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Breathing pattern in humans: diversity and individuality

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Abstract

In adult awake human subjects at rest, there exists a diversity in the breathing pattern not only in terms of tidal volume and inspiratory and expiratory duration and derived variables (TTOT, VT/TI and TI/TTOT) but also in the airflow profile. Besides this diversity, in every recording of ventilation at rest in steady-state condition breath-to-breath fluctuations are observed in ventilatory variables. This variability is non random and may be explained either by a central neural mechanism or by instability in the chemical feedback loops. Beyond this variability, each individual appears to select one particular pattern among the infinite number of possible combination of ventilatory variables and airflow profile. This one particular pattern appears to be a relatively stable characteristic of an adult individual being reproducible in several conditions and above all, after a long period of time. Consequences of this individuality of breathing pattern are discussed with regard to the selection of control subjects for a study and also per se: are there physiological situations where differences may be observed solely because of the differences in the pattern of breathing? © 2000 Elsevier Science B.V. All rights reserved.

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The objective of this article is an to attempt to review the concepts relating to the pattern of breathing in adult awake human subjects at rest. Indeed, changes in the rate and depth of breathing have been used as indicators of the regulatory processes during respiration in the state of health and disease before any research was undertaken to find the significance of the various components of the breathing pattern and the physiological relevance of the diversity and variability of these components.

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1. Diversity in the pattern of breathing: description and hypotheses

1.1. Breathing frequency

The earliest data available on spontaneous breathing frequency values are those of Quetelet (1842) on 300 subjects and of Hutchinson (1850) on 1714 adult subjects. These data appear to be the most extensive so far published and show the

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very wide frequency range (between 6 and 31 breaths per minute) observed in adults. In addition, they have the merit of being obtained by observation and thus not being altered by the use of any measuring device.

The large range of breathing frequencies observed in human subjects at rest led to a search to determine an optimal breathing frequency. Whichever the variable to be minimized, it appears that, at rest, a large range of frequencies fulfil the optimization criterion. Several studies have examined this problem, a documented analysis of which is given by Poon (1991).

1.2. Inspiratory and expiratory duration

The inspiratory and expiratory durations introduce an additional factor of diversity into the breathing pattern. For a given duration of respiratory cycle (T_{TOT}) there may be several combinations of inspiratory (T_I) and expiratory (T_E) times within, however, the constraint that T_I is less than T_E ($T_I < T_E$).

1.3. Tidal volume

The diversity in tidal volume was first described by Dejours et al. (1961), the range of V_T observed in human subjects at rest being from 442 to 1549 ml. These values were neither related to the height of the subjects, the vital capacity, FEV1, nor to the inspiratory and expiratory resistances.

The devices used for measuring V_T have been blamed for introducing errors not only in the values of V_T but also in the values of timing components of the breathing pattern. However, these errors appear to affect only the base line values and not the range of the diversity. Indeed, in one of the most recent studies (Perez and Tobin, 1985) conducted on 16 subjects the mean $\pm$ S.D. values of the respiratory variables remained approximately the same whatever the instrumentation used for recording breathing.

1.4. V_T/T_I and T_I/T_{TOT}

The drive and timing components of ventilation introduced by Milic-Emili and Grunstein (1976), are widely used because of their physiological significance and relevance. However, being ratios, the diversity in their values may be reduced if both terms of the ratio vary in the same direction or, alternatively, may derive from the diversity of one or both of the ratio terms. Thus, they are not the most adequate descriptors of the diversity of the breathing pattern. Indeed, Proctor and Hardy (1949) reported that there were global qualitative differences in the breathing pattern between people but that single measurement of slopes, ratios or instantaneous flows failed to yield significant differences between people. Benchetrit et al. (1989) showed that when comparing breathing pattern at rest, the ensemble (V_T, T_I and T_E) may better characterize a pattern than any of the traditionally used single respiratory variables V_T, T_I, T_E or the ratios V_T/T_I and T_I/T_{TOT}.

1.5. Flow profile

Very shortly after the publication of Der Pneumotachograms by Fleisch, Bretschger (1925) analyzed and classified patterns of pneumotachograms and concluded that the optimal airflow pattern minimizing mechanical work is rectangular with constant airflow rates during inspiration and expiration.

