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Breath-to-breath "noise" in the ventilatory and gas exchange responses of children to exercise

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Abstract The purposes of this investigation were to quantify the noise component of child breath-by-breath data, investigate the major determinants of the breath-to-breath noise, and to characterise the noise statistically. Twenty-four healthy children (12 males and 12 females) of mean (SD) age 13.1 (0.3) years completed 25 min of steady-state cycle ergometry at an exercise intensity of 50 W. Ventilatory and gas exchange variables were computed breath-by-breath. The mean (SD) oxygen consumption ($\dot{V}O_2$) ranged from 0.72 (0.16) to 0.92 (0.26) $l \cdot min^{-1}$; mean (SD) carbon dioxide production ($\dot{V}CO_2$) ranged from 0.67 (0.20) $l \cdot min^{-1}$ to 0.85 (0.16) $l \cdot min^{-1}$; and mean (SD) minute ventilation ranged from 17.81 (3.54) $l \cdot min^{-1}$ to 24.97 (5.63) $l \cdot min^{-1}$. The majority of the breath-to-breath noise distributions differed significantly from Gaussian distributions with equivalent mean and SD parameters. The values of the normalised autocorrelation functions indicated a negligible breath-to-breath correlation. Tidal volume accounted for the majority of the $\dot{V}O_2$ (43%) and $\dot{V}CO_2$ (49%) variance. The breath-to-breath noise can be explained in terms of variations in the breathing pattern, although the large noise magnitude, together with the relatively small attainable response amplitudes in children reduces the certainty with which ventilatory and gas exchange kinetics can be measured.

Key words Exercise · Children · Ventilation Gas exchange

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Introduction

The ventilatory and gas exchange responses of children to maximal and steady-state submaximal exercise (Armstrong and Welsman 1994; Rowland 1996) fail to replicate the most common pattern of activity exhibited by children, namely the non-steady-state (see Armstrong 1998 for review). A more appropriate measure of a child's cardiorespiratory function may be gained by quantifying the rate of ventilatory and gas exchange adjustments that occur during exercise transitions. Breath-by-breath data are routinely collected and the rate of adjustment during square-wave transitions below the anaerobic threshold (Th_{an}) is characterised by extraction of the time constant (τ) of a monoexponential model, although more complex formulations are frequently used for transitions above Th_{an} (Casaburi et al. 1989; Cochrane and Hughson 1992; Barstow et al. 1996). The τ of oxygen uptake ($\dot{V}O_2$) is an important parameter of aerobic function (Whipp et al. 1981) which Barstow (1994) has speculated "...may provide a non-invasive window into the kinetics of skeletal muscle respiration...". These techniques have been utilised to investigate the responses of children to exercise (Cooper et al. 1985; Armon et al. 1991a; Springer et al. 1991).

The values of breath-by-breath responses typically fluctuate from one breath to the next. Lamarra et al. (1987) have defined breath-by-breath gas exchange responses as consisting of both an underlying physiological response and a noise component to which breath-to-breath fluctuations are attributed. From this analysis, the noise is physiological in origin and not the result of some extraneous factor such as measurement error. This contention is supported by Myers et al. (1990), who investigated the source of variability in adult $\dot{V}O_2$ data and found that the predominant variability could be attributed to fluctuations in the breath-to-breath ventilatory profile rather than to differences in "true O_2".

Before attempting to estimate the τ of minute ventilation ($\dot{V}_E$), $\dot{V}O_2$ or carbon dioxide production ($\dot{V}CO_2$) in children, consideration should be made of the most appropriate parameter estimation technique. Non-linear regression estimates τ by varying its value and iterating until the modelled response matches the measured response according to a given criterion (e.g. minimum mean squared error, Lamarra 1990). The least squares estimate will be unbiased if the residuals are uncorrelated and normally distributed with a mean of zero and constant variance (Quadling 1987). While the breath-to-breath noise in adult responses has been demonstrated to be Gaussian and uncorrelated (Lamarra et al. 1987), the noise content of data from children remains to be systematically examined. Without knowledge of the nature of the noise characteristics present in child breath-by-breath data, it is possible that the use of least squares non-linear regression is inappropriate. In this case, it is unlikely that unbiased parameter estimates would be calculated using the least squares method.

