Influence of Age on the ‘Nasal Cycle’

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The nasal cycle is classically defined as a side-to-side fluctuation in nasal engagement and airflow, with period lengths ranging from approximately 1 to 5 hours. This cycle, as well as its variants (e.g., cyclic changes on one side of the nose only), is produced by alterations in autonomic tone of the nasal vasculature and reportedly correlates with a number of ultradian rhythms, including asymmetries in left/right cerebral electroencephalographic (EEG) activity and differential performance on visual/spatial psychological tasks. Since the pacemaker for the nasal cycle is believed to lie within the suprachiasmatic nucleus of the hypothalamus, and this nucleus evidences degeneration in later life, we sought to determine whether the nasal cycle or its variants changes with age. To achieve this end, we used a liquid crystal thermography exhalation monitor to measure relative airflow of the two nasal chambers at 15-minute intervals for 6 hours in 60 people representing four age categories: 18 to 29 years (n=12); 30 to 49 years (n=15); 50 to 69 years (n=13); and 70 to 85 years (n=20). Overall, the proportion of subjects exhibiting the alternating rhythmicity associated with the classic nasal cycle decreased with age. No association was present between nasal cycle parameters and scores on the Mini-Mental State Examination (MMSE). The results suggest that the classic nasal cycle may be a marker for age-related central nervous system changes.

Key Words: Nasal cycle—Ultradian rhythm—Suprachiasmatic nucleus—Hypothalamus—Central nervous system.


INTRODUCTION

The nasal cycle, traditionally defined as a side-to-side fluctuation in nasal engagement with period lengths ranging from 1 to 5 hours, is of considerable interest to otorhinolaryngologists and neurobiologists. This is due, in part, to the fact that it reportedly correlates strongly with a number of indices of bodily function, including 1. the relative electroencephalographic (EEG) activity of the two cerebral hemispheres, 2. rapid eye movement (REM) and non-REM sleep activity patterns, 3. verbal and spatial cognitive processing, and 4. the release of neuroendocrine agents. The pacemaker for this cycle may be located within the suprachiasmatic nucleus of the hypothalamus, a nucleus associated with the control of a number of circadian and ultradian rhythms.

To date, no studies have examined whether the nasal cycle is altered in old age. One might expect such alteration, since the suprachiasmatic nucleus evidences degeneration in later life, 2. patients with Kallmann’s syndrome (a syndrome associated with hypothalamic dysfunction) reportedly evidence no nasal cycle, 3. age-related changes may occur in the development of the nasal cycle prepubertally; however, please see Fox and Matthews, Mayer et al., and Fisher et al. Thus, in this study we sought to examine nasal cycles from a relatively large number of people spanning a wide age range and to determine whether age-related changes occur in components of the cycle, such as amplitude, period length, and left-right coupling.

MATERIALS AND METHODS

Study Group

Sixty subjects—29 men and 31 women—ranging in age from 18 to 85 years were recruited from the Veterans Administration Medical Center of Philadelphia, the campus of the University of Pennsylvania, and the Medford Leas Retirement Community, Medford, N.J. Forty were Caucasian, 18 were African American, and 2 were Asian American. They comprised four age categories: 18 to 29 years; 30 to 49 years; 50 to 69 years; and 70 to 85 years (respective mean ages, standard deviations (SDs), and sample sizes were as follows: 22.00, 3.79, 12; 39.73, 6.10, 15; 61.61, 7.03, 13; 77.40, 4.46, 20).

At the time of testing, all subjects were free of allergies, nasal sinus disease, active upper respiratory infections, and major medical or sleep disorders, as determined by self-report and anterior rhinoscopy. The subjects were administered the Mini-Mental State Exam (MMSE) and provided...
written informed consent, in accord with the requirements of the Committee for the Study of Human Beings at the University of Pennsylvania and the Human Research Committee of the Veterans Administration Medical Center of Philadelphia.

**Testing Procedure**

The relative airflow patency of the two sides of the nose was determined using a liquid crystal thermography exhalation monitor similar to that described by Canter17 (Fig. 1). To obtain a reading, each subject exhaled through the nose with mouth closed onto an 8 × 10-in heat-sensitive Mylar sheet once every 15 minutes for 6 hours (total of 24 measurements per subject). The distance of each subject from the Mylar sheet was standardized using a chin and head rest. The area of color change produced by the warm exhalation air was quantified, for each side of the nose, using a grid containing 1-in squares located on the side of the monitor facing the investigator. Subjects were given a 30- to 45-minute break midway through testing. Testing occurred between 9 a.m. and 3 p.m.

