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ORIGINAL ARTICLE

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Interindividual differences in the thermoregulatory response to cool exposure in sleeping neonates

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Abstract The responses of the thermoregulatory effectors vary greatly among neonates. Therefore, we assume that a small decrease in air temperature from thermoneutrality induces various thermoregulatory responses within neonates that represent an energy cost due to the cold defence processes. To determine the importance of this variability in nursing, 26 neonates were explored at thermoneutrality and in a cool environment (−1.5 °C from thermoneutrality) similar to that which occurs currently in clinical procedure. Oxygen consumption ($\dot{V}O_2$), oesophageal and skin temperatures, as well as sleep parameters were recorded continuously in both conditions. Analysis of all of the data from all of the neonates revealed that the cool exposure induced thermal and sleep disturbances, but $\dot{V}O_2$ did not increase and was not negatively correlated to body temperature (as might be expected). Analyses of individual data showed large variability in body temperature regulation: the neonates could be assigned to one of three groups according to the direction of the individual slopes of $\dot{V}O_2$ versus oesophageal or skin temperature. The groups also differed according to the sleep changes recorded in the cool condition. The results show that the definition of thermoneutrality should be revised by incorporating non only changes in the body temperature, but also the sleep disturbances (increased wakefulness and active sleep, decreased quiet sleep), which are criteria that are more sensitive to mild cool exposure. Thermoneutrality should be defined for each individual, since the results stress that the variability does not help to predict a general pattern of thermoregulatory responses in cool-exposed neonates.

Key words Neonate · Thermoregulation · Sleep · Body temperatures

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Introduction

In neonatal units, in order to improve growth pre-term neonates are nursed in a thermoneutral environment, defined as the narrow range of ambient temperatures under which metabolic heat production, as assessed from the rate of oxygen uptake ($\dot{V}O_2$), is minimum (Glass et al. 1968). Above the upper limit, body temperature increases slightly and sweating starts to prevent a further temperature increase. At the same time, $\dot{V}O_2$ can slightly increase through the energetic cost of thermolysis and/or a Q_{10} effect, according to Van't Hoff's law (Adams et al. 1964; Bligh and Johnson 1973; Brück 1992; Heim 1981). Similarly, below the lower limit, the body temperature falls slightly. Thermogenesis, and therefore $\dot{V}O_2$, is increased to prevent any decrease in core temperature. Body temperature stops falling when thermogenesis balances heat loss, and a new steady state is reached.

For practical purposes, some guidelines (Hey 1971; Sauer et al. 1984) define a value of thermoneutral air temperature as assessed on the basis of the age and morphometric parameters of several neonates. But these should be used strictly in the specific environmental conditions for which they were established. They do not take into account interindividual variability, and the thermal condition thus defined does not necessarily fit each neonate's thermal need. Sauer et al. (1984) define thermoneutrality as an ambient temperature at which oesophageal temperature (T_{es}) lies between 36.7 and

37.3 °C, whereas time-derivative patterns of core and skin temperatures (T_{sk}) are less than 0.2 and 0.3 °C h^{-1}, respectively. This definition has the advantage of not referring to an average value, which might hide the interindividual variability. Individual thermal needs and environmental parameters are taken into account since the body temperature equilibrium(T_{eqb}) depends upon both thermoregulatory processes and physical heat exchanges with the environment.

In neonates, there is a large variability in the thermoregulatory responses (Bach et al. 1994; Brück 1961; Edson and Hull 1977; Hull 1976; Smales 1978) that is probably due to the reactivity of the thermoregulatory system, which differs according to the morphofunctional neural organisation of the central nervous system (Murakami and Sakata 1980). Considering this, we assumed that the impact of a small decrease in air temperature (−1.5 °C) from thermoneutrality, as often occurs during nursing care, could induce various thermoregulatory responses within neonates.

The purpose of the present study was to test whether the definition of thermoneutrality should be revised by taking into account the variability of the thermal responses observed in neonates. Since sleep parameters and body movements are both sensitive to cooling (Azaz et al. 1992; Bach et al. 1994; Brück et al. 1962; Fleming et al. 1988), it is held that these variables should be incorporated into the revised definition of thermoneutrality.

Methods

Subjects

Observations were made on 26 healthy neonates (11 boys and 15 girls). Their parents were informed of the protocol and the potential risks and gave their informed consent. The protocol was approved by the local ethics committee (CCPPRB Picardie: 93/18). The neonates were born at [mean (SD)] 34 (2) weeks of amenorrhoea. At the time of the study, the neonates were 22 (10) days old and weighed 2159 (222) g. Neonates who exhibited apnoeas longer than 15 s or bradycardias (fast decrease of instantaneous heart rate below 70 beats min^{-1}) were excluded from the study.