Furthermore, the confidence with which τ can be estimated using the least squares method, is dependent upon the magnitude of both the response amplitude and the breath-to-breath noise. Lamarra et al. (1987) demonstrated that the confidence interval for the estimated value of τ ($\hat{\tau}$), derived from data containing uncorrelated and Gaussian noise, is inversely proportional to the amplitude of the response if the average amplitude of the noise is constant and, conversely, the greater the magnitude of the noise as a proportion of the total response, the less confidence we can have in $\hat{\tau}$ (Lamarra et al. 1987; Lamarra 1990). As a result, characterisation of the non-steady-state gas exchange responses in subjects with a low response amplitude, such as children, may be problematic because the noise occupies a larger proportion of the total response amplitude (Lamarra et al. 1987; Whipp 1997). Characterisation will be further confounded if the magnitude of absolute noise is also large. The noise magnitude and its possible effects on the confidence with which τ can be estimated from child breath-by-breath data has yet to be determined. The purposes of this investigation therefore, were to quantify the noise component of child breath-by-breath data, to investigate the major determinants of the breath-to-breath noise, and to characterise the noise statistically.

Methods

Population

Twenty-four healthy children (12 males and 12 females) with a mean (SD) age of 13.1 (0.3) years comprised the study population. The mean stature and body mass of the group was 1.55 (0.10) m and 46.5 (11.3) kg, respectively. Ethical approval for the study was obtained from the Local Health Authority Ethical Committee.

Gas exchange measurement

Inspired and expired gases were analysed by a mass spectrometer (Airspec QP9000, Case, Kent, UK). Analog-to-digital (A/D) conversion factors for gases were determined using calibration gas mixtures. Expired volume was measured using a turbine flowmeter (VMM-401, Interface Associates, California, USA). The mouthpiece dead space volume was 40 ml. Determination of the A/D volume conversion factor was achieved using a 2-l syringe (Hans Rudolph, Kansas City, USA). The volume calibration procedure was carried out while the mass spectrometer was sampling gas so that testing conditions were replicated. The sum of the gas transport and analyser response delay times were determined and appropriate adjustments made in the software. All calibration procedures were repeated prior to each experimental test. Ventilatory and gas exchange variables were computed for each breath in accordance with the algorithms of Beaver et al. (1973). Subjects wore nose-clips throughout experimental testing.

Experimental protocol

The exercise stress was applied using an electromagnetically braked cycle ergometer (Lode Excalibur Sport, Lode, Groningen, The Netherlands) that enables a cadence-independent power to be produced at between 30 and 120 rpm. The children were habituated to the laboratory environment, personnel, protocol and equipment during a session prior to experimental testing. The experimental protocol and procedures were explained to each subject separately prior to both habituation and experimental testing. Subjects completed a 3-min warm-up at a work rate that was 50% of the work rate applied during experimental testing. Subjects were required to cycle at a cadence of 60 rpm during experimental testing and were encouraged to keep pedalling at all times. This was to avoid any possible metabolic consequences of a varying cadence. The cadence was monitored remotely by the experimenter and appropriate verbal instructions given to the subject if the cadence differed from 60 ± 5 rpm. A work rate of 50 W was selected for all subjects, which was designed to allow a steady-state to be attained. The attainment of a steady-state was examined as part of the subsequent data analysis. Subjects exercised for 25 min, during which time periodic verbal encouragement was given. All subjects completed the test in the morning.

Data analysis

For the purpose of this study only the steady-state responses were required; data from the first 3-min of exercise were therefore removed from the analysis (Whipp 1987). Data were analysed in this way to enable variations about a steady-state mean value to be investigated. As noted by Lamarra et al. (1987), breath-by-breath responses occasionally contain values that are clearly artefactual, for example $\dot{V}O_2$ values ≤ 0. Such breaths are the result of swallowing or coughing, for example, and were therefore removed from the analysis. In addition, values exceeding the steady-state mean by 4 standard deviations were excluded from the analysis. This technique was proposed by Lamarra et al. (1987) to improve the statistical confidence of parameter estimates.