**Statistical Analyses**

Periodicity of cyclic trends in the exhalation data for each side of the nose was estimated using autocorrelation analysis.18 In this procedure, the time series observations are correlated with one another in successive steps, or lags, and a plot of resulting correlation coefficients, or a correlogram, is produced. A series of observations that alternates above and below a mean value results in an alternating correlogram. A correlation coefficient at a given lag value is considered significantly different from zero when it is greater in absolute value than the result of $2\sqrt{N}$, where $N$ = the total number of observations in the series.19

The relationship between the left and right patterns of exhalation was assessed using Pearson correlation coefficients. A correlation between complete sets of observations for the right and left sides of the nose produced a single correlation coefficient for each subject, termed the bilateral $r$. A negative bilateral $r$ indicates an alternating cycle of nasal patency between nostrils, whereas a positive bilateral $r$ indicates a tendency toward parallel or non-alternating side-to-side cycle of patency. The statistical significance of the coefficients was determined using the procedure noted above. Analysis of variance with post hoc Bonferroni pairwise comparison was used to compare the bilateral $r$ values among the four age groups. The non-parametric Kruskal-Wallis Analysis of Variance and the Mann-Whitney $U$ test were used to compare the amplitude values among the four groups, since the amplitude values were not normally distributed.

Chi-square analyses were performed on categorical data, as described in “Results.” Depending upon the nature of the underlying distributions, either Pearson or Spearman correlation coefficients were used to examine associations.
Although approximately half of our sample was female, the sex of the subjects, we subjected the data to a Kruskal-Wallis one-way analysis of variance (ANOVA). No significant differences among the age groups were observed \( H_{\text{right}} (3) = 3.80, P = .28; H_{\text{left}} (3) = 6.15, P = .11 \). To address the possibility that the age groups might differ in terms of left or right bias in nasal exhalation, we calculated a measure of the exhalation area on one side of the nose relative to the total exhalation area from both sides \( i.e., \text{right exhalation area/ (right + left exhalation area)} \), and subjected this measure to the same analysis. Again, no significant difference across age categories was present \( H (3) = 3.69, P = .30 \).

A range of MMSE scores was present within the 71 to 85 year age category \( i.e., \text{less reciprocal cyclicitiy and more disintegration or parallel cyclicitiy} \) as age increases.

The amplitude data for each subject were separately averaged for the left and right sides of the nose and subjected to nonparametric analysis using a Kruskal-Wallis one-way analysis of variance (ANOVA). No significant differences among the age groups were observed \( H_{\text{right}} (3) = 3.80, P = .28; H_{\text{left}} (3) = 6.15, P = .11 \). To address the possibility that the age groups might differ in terms of left or right bias in nasal exhalation, we calculated a measure of the exhalation area on one side of the nose relative to the total exhalation area from both sides \( i.e., \text{right exhalation area/ (right + left exhalation area)} \), and subjected this measure to the same analysis. Again, no significant difference across age categories was present \( H (3) = 3.69, P = .30 \).

Between the MMSE scores and indices of the cycle (e.g., bilateral \( r \) values).

**RESULTS**

The exhalation data were classified into four categories similar to those described by Kern\(^20\) and Fisher et al.\(^21\). Exhalation data with a statistically significant negative bilateral \( r \) were assigned to the category “classical alternating cycle.” Those with a significant positive bilateral \( r \) were assigned to the category “parallel cycle.” Data which did not have significant bilateral \( r \) values but which exhibited systematic fluctuations on one side or the other, as determined by autoregression analysis, were classified as “hemicyclic.” When no systematic fluctuations on either side were apparent, the data were categorized as “acyclic.”

As can be seen in Table I, only a minority of the subjects in any age group exhibited the classical nasal cycle. Interestingly, however, the number of subjects exhibiting the classical cycle fell from 25% to 5% across the four age categories, whereas the number of subjects exhibiting no cyclic activity rose from 17% to 50% across these age categories. Because of low frequencies within the classical and hemicycle categories in the oldest age group, we collapsed the data into categories greater and less than 50 years of age for analysis. A Chi-square analysis of these data was significant at the 0.06 \( \alpha \) level [Chi square (3) = 7.29]. Although approximately half of our sample was female, the frequencies were too low to determine, using Chi-square analysis, whether sex meaningfully influenced the aforementioned categorization.

The tendency toward age-related disintegration or desynchronization of the cycles across the two sides of the nose was supported by the fact that the mean bilateral \( r \) values were more positive in the older than in the younger groups (Fig. 2). To establish if this effect was statistically significant, and whether it was related to the sex of the subjects, we subjected the data to an age category \( \times \) sex analysis of variance. Both main effects, age category and sex, were statistically significant [\( F_{\text{age category}} (3,52) = 3.39, P = .025; F_{\text{sex}} (1,52) = 6.41 P = .014 \). The age category \( \times \) sex interaction was not significant [\( F (3,52 = 0.95, P = .426 \), implying that males and females performed similarly, relative to one another, within each age category. The overall mean (SD) bilateral \( r \) values for the men and women were 0.02 (0.45) and 0.24 (0.36), respectively, indicating that, on average, women exhibited a tendency toward a less random and more parallel cycle than that observed in men. This sex effect, however, is weak; thus, when we performed a similar analysis using multiple linear regression treating age as a continuous variable, the main effect of sex was not significant [\( F (1,56) = 2.26, P = .138 \). Age remained significant [\( F (1,56) = 5.97, P = .018 \].