Each neonate was nursed in his or her own incubator at a thermoneutral air temperature, taking into account birthweight and postnatal age (Hey 1971). The humidity of the air circulating in the incubator was set at 55%. Thermal management before and during the experiments was similar for all of the neonates. All were bottle fed with milks of similar composition. The nursing rooms of the Department of Neonatology were climatically controlled (air temperature ≅ 25 °C, relative humidity ≅ 50%).

Physiological recordings

The diaper-clothed neonate was laid in a supine position on a mattress in a closed, convectively heated research incubator in which sleep, $\dot{V}O_2$, and body and air temperatures were monitored continuously.

Sleep and body movements

Sleep was scored from electrophysiological parameters as active sleep, intermediate sleep or quiet sleep (Curzi-Dascalova and Mirmiran 1996). Continuous observations of the behaviour of these babies were performed, noting the duration of whole-body movements accompanied by an increase in instantaneous heart rate. The total duration of body movements is expressed as a percentage of total sleep time. The longest quiet sleep episode (expressed in minutes and in percentages of total sleep time) was analysed. As shown by Parmelee et al. (1961, 1964), the ability to prolong quiet sleep depends upon the development of the central nervous system: as neonates mature the quiet sleep period steadily becomes longer.

Energy expenditure

Metabolic heat production, approximated from $\dot{V}O_2$, was continuously monitored on-line using open-circuit indirect calorimetry. The neonate's head and chest were covered by a Perspex canopy (0.014 $m^3 = 0.25 \times 0.28 \times 0.20$ m), the aperture at the waist being partially closed by a detachable packing to allow passive air entrance. Air inside the canopy was evacuated over the infant's head through a manifold and a mixing box ($0.17 \times 0.12 \times 0.06$ m) at a constant continuously monitored rate of 4.0 l min^{-1} (mass flow controller, Hastings HFC-Series, Teledyne Hastings-Raydist, Hampton, Va., USA; accuracy and linearity: ±1% full scale, reproducibility: ±0.2% full scale 0–10 l). The expired gas from the neonate was carried along with in this gas flow. Gas was pumped from the mixing box at a rate of 18 ml min^{-1} and run through a mass spectrometer (MGA-1100, Perkin-Elmer, Milwaukee, Wisc., USA) to measure on-line O_2 concentration (accuracy better than 1% full scale: O_2: 100%). A secure airtight seal at the waist of the neonate was not essential since the distance between the mouth and the aperture, the high sample flow rate (four times the respiration rate) and a slight subatmospheric pressure within the canopy ensured that the expired gas could not escape from the canopy except via the manifold.

Calibration

The performance of the system was checked, simulating $\dot{V}O_2$ by the injection of gas of known concentrations (Nelson et al. 1987) at the level of the mouth of a doll (the size of a pre-term neonate, with a diaper) placed under the canopy. A flow rate of 1.0 l min^{-1} (mass flow controller, full scale 0–1 l) was chosen because this is approximately the pulmonary ventilation minute volume of a 2-kg neonate.

Repeated measurements were made with different gases [N_2 = 100% (Woodson et al. 1983); O_2 = 12%, CO_2 = 5%, N_2 = 83%; O_2 = 20%, CO_2 = 5%, N_2 = 75%] to check the O_2 detection efficiency as a function of airflow rate out of the canopy. Simulated $\dot{V}O_2$ was calculated continuously according to the formula: "respiratory" flow rate × (0.209−oxygen concentration of the injected gas). Results exhibit increased efficiency (ratio of measured $\dot{V}O_2$/simulated $\dot{V}O_2$) with increased outflow, the maximal efficiency being observed with levels over 3.5 l min^{-1}. At 4.0 l min^{-1}, the accuracy of the system in measuring $\dot{V}O_2$ was better than ±5%, and the efficiency was 94%. There was no effect of incubator temperature (20 °C versus 35 °C). Validation with neonates showed that there was no rebreathing at a flow rate of 4.0 l min^{-1}. At higher flow rates, the frequency of apnoeas increased, or rapid haemoglobin desaturations occurred.

Therefore, $\dot{V}O_2$ (ml min^{-1} kg^{-1}) was calculated on-line according to the formula:

$$\dot{V}O_2 = \frac{1}{m_b} \times \frac{1}{0.94} \times \dot{Q}_{out}(0.209 - F_{out,O_2}) \quad (1)$$

where m_b is body mass (kg), 0.94 is the efficiency of O_2 detection, $\dot{Q}_{out}$ is air outflow (4.0 l min^{-1}), 0.209 is O_2 concentration in the inflowing air, and F_{out,O_2} is the O_2 concentration in the outflowing air. $\dot{Q}_{out}$ and F_{out,O_2} were recorded continuously. Volumes were corrected to standard temperature and pressure dry.