Confirmation of steady-state

Two strategies were employed to confirm steady-states of $\dot{V}_E$, $\dot{V}O_2$ and $\dot{V}CO_2$. Firstly, a linear regression analysis was performed for the three breath-by-breath variables against time. A steady-state was accepted if the slope of the regression line was not significantly greater than zero at the $P > 0.05$ level. A second analysis was considered necessary since the characteristics of a particular data set may have precluded the calculation of unbiased parameter estimates by least squares linear regression. Using paired *t*-tests, this analysis compared the value of the means of the breath-by-breath responses in the first and last minute of steady-state exercise. A steady-state was accepted if the mean response in the last minute was not significantly larger than that in the first minute ($P > 0.05$).

Noise analysis

Firstly, the means and standard deviations of the steady-state $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}_E$ responses were calculated. The amplitude and time statistics were investigated by calculating the amplitude probability density function and time autocorrelation function of the steady-state data (Lamarra et al. 1987). The probability density function $f(x)$ of a random variable X, where X denotes any particular value X can take (denoted by x), is such that the integral $\int_a^b f(x)\,dx$ gives the probability that the value of X lies between a and b (Quadling 1987; Hugill 1988). The autocorrelation function is a measure of the association of the present value of the response $x(n)$, on the value of the response some time in the past or future $x(n+i)$, and can be defined as the time average of the product $x(n) \cdot x(n+i)$ (Davies 1970).

The distributions of the breath-to-breath $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}_E$ noise were compared to Gaussian distributions with equivalent parameters, and their "goodness of fit" was evaluated using the chi-squared (χ^2) test. Breath-to-breath variability was further examined by computing the means and standard deviations of the steady-state tidal volume (V_T) responses and the calculated breathing rate (f_b) for individual breaths. The source of $\dot{V}O_2$ and $\dot{V}CO_2$ variability was investigated by performing stepwise multiple regression analyses using V_T, f_b and true O_2 for $\dot{V}O_2$ and V_T, f_b and the fractional CO_2 production ($F_ECO_2 - F_ICO_2$) for $\dot{V}CO_2$ as the independent variables. Data were analysed using Mathcad 7 (MathSoft International, Surrey, UK) and SPSS (SPSS, Chicago, Illinois, USA).

Results

The mean (SD) number of breaths used for the steady-state analyses was 568 (113) per subject. Linear regression of the steady-state $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}_E$ responses of all subjects revealed slopes that were not significantly different from zero. The mean responses of all subjects in the first and last minute of steady-state exercise were not significantly different. All responses were therefore accepted as steady-state.

The means and standard deviations of the steady-state $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E$, V_T and f_b responses of all 24 subjects are presented in Table 1. Also indicated in Table 1 are the findings of the χ^2 goodness of fit tests for $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}_E$. Out of the 72 distributions compared, 18 were not significantly different from a Gaussian distribution with equivalent mean and standard deviation parameters. Figure 1 shows the $\dot{V}O_2$ breath-to-breath noise distribution that elicited the smallest χ^2 value (i.e. that which most closely approximated a Gaussian distribution) and the distribution yielding the largest χ^2 value. The noise distributions of $\dot{V}CO_2$ and $\dot{V}_E$ were similar to those shown for $\dot{V}O_2$.

The normalised autocorrelation coefficients of the breath-to-breath noise for $\dot{V}O_2$,$\dot{V}CO_2$ and $\dot{V}_E$ are presented in Table 2. Coefficients for breath delays ranging from 1 to 3 are shown. A typical example of a normalised autocorrelation function plot obtained for $\dot{V}O_2$ is presented in Fig. 2. Plots of the normalised autocorrelation functions for $\dot{V}CO_2$ and $\dot{V}_E$ were similar to that shown for $\dot{V}O_2$. Individual results of the stepwise multiple regression analyses demonstrated a common pattern; for this reason group mean values are presented. The mean $\dot{V}O_2$ variance accounted for by V_T, f_b and true O_2 was 43%, 22% and 19%, respectively; the $\dot{V}CO_2$ variance accounted for by V_T, f_b and fractional CO_2 production was 49%, 25% and 11%, respectively.

