at the same delay from the start of the expiratory phase. At lower current strengths, each train had little or no effect; at intermediate strengths, some individual trains had little effect while others produced switching to the inspiratory phase, finally, at each of the highest current strengths, all trains produced switching to the inspiratory phase [12]. Once the threshold for switching from the expiratory to the inspiratory phase had been reached, further increase of stimulus efficacy resulted in decrease of the latency from start of the stimulus train to start of the inspiratory phase. This latency decrease also occurred as a stimulus train with particular parameters was delivered later in the expiratory phase. The graph shows the effects of stimulus trains of given parameters delivered at different times during the expiratory phase. The trains delivered in

the first half of the expiratory phase caused moderate shortening of the phase, which was about the same for each time of stimulus delivery; while those starting 2\*2 see or more after the start of the phase caused drastic shortening of the phase and switching to the inspiratory phase [13]. The sharpness of threshold for the production of the switching response is indicated by the discontinuity in the curve. Beyond this 2-2 see delay, as the trains were delivered later, the median latency from train onset to onset of the inspiratory phase decreased progressively. Additional features of this decrease of latency with later stimulus delivery can be seen in the traces of summed phrenic potentials [14]. The stimulus-evoked inspiratory phase can start even after the stimulus train has ended, indicating that an effective switching process had been set into motion by the earlier stimuli of the train. Further, with later stimulus delivery, the dispersion of the onset of individual inspiratory phases is reduced, as indicated by, the sharp peak at the onset of the summed phrenic burst activity and the small range of the times of occurrence of the trigger. Most commonly, stimulus trains which were sub threshold for switching to the inspiratory phase produced either no discernible phrenic activity; or small phrenic bursts, barely above noise level, which could only be made apparent by computer summation of activity evoked by 50-100 stimulus presentations. These bursts, which were produced only when stimuli were delivered in the early expiratory phase, had latencies of 30-60 msec. However, in a few cases, stimulus trains delivered to inspiratory- facilitator points during the early expiratory phase produced phrenic bursts of appreciable size which, however, did not lead to a complete inspiratory phase.

#### Acknowledgement

None

# **Conflict of Interest**

None

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