Following Bretschger's (Bretschger, 1925) study the hypothesis of an optimal flow shape has been considered by several authors. An analysis of these studies and models is given by Hämäläinen (1983). In addition to the mechanical work, work rate, mean squared volume acceleration, average pressure, are among the minimization criteria used. The rectangular or parabolic airflow curves predicted by these models are not close to the observed patterns of breathing at rest, although breathing patterns in exercise, are indeed, of the rectangular type. Thus, the related criteria are not able to explain individual variations in breathing pattern nor can they predict effects of added external loads. The flow profile was also analyzed to determine, as in Proctor and Hardy (1949) subtitle to their article, the significance of the normal pneumotachogram. The quantitative analysis performed by these authors, include measurements of acceleration, velocity and time relationships at various points during the cycle. Patterns that seem quite similar in shape, when submitted to such methods of quantitative analysis yield widely differing figures. One of the possible explanations they proposed was that 'the methods of quantitative analysis may not include the fundamental characteristics of the pattern. Perhaps an analysis of the total shape of the curve is required'. Gray and Grodins (1951) have further proposed that transformation of the tracings to a completely non-dimensional form should be the first step in analyzing the significance of their shape as far as no two respiratory cycles yield identical curves with respect to both shape and dimensions. Such methods of global flow profile analysis have been proposed by several authors (Bachy et al., 1986; Painter et al., 1987; Sato and Robbins, 1998). These methods provide the possibility of obtaining mean flow profiles under different conditions and of comparing resting and stimulated patterns.

2. Breath-to-breath variations in the pattern of breathing

Priban (1963) was the first to demonstrate that the breath-to-breath fluctuations in respiratory cycle variables were not purely random. He concluded that, "it is not unlikely that some system would be able to compare one breath to its predecessor and adjust it or the following one with respect to frequency and volume and so produce the observed pattern of breathing".

Using mainly time-series analyses and statistical models, several studies confirmed the non random nature of the fluctuations of the ventilatory variables and showed that there was a significant positive autocorrelation between X_n and X_{n-1}, X_n being the generic term of a series of VT or TTOT (Benchetrit and Pham Dinh, 1974; Gallego et al., 1985), TI or TE (Bolton and Marsh, 1984), VTI or VTE (Busso et al., 1996). The simplest autoregressive model proposed was:

$$(X_n - X) = a(X_{n-1} - X) + \varepsilon_n$$

where, X is the mean value of the series, a is a constant and ε is the disturbance and should be positive, negative or nil.

In order to identify the system that is 'able to compare' and to specify the structure of interrelationships within and between cycle's variables recordings were made under various conditions.

Autocorrelation function were calculated while breathing different gas mixtures, air; hypoxic ($FI_{O_2} = 0.14$); hyperoxic ($FI_{O_2} = 1.0$) and hypercapnic ($FI_{CO_2} = 0.03$), it was found that there were no significant differences between these conditions for a given subject and also there were no significant differences in the autocorrelation coefficients between subjects for a given gas mixture (Benchetrit, 1976). Modarreszadeh et al. (1990) reported a similar autoregressive structure for VI, TI and not for TE during stage II sleep. Liang et al. (1996) observed that at constant end tidal P_{O_2} and P_{CO_2} the breath-to-breath variations in ventilation were not random and that the autocorrelation in the sequence can usefully be described by a simple autoregressive model.

In addition to these studies on human subjects, animal experiments were performed to clarify the mechanisms contributing to the breath-to-breath correlations seen in respiratory cycle characteristics. Whether the dependency between the characteristics of successive breaths resides solely in a central neural mechanism or results in part from instability in the chemical feedback loop is still matter of debate.

It is noteworthy that breath-to-breath dependency in respiratory variables suggested to Priban and Fincham (1965) that the respiratory controller may be an adaptive or a self-optimizing system which predicts the activity which will keep the performance of the respiratory system at its minimum, the prediction being conditioned by the response of the system during previous breaths.