Discussion

Noise magnitude

The child breath-by-breath $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}_E$ responses contained relatively large variations from one breath to the next, as evidenced by the large standard deviations (see Table 1). The standard deviations of the child breath-by-breath data are larger than those reported for adult subjects during moderate-intensity, constant work rate cycle ergometry by Lamarra et al. (1987). For example, the largest $\dot{V}O_2$ standard deviation reported by Lamarra et al. (1987) was 0.11 $l \cdot min^{-1}$, whereas the largest $\dot{V}O_2$ standard deviation found in the present investigation was 0.37 $l \cdot min^{-1}$. Similarly, for $\dot{V}CO_2$ and $\dot{V}_E$ the largest standard deviations reported by Lamarra et al. (1987) were 0.11 and 4.2 $l \cdot min^{-1}$, respectively, and in the present study were 0.32 $l \cdot min^{-1}$ and 8.81 $l \cdot min^{-1}$, respectively. Together with large standard deviations, the small response amplitudes of children reduces the certainty with which parameters such as $\tau\dot{V}O_2$ can be estimated. This problem is exacerbated for studies designed to investigate children's ventilatory and gas exchange kinetic responses to low- and moderate-intensity exercise, where the already small attainable response amplitudes are reduced even further.

The predominant source of variability in child breath-by-breath $\dot{V}O_2$ was found to be V_T, followed by f_b and true O_2; for $\dot{V}CO_2$, V_T, f_b and the fractional CO_2 production. Interestingly, true O_2 accounted for a considerably larger proportion of $\dot{V}O_2$ variance compared to the $\dot{V}CO_2$ variance accounted for by the fractional CO_2 production (19% vs 11%). This is likely to be the result of high CO_2 solubility in the lung tissue buffering changes in the alveolar CO_2 partial pressure (P_ACO_2; Hlastala 1972). Alterations in the respiratory pattern will therefore affect the alveolar partial pressure of O_2 to a greater extent than P_ACO_2 (Hlastala et al. 1973).

All subjects demonstrated a large V_T and f_b variability (Table 1), and subject 12 was found to have the largest standard deviation for V_T (0.36 l). Of particular relevance is the large range, with values from 0.15 l to 2.29 l, compared to a mean V_T of 1.15 l. A similar variability was found in the breathing rate values, with subject 2 having the largest f_b standard deviation (12 breaths $\cdot$ min^{-1}). The sources of $\dot{V}O_2$ variability in adult subjects are similar to those of the present investigation. Myers et al. (1990) found 51% of $\dot{V}O_2$ variance to be accounted for by V_T, 25% by f_b and 19% by true O_2, and resting data from Hlastala et al. (1973) found $\dot{V}O_2$ variance to be accounted for by V_T,f_b and changes in functional residual capacity, in that order. These findings also concur with those of Lamarra et al. (1987) who asserted that the breath-to-breath noise was a result of natural breathing irregularities.

Table 1 Means and standard deviations of the steady state oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), minute ventilation ($\dot{V}_E$), tidal volume (V_T) and frequency of respiration (f_b) responses of all subjects. Goodness of fit with Gaussian distribution for $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}_E$ is also indicated