Body temperatures

T_{es} (°C) was recorded by a thermistor probe that was introduced 10 cm into the neonate's oesophagus via the mouth. The thermistor was located close to the segment between the left atrium and the aorta. Mean T_{sk} ($\bar{T}_{sk}$, °C) was calculated from two local skin sensors, one on the right side of the abdomen and one on the right cheek, which represented 30% and 22% of the total body surface area, respectively. Cheek temperature plays an important role in body temperature regulation, since the trigeminal area exhibits a high sensitivity to thermal stimuli (Brück 1961; Mestyan et al. 1964a, b). The temperature probes were stuck onto the skin surface by rubber tape and without any pressure, so that it would not modify temperature measurement. The sensors were shielded by insulated reflective covers to avoid a possible effect of thermal radiation from the surroundings on the temperature measure. Body temperatures, as well as $\dot{V}O_2$, were recorded at 10-s intervals. The accuracy of all temperature readings was 0.05 °C, and the sensitivity to variations was 0.01 °C.

Thermal conditions

The incubator temperature was regulated by controlling the air circulating inside the canopy (T_{inc}, °C), measured by a thermistor located 5 cm below the top of the canopy. This location was chosen to rule out a greenhouse effect inside the canopy. Two different heating programs were used to control T_{inc}. One was based on a set-point value, where T_{inc} was kept constant by a servosystem at a target level set by the experimenter (i.e. heating was provided when T_{inc} fell below the imposed set-point value). The other program (Telliez et al. 1997a, b) dealt with the time derivative of the skin temperature, so that when $\bar{T}_{sk}$ decreased over the last minute (six measurements), the heating of the air entering the incubator was activated for 10-s periods until $\bar{T}_{sk}$ stopped decreasing. This $\bar{T}_{sk}$ servocontrol allows a thermal equilibrium between the air temperature and the neonate's body temperature to be attained after 17 (18) min. Therefore, to ensure that the T_{eqb} had been reached, only the last hour of temperature data recording was taken into account (see Table 1). T_{eqb} is specific to each neonate and fulfils the definition of thermoneutrality as far as body temperatures are concerned. In Table 1, this measure is compared with the thermoneutral air temperature (T_N) formulated by Sauer et al. (1984) [after the first week of life: $T_N = 36.00 - 1.4 \times$ body mass (kg)$-0.03 \times$ postnatal age (days)] and corrected to take into account heat radiation (Hey and Katz 1970: $T_{N\,corrected} = 0.4 \times T_N + 0.6 \times T_{wall}$). At T_{eqb}, body temperatures were compared to the values that fulfil the thermoneutral condition according to Sauer et al. (1984): T_{es} lies in the range 36.7 – 37.3 °C, whereas time variations of T_{es} and $\bar{T}_{sk}$ should be lower than 0.2 and 0.3 °C h^{-1}, respectively.

Experimental design

After being fed by bottle, the neonate was placed in the incubator. The experiment went on until a long period of spontaneous wakefulness occurred, or until feeding or nursing time (approximately 3 h later). The experiments were performed on three consecutive mornings to minimise the strong effects of fast nervous maturation. A first, screening experiment (not analysed in the present paper) was performed at thermoneutrality to ensure that normal sleep was present and to reduce the influence of the "first experiment effect" on sleep. The reference condition was also carried out at thermoneutrality. The T_{eqb} reached during the last hour of the reference condition was used to define the thermal load of the cool condition. The cool condition was set 1.5 °C lower than T_{eqb} to standardise the cool exposure according to each neonate's thermoregulatory requirements. This sequence rules out a possible adaptation of thermoregulatory mechanisms due to cool exposure (Glass et al. 1968).

Statistical analysis

One-sample analyses were performed to compare our thermal results with the values proposed by Sauer et al. (1984) to define thermoneutrality. The variance of T_{eqb} was compared to the expected variance of $T_{N\,corrected}$ (Sauer et al. 1984) by a χ^2 test.

Comparisons between reference and cool conditions for the whole group of neonates were performed using paired t-tests. Analyses of variance, with Greenhouse and Geisser correction (Geisser and Greenhouse 1958), were performed to compare the different thermal conditions and the different groups of neonates. Post hoc t-tests were also performed.

Individual linear regressions were calculated between the $\dot{V}O_2$ values and body temperatures recorded during each sleep stage episode that lasted more than 5 min. In the present study, the regressions were calculated for the three sleep stage values pooled, after verification that for each sleep stage there was no sleep stage effect present on the slope of the regression.

The significance level was set at $P < 0.05$. Indicative results are given when relevant. Data are expressed as the mean values (SD). Results for one neonate were not available under the cool condition because of technical problems.