3. Individuality of breathing pattern

The existence of the individuality of the breathing pattern has been observed by all the investigators who have had to perform several recordings on one subject. Thus, from the observation of pneumotachograms, Proctor and Hardy (1949) reported that "the comparison of consecutive cycles or cycles taken on different days from records on any single subject impresses one with the consistency with which an individual pattern is reproduced''. Morrow and Vosteen (1953) confirmed these observations and even suggested that subjects could be identified from 'gross judgment' of the pneumotachogram. It was Dejours et al., (1961) who introduced the concept of 'la personnalité ventilatoire', claiming that different people breathe in different ways in terms of tidal volume, respiratory frequency and airflow shape, and that this is a relatively stable characteristic of an adult individual. In addition, Golla and Antonovich (1929) found that some normal subjects had habitually a regular breathing pattern whilst others a habitually irregular one. We have also observed (unpublished observation) this phenomenon and found that the regular or irregular breathing pattern was reproducible for the same subjects under the same conditions, and that the regular or irregular nature of the breathing pattern is thus part of the *personnalité respiratoire*.

Several further studies have been carried out on this subject revealing the persistence of this respiratory personality under diverse conditions. In these studies, the airflow shape was quantified by a harmonic analysis providing eight variables, which contained more than 95% of the power of the original signal. However, these eight variables have no physiological 'meaning' or 'correspondence', they merely quantify a shape. The ventilatory variables and the airflow shape were then compared using a test of similarity. For example, to assess the individuality of breathing pattern over time, a multivariate statistical test was used to compare differences between the first and second recording within individuals with those differences observed between random pairs of recordings from the two studies on the same group of individuals. Thus, the test provides a result on the group and not of each individual. Such an analysis allows for differences within an individual, but implies that the individual has a certain 'trait' that can be recognized amongst other individuals. This is analogous to the fact that one can recognize a person's face in a crowd, even after a number of years, despite any changes which may have occurred in their facial appearance. However, these tests are a comparison between individual variables and are designed to detect any kind of deviation from the hypothesis but not a specific alternative. This is similar to the χ^2 goodness-of-fit test in which no alternative hypothesis is specified. On the other hand, because of the natural large variability of the descriptive variables associated with each individual and the lack of models as to their variation, it is difficult to perform comparisons within individual without reference to the between-individual variability. In the proposed similarity tests, this between individual variability is used precisely as the basis for assessing whether the variability within an individual of the descriptive variables is meaningful or not.

This test was applied to show similarity in the flow profile within an individual (i) on repeated recordings, (ii) on recordings performed 4 years apart and (iii) on recordings in seated and supine conditions. In addition, it was found that identical twins breathe in a more similar way than any other pair of individuals from the same population. Considering conditions other than control, it was found that the airflow shapes are maintained during hypoxia (simulated altitude of 4500 m), but they are significantly modified during exercise (at 50% of their maximal oxygen consumption). Comparison of airflow shapes at this level of exercise between normoxia and hypoxia (simulated altitude of 4500 m), showed resemblance which suggests that when exercising, subjects adopt another individuality unchanged by hypoxia. A summary of these studies is given by Benchetrit and Guz (1993) and the topic has been overviewed by Shea and Guz (1992).

It was also shown that during resistive loading some individual characteristics (flow profile and T_I/T_{TOT} were maintained despite being proportional to the loads changes in the other ventilatory variables (Calabrese et al., 1998).

These observations suggest that a resting individual pattern, at least in the airflow profile, is maintained over a certain extent of changes in the minute ventilation, thereafter, there are also changes in the airflow profile. It has been hypothesized, that the characteristics of the changes would be common to all subjects and a model was proposed where there will be a sudden change in the airflow profile at some value of ventilation, this value varying from one individual to another (Benchetrit et al., 1995).

4. Consequences of the diversity and individuality of the breathing pattern

4.1. How are control subjects to be chosen?

In most studies on ventilatory changes, control experiments are carried out on subjects matched by age, weight and sex. Given the diversity of the breathing pattern the question arises as to whether this age and morphology matching yields adequate control subjects.