Subject	$\dot{V}O_2(l \cdot min^{-1})$		$\dot{V}CO_2(l \cdot min^{-1})$		$\dot{V}_E(l \cdot min^{-1})$		V_T (l)		f_b (breaths $\cdot$ min^{-1})	
	$\bar{x}$	SD	$\bar{x}$	SD	$\bar{x}$	SD	$\bar{x}$	SD	$\bar{x}$	SD
1	0.87	0.19	0.78	0.18	24.97	5.63	0.81	0.31	34	9
2	0.76*	0.24	0.67*	0.20	19.14*	5.89	0.66	0.28	32	12
3	0.81*	0.26	0.68*	0.21	18.68*	4.66	0.66	0.19	29	5
4	0.88*	0.33	0.80*	0.30	21.04*	6.90	0.94	0.33	25	9
5	0.78*	0.19	0.72*	0.16	18.39*	3.98	0.66	0.13	28	4
6	0.79*	0.17	0.72	0.15	19.38	3.88	0.91	0.18	22	4
7	0.92	0.29	0.81	0.26	24.47*	7.67	1.01	0.29	25	6
8	0.86*	0.32	0.74	0.27	20.24	6.84	0.94	0.32	23	6
9	0.79*	0.13	0.73*	0.11	19.21*	3.26	0.67	0.13	29	5
10	0.89	0.21	0.79*	0.19	23.51*	5.70	0.77	0.22	31	6
11	0.87*	0.21	0.80	0.19	22.13*	5.08	0.71	0.16	31	6
12	0.91*	0.16	0.85*	0.16	21.62*	4.48	1.15	0.36	20	5
13	0.92	0.26	0.78	0.22	22.77	6.31	0.88	0.28	27	6
14	0.81*	0.16	0.76*	0.15	19.79	4.22	0.95	0.28	22	7
15	0.87*	0.17	0.77*	0.14	22.44*	4.11	0.87	0.22	26	5
16	0.83*	0.13	0.77*	0.13	22.90*	4.33	0.86	0.24	28	7
17	0.73*	0.16	0.67*	0.14	17.81*	3.54	0.65	0.18	28	6
18	0.79	0.18	0.71*	0.16	20.42*	5.21	0.75	0.15	27	6
19	0.78*	0.14	0.71*	0.13	23.01*	4.60	0.65	0.16	36	9
20	0.83*	0.17	0.76*	0.15	24.56*	4.99	0.84	0.15	29	4
21	0.87*	0.37	0.77*	0.32	23.73	8.81	0.79	0.32	31	9
22	0.79*	0.22	0.69*	0.19	22.49*	5.33	0.65	0.20	37	10
23	0.72*	0.16	0.69*	0.15	21.97*	4.61	0.64	0.15	35	7
24	0.73*	0.18	0.68*	0.16	20.28	4.35	0.62	0.15	33	7

* Significantly different from Gaussian distribution ($P \leq 0.05$)

Identification of the respiratory pattern as the major source of variability in $\dot{V}O_2$ in adults (Myers et al. 1990), and $\dot{V}O_2$ and $\dot{V}CO_2$ in children (present study), and the relatively larger noise in child breath-by-breath ventilatory and gas exchange responses compared to those reported for adult subjects by Lamarra et al. (1987) may be indicative of maturational changes in ventilation. While only speculative, this assertion is supported by incomplete maturation of ventilatory control mechanisms, such as the peripheral chemoreceptors in children (Springer et al. 1988). Others have found evidence for a lower arterial CO_2 partial pressure set-point, (Brady et al. 1964; Brady and Ceruti, 1966) causing higher levels of ventilation for a given $\dot{V}CO_2$ (Cooper et al. 1987; Armon et al. 1991b; Pianosi and Wolstein 1996; Nagano et al. 1998), increased ventilatory sensitivity to CO_2 and greater respiratory responsiveness (Gratas-Delamarche et al. 1993) in children compared to adults.

A means of reducing the distorting effects of breath-to-breath noise and improving the strength of the underlying physiological kinetic response has been implemented by Linnarsson (1974), Whipp et al. (1982) and Lamarra et al. (1987). Several identical trials of the work rate profile are repeated and the breath-by-breath responses averaged together to form a single data file which is used for parameter estimation. By the equation of Lamarra et al. (1987), it is possible to calculate the number of repeated transitions that would be required to obtain a parameter estimate with a specified confidence interval for data containing noise which is Gaussian and uncorrelated:

$$n = \left(\frac{\hat{L} \cdot s}{K_n \cdot \Delta Y_{ss}}\right)^2$$

where n is the number of transitions required, $\hat{L}$ is a constant whose value is contingent upon the response time constant and the fitting window, s is the standard deviation of the variable Y, K_n is the confidence interval, and ΔY_{ss} is the steady-state amplitude of Y above the prior control value.