Table 1 Thermal parameters measured during the last hour of recording during reference and cool conditions, and compared (t-values, degrees of freedom, probabilities) with thermoneutrality as defined by Sauer et al. (1984). Also given are time variations of oesophageal temperature (dT_{es}/dt, absolute value, °C h^{-1}) and mean skin temperature ($d\bar{T}_{sk}/dt$, absolute value, °C h^{-1}) compared with 0.2 and 0.3 °C h^{-1}, and mean oesophageal temperatures ($\bar{T}_{es}$, °C) compared with the range of 36.7 – 37.3 °C. Mean incubator air temperatures ($\bar{T}_{inc}$, °C) measured at thermal equilibrium (T_{eqb}, °C) have been compared with the temperature given by the equation for neutral air temperature as recommended by Sauer et al. (1984) after the 1st week of life, and corrected by Hey and Katz (1970). Data are given as means (SD). (*NS* Non-significant)

Parameter	Reference	Cool	Comparisons with Sauer et al. (1984)	
			Reference versus Sauer	Cool versus Sauer
dT_{es}/dt (absolute value)	0.08 (0.07)	0.13 (0.11)	versus 0.2 °C h^{-1} $t_{25} = 8.78$, $P < 0.001$	versus 0.2 °C h^{-1} $t_{23} = 3.03$, $P = 0.006$
$d\bar{T}_{sk}/dt$ (absolute value)	0.12 (0.07)	0.29 (0.19)	versus 0.3 °C h^{-1} $t_{24} = 12.24$, $P < 0.001$	versus 0.3 °C h^{-1} $t_{18} = 0.33$, NS
$\bar{T}_{es}$	37.11 (1.11)	36.86 (0.23)	versus 36.7 °C h^{-1} $t_{25} = 8.23$, $P < 0.001$	versus 36.7 °C h^{-1} $t_{23} = 3.37$, $P = 0.003$
			versus 37.3 °C h^{-1} $t_{25} = 3.94$, $P < 0.001$	versus 37.3 °C h^{-1} $t_{23} = 9.57$, $P < 0.001$
$\bar{T}_{inc}$ (at T_{eqb})	33.34 (1.11)	31.62 (0.57)	versus Sauer's corrected value = 33.47 (0.17 °C) $t_{25} = 0.55$, NS	$t_{25} = 15.26$, $P < 0.001$

Results

During the last hour of the reference condition, the body temperatures and their rate of change (Table 1) were representative of thermoneutrality as defined by Sauer et al. (1984): the absolute values of the rates of change of body temperature were significantly lower than those recommended, while T_{es} was significantly higher than 36.7 °C and lower than 37.3 °C. In the same way, T_{eqb} did not differ significantly from the mean value of thermoneutrality [$T_{N\,corrected} = 33.47$ (0.17) °C]. T_{eqb} varied widely from one neonate to another, as shown by the magnitude of the SD (1.11) °C, which is larger than Sauer et al.'s predicted SD of 0.65 °C ($\chi^2_{25} = 72.292$, $P < 0.001$).

The cool condition also fulfilled Sauer et al.'s thermoneutrality criterion as far as T_{es} is concerned. However $d\bar{T}_{sk}/dt$ was larger than 0.3 °C h^{-1} in 47% of the neonates, and T_{inc} was lower than the value T_N calculated from the formula of Sauer et al. (1984) and corrected according to Hey and Katz (1970).

Analyses of pooled data

Compared with the reference condition, the cool exposure (Table 2) caused a significant reduction in T_{es} and $\bar{T}_{sk}$. Strikingly, the expected significant increase in the mean value of $\dot{V}O_2$ did not occur ($\dot{V}O_2$ increased in only 10 out of the 25 neonates). $\dot{V}O_2$ was not correlated with T_{inc} in any thermal condition ($P = 0.11$). In the reference condition (Fig. 1), $\dot{V}O_2$ was positively related to T_{es}($F_{1,24} = 6.082$, $P = 0.021$, $r^2 = 0.202$) and to $\bar{T}_{sk}$ ($F_{1,22} = 6.179$, $P = 0.021$, $r^2 = 0.219$), whereas, in the cool exposure, these relationships were not significant (T_{es}: $F_{1,23} = 0.256$, $P = 0.618$, $r^2 = 0.011$; $\bar{T}_{sk}$: $F_{1,20} = 1.187$, $P = 0.289$, $r^2 = 0.056$).

Cool exposure increased the body movements when expressed as percentage of total sleep time [reference: 7.5 (2.6)% versus cool condition: 13.8 (6.1)%; $t_{24} = 5.258$; $P < 0.001$]. It also decreased the total sleep time [reference: 118 (34) min versus cool: 95 (40) min; $t_{25} = 2.74$; $P = 0.