![Fig. 2. Mean (± SEM) bilateral \( r \) values for the four age groups. Note the tendency toward higher positive values (i.e., less reciprocal cyclicitiy and more disintegration or parallel cyclicitiy) as age increases.](image)

<table>
<thead>
<tr>
<th>Age Group (Years)</th>
<th>Classical (%)</th>
<th>Alternating (%)</th>
<th>Parallel (%)</th>
<th>Hemicyclic (%)</th>
<th>Acyclic (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18–29 (n=12)</td>
<td>3 (25)</td>
<td>3 (25)</td>
<td>4 (33)</td>
<td>2 (17)</td>
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<tr>
<td>30–49 (n=15)</td>
<td>3 (20)</td>
<td>2 (13)</td>
<td>5 (33)</td>
<td>5 (33)</td>
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</tr>
<tr>
<td>50–69 (n=13)</td>
<td>2 (15)</td>
<td>5 (38)</td>
<td>3 (23)</td>
<td>3 (23)</td>
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</tr>
<tr>
<td>70–85 (n=20)</td>
<td>1 (5)</td>
<td>7 (35)</td>
<td>2 (10)</td>
<td>10 (50)</td>
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*cf. text for detailed definitions of categories.
DISCUSSION

The present study demonstrates that elements of the so-called nasal cycle, particularly those related to the coordination of side-to-side changes, are influenced by older age. Thus, the exhalation data from over half of the subjects under the age of 50 years reflected classical alternating (22%) or hemicycle patterns (33%), whereas those from only a quarter of the subjects over the age of 50 reflected such patterns (9% and 15%, respectively). The older subjects were much more likely to exhibit data indicative of acyclic or parallel patterns of airflow. Only 1 (5%) of the 20 subjects over the age of 69 exhibited the classical nasal cycle.

Traditionally, the nasal cycle has been defined as “the alternating congestion and decongestion of the nasal turbinates” or “rhythmic and bilaterally reciprocal alterations of nasal airway patency such that total airway resistance remains constant.” Haight and Cole, in their classic studies of asymmetrical body pressure on unilateral nasal resistance, define the nasal cycle succinctly: “One nasal cavity is more congested than the other. Periodically the congestion switches sides.” It has been generally assumed that most humans exhibit this cycle. Thus, Heetderks on the basis of clinical inspection of the nose, reported that 80% of adults exhibit the cycle, and Hasegawa and Kern reported that 72% of 50 subjects studied over a 7-hour period “had at least one nasal cycle” during the period of observation. However, the latter study used a comparatively liberal criterion of “cycle” which was based neither upon statistical nor rhythmic considerations (namely, that a 20% left:right nasal resistance difference be present for two consecutive observations separated from one another by at least 15 minutes within a 7-hour session).

In contrast to such reports, it is clear from the present data that if one accepts the commonly held definition of “cycle” (e.g., Webster’s definition: “a course or series of events or operations that recur regularly and usually lead back to the starting point”) and assumes that the nasal cycle requires reciprocity of change across the sides of the nose, very few humans have a “nasal cycle.” In the present study, only 9 (15%) of 60 subjects exhibited the classical nasal cycle; 28.3% exhibited parallel cycles, 23.3% exhibited hemicycles, and 33.3% were acyclic. These figures are in rough accord with those reported in a smaller study by Gilbert and Rosenwasser who, using statistical criteria similar to our own, found a classical nasal cycle in only 2 (13%) of 16 subjects and hemicycles in 7 (44%) of the subjects.

The basis for the age-related change in the occurrence of the nasal cycle and its variants is not clear. While age-associated peripheral factors, such as decreased intramucosal blood flow and changes in the vascular elasticity of the nasal epithelium, might play some role, most authorities believe that alterations in central brain mechanisms are involved, perhaps reflecting centers controlling a constellation of autonomic and other biological rhythms (e.g., changes in sleep-wake and body temperature patterns). Although the medulla has been associated with the control of the autonomic tonicity of the nasal vasculature, perhaps through an N-methyl-D-aspartate-mediated system, pacemakers within the suprachiasmatic nucleus of the hypothalamus have been most frequently suggested as the central basis for the cycle. This idea stems, in part, from evidence that this nucleus contains pacemakers for a number of circadian and ultradian rhythms, the observation that nasal vasoconstriction follows electrical stimulation of this nucleus in the cat, and evidence that patients with Kallmann’s syndrome, a congenital hypogonadal disorder associated with hypothalamic dysfunction, do not have a nasal cycle. Importantly, the suprachiasmatic nucleus shows a loss in cell number and nuclear volume with aging, losses which are reportedly exacerbated in Alzheimer’s disease.

In summary, the present study clearly demonstrates that the proportion of subjects exhibiting the alternating rhythmicity associated with the classic nasal cycle (i.e., left:right coupling) decreases with age. Other components of the cycle, such as amplitude, appear not to be influenced markedly by age. No association was found between nasal cycle parameters and scores on the MMSE (an association that would have been expected if damage to the suprachiasmatic nucleus was systematically related to both dementia and the measured parameters of the nasal cycle). The results of this study do suggest, however, that the nasal cycle and some of its variants may be a marker for age-related central nervous system changes.

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BIBLIOGRAPHY