Although it is not possible to calculate amplitudes of the responses in the present study because measurements were not made at baseline, we can make an assumption of its value. If we assume a mean loadless pedalling $\dot{V}O_2$ of 0.35 $l \cdot min^{-1}$, the largest mean $\dot{V}O_2$ amplitude would be 0.57 $l \cdot min^{-1}$ (subject 7); the corresponding SD is 0.29. In order to gain an estimate of the time constant (approximately 30 s) with a 95% confidence interval of ± 1 s, approximately 232 repetitions would be required. If we accept a 95% confidence interval of ± 2 s, 58 repetitions would be needed, and for a 95% confidence interval of ± 10 s, 2 repetitions would be sufficient. From this analysis the prescription of a set number of repetitions for all subjects may be undesirable. As noted by Whipp (1997), it is imperative that confidence limits be reported so that apparent differences can be evaluated

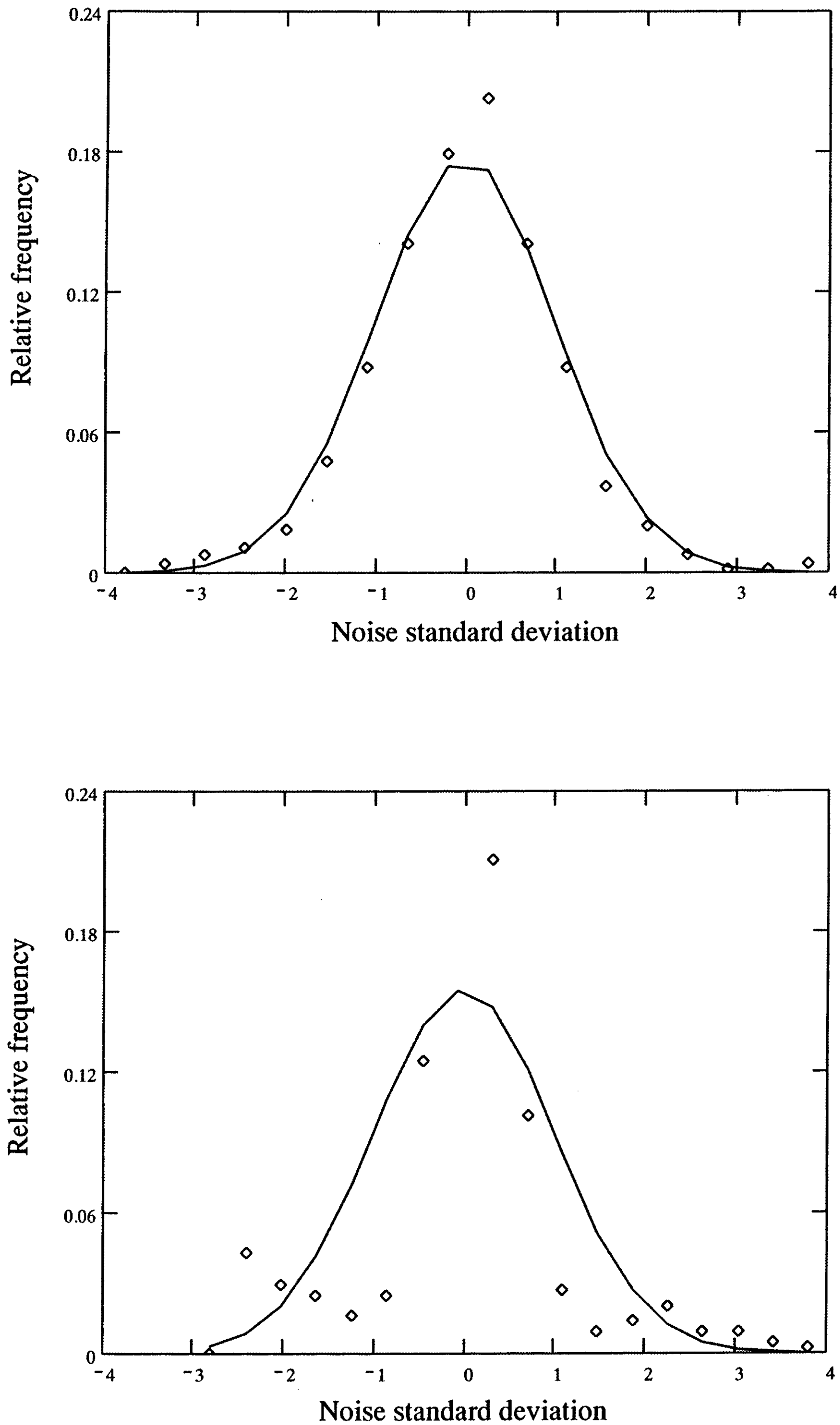

Fig. 1 Oxygen consumption ($\dot{V}O_2$) distribution (*diamonds*) that yielded the smallest (top) and largest bottom χ^2 values when compared to a Gaussian distribution with equivalent parameters (*line*)