It has not been clearly established whether in adult human subjects, there is a relationship between these characteristics and the components of the breathing pattern. Jammes et al. (1979) reported a study on 235 subjects of both sexes aged between 6 and 80. They found no significant sex-related differences in any group when V_T, f_R, T_I and T_E were compared. Whereas the changes with age in the range 6–25 were clearly obvious, variations according to age in adults were less conclusive. They also compared the coefficient of variation of these variables and found that they were independent of age. Tobin et al. (1983) found that the mean values of ventilatory variables were not affected by age but the rhythmicity was more irregular in the elderly. Hudgel et al. (1993) reported a greater variability of breathing characteristics in the elderly compared with that in younger subjects during sleep but not during wakefulness. Whereas Hak et al. (1999) observed that in elderly subjects without sleep disordered breathing the change in the coefficient of variation of ventilatory variables between wakefulness and sleep was similar to that reported in the younger group of Hudgel et al. (1993). It is possible that some, if not all, of the discrepancies between these results may be explained by the diversity of breathing pattern within the group of subjects.

Dejours et al. (1961) reported that the diversity of V_T and f_R, of the subjects was related neither to their height, their vital capacity (VC), maximal inspiratory and expiratory volumes, forced expiratory volume in 1 sec (FEV1) nor to their FEV1/VC ratio. They also found that there was no correlation between f_R and the respiratory resistance or compliance or resistance x compliance product.

As to the flow profiles, in a tentative classification (Benchetrit et al., 1987) it was found that no noteworthy features attributable to differences in size, weight, body surface area, sex or smoking habits were observed in the clusters of flow profiles.

The selection of control subjects remains a matter to be resolved. Whoever these control subjects are, one reasonable comparison to be considered would be that of the perturbation response parameters (slope, delay etc). Indeed, changes between the resting pattern and the perturbed pattern are likely to be similar in different individuals and to lead to elaborate a control response function with which an 'abnormal' response function may be compared.

4.2. How important are these differences in resting pattern?

In addition to the question of the choice of control subjects, at least two situations may be evoked where the differences in pattern of breathing are pertinent.

1. In a recent study Salerno et al. (1999) have shown that methacholine induced bronchoconstriction was modulated by the amplitude of the tidal ventilation. In these experiments carried out on open chest dogs the two lungs were ventilated separately with different V_T and lungs ventilated with higher amplitudes always demonstrated lesser increases in resistance and elastance during induced constriction. When mean bronchial pressure was kept constant, the discrepancy in the contractile response between the two lungs was again evident. This demonstrates that large V_T inhibits airway smooth muscle contraction, regardless of mean bronchial pressure. Although these observations were obtained during induced bronchoconstriction, it may be suggested that airway contractility may also change with V_T in normal lung. Thus, there may be ventilatory

(in the broadest sense) differences between subjects with high and low V_T, 'high' and 'low' needing to be defined. Intuitively, one would define high and low V_T according to the stature of the subject. One possible estimation would be the use of the ratio of V_T to the vital capacity. For example, an individual using one tenth of his vital capacity in tidal breathing may be defined as having a low V_T whereas an individual using one fifth of his VC would have a high V_T.

2. The breathing rate becomes important when considering its interrelation with other rhythms. For example, for a heart rate of 60 beats per minute in the range of normal breathing rate between 6 and 30 breaths per minute, there will be ten heart beats per breath for the slowest breathing rate and two for the fastest. Apart from the role of the breathing rate in respiratory sinus arrhythmia which is well documented, this heart rate/breathing rate ratio may result in more than anecdotal outcomes; mechanical effect of intrathoracic pressure changes, the time necessary to transport the information from the lungs to chemoreceptors, delay and gain in the reflex loops, etc.

There are other rhythms also which are known to influence the breathing rhythm, walking, pedaling or mechanical ventilation may entrain the breathing rate. Does the resting breathing rate determine the parameters (ratio, range, boundaries) of entrainment?

To summarize, the existence of the diversity and individuality in breathing pattern suggests that there are degrees of freedom in the resting pattern, and as pointed out by Dejours et al. (1961), an infinite number of possible combinations of the ventilatory components and airflow shape exists capable of achieving the same minute ventilation. The number of combinations decreases when the demand for ventilation increases and at maximal ventilatory values all individuals tend to exhibit more similar patterns, such as a rectangular air flow profile or equal inspiratory and expiratory times.

The diversity and individuality of the resting breathing pattern is worth being taken into account when studying changes in ventilation and the individual results are as meaningful as the group results. However, until we find out why individuals do breathe in different ways, the method we adopt to take into account these resting patterns will proceed by trial and error and thus remain empirical.

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