statistically. For example, by rearranging the equation, we can calculate the confidence interval that would be associated with a given response amplitude and standard deviation from a single transition. Using the amplitude and standard deviation of subject 7, and an estimated $\tau\dot{V}O_2$ of 30 s as above, a confidence interval of ± 15 s would be gained. For subject 21, whose $\dot{V}O_2$ response produced the highest standard deviation ($0.37\ \mathrm{l \cdot min^{-1}}$), if we assume the same $\dot{V}O_2$ baseline and $\hat{\tau}$, the confidence interval associated with a single transition would be ± 21 s.

It is unwise to attempt to evaluate the effects of maturity or possible adult-child differences on $\tau\dot{V}O_2$ using an estimated value of 30 s with a 95% confidence interval of ± 21 s. Lamarra (1982) asserted that differences in parameter estimates could not be accurately distinguished if their confidence intervals appreciably overlapped. While it is desirable to obtain an estimate of τ

Table 2 Normalised autocorrelation coefficients of the $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}_E$ breath-to-breath noise for breath delays ranging from 1 to 3

Subject	$\dot{V}O_2$			$\dot{V}CO_2$			$\dot{V}_E$		
	Breath delay			Breath delay			Breath delay		
	1	2	3	1	2	3	1	2	3
1	−0.05	−0.15	−0.11	−0.06	−0.15	−0.09	0.06	−0.13	−0.10
2	−0.21	0.15	−0.04	−0.20	0.18	−0.05	−0.06	0.21	0.07
3	−0.16	−0.11	0.01	−0.16	−0.10	0.03	−0.05	−0.01	0.05
4	−0.26	0.13	−0.01	−0.25	0.14	0.01	−0.22	0.15	0.01
5	0.08	−0.18	−0.10	0.06	−0.16	−0.09	0.12	−0.14	−0.09
6	−0.14	0.05	0.03	−0.14	0.05	0.09	0.05	0.15	0.12
7	−0.05	−0.12	−0.09	0.01	0.00	0.00	0.28	0.19	0.15
8	−0.05	−0.12	−0.09	−0.05	−0.11	−0.07	−0.03	−0.09	−0.10
9	−0.01	−0.10	−0.01	0.06	−0.02	0.07	0.16	0.02	0.05
10	0.04	−0.13	−0.08	0.01	−0.12	−0.07	0.13	−0.07	−0.08
11	0.01	−0.07	−0.03	0.03	−0.04	−0.01	0.16	0.05	0.05
12	−0.00	−0.09	−0.02	0.05	−0.04	0.00	0.17	−0.06	0.06
13	−0.03	−0.15	−0.05	0.00	−0.10	−0.01	0.16	−0.02	0.04
14	0.00	−0.11	−0.05	0.03	−0.10	−0.03	0.11	−0.04	0.03
15	0.02	−0.07	−0.01	−0.03	−0.07	0.02	0.08	−0.02	−0.01
16	−0.14	−0.19	0.04	−0.10	−0.12	0.04	0.04	−0.07	0.05
17	0.04	−0.09	−0.13	0.02	−0.08	−0.11	0.09	−0.07	−0.11
18	−0.13	−0.23	−0.10	−0.16	−0.23	−0.07	−0.14	−0.22	−0.08
19	0.04	−0.02	−0.06	0.11	0.06	0.04	0.34	0.17	0.14
20	−0.06	−0.15	−0.07	−0.07	−0.14	−0.07	−0.03	−0.15	−0.09
21	−0.05	−0.07	−0.03	−0.01	−0.02	0.00	0.14	0.04	0.05
22	−0.03	−0.13	−0.11	−0.03	−0.11	−0.09	0.09	−0.04	−0.06
23	−0.11	−0.10	−0.09	−0.12	−0.10	−0.06	0.03	−0.05	−0.05
24	0.01	−0.20	−0.06	0.00	−0.18	−0.04	0.09	−0.12	−0.03

with the highest possible accuracy, a large confidence interval may be acceptable when comparing $\hat{\tau}$ values that are substantially different. Indeed, an appropriate confidence interval may be dependent upon the magnitude of the difference between the values being compared and, as such, will vary.

Lamarra et al. (1987) proposed that prospective experimental subjects should complete a short steady-state exercise test to enable the noise standard deviation inherent in their breathing to be determined. An estimate of the number of transitions that would be required to achieve a nominal parameter accuracy could then be calculated using the equation. The results of the present investigation suggest that such a practice is essential for research projects involving children.

Characterisation of the noise

The autocorrelation function analysis of $\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}_E$ demonstrated very little correlation in the breath-to-breath noise. Autocorrelation function values close to zero indicate rapid variations in the noise from one breath to the next and are characteristic of a response containing noise frequencies covering the entire spectrum (Lamarra et al. 1987). The small autocorrelation function coefficients detected in the present data justify the description of the breath-to-breath noise as uncorrelated (Lamarra et al. 1987).

The distribution of the breath-to-breath noise differed considerably between subjects. In the majority of cases (75%), the distribution of the noise was found to

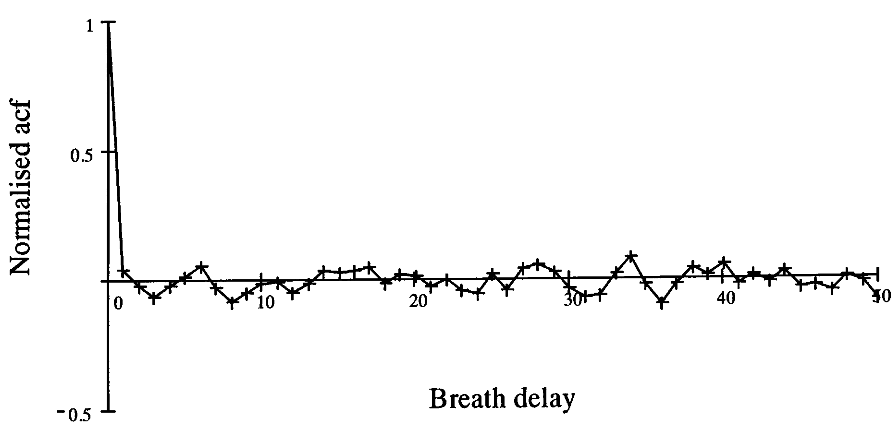

Fig. 2 An example of the normalised autocorrelation function (*acf*) obtained for $\dot{V}O_2$

be significantly different ($P \leq 0.05$) from a Gaussian distribution using the χ^2 goodness of fit test. Although a study involving adult subjects (Lamarra et al. 1987) did not evaluate statistically the goodness of fit of their data to a Gaussian distribution, the adult responses were described as being well approximated by the Gaussian probability density function.

The identification of a non-Gaussian noise distribution in child breath-by-breath ventilatory and gas exchange data may have implications for the characterisation of non-steady-state kinetic responses. It is possible that parameter estimates derived using a non-linear least squares regression may be biased, by an amount that will be dependent upon the bias of the noise. If so, alternative methods for dynamic parameter estimation may have to be considered. Furthermore, averaging several identical repetitions may produce an ensemble data file that is also biased. Although such consequences must be balanced against the effects of using single transitions for parameter estimation that may produce estimates with confidence intervals so large, as demonstrated above, that their value may have little meaning.

Alternatively, the distribution of the breath-to-breath noise may not introduce any significant bias into parameter estimates. This may be the case, for example, if positive and negative noise samples effectively cancelled each other out. Regardless of the possible effects of non-Gaussian noise, it is clear that the assumption of a Gaussian distribution for all experimental subjects is likely to be incorrect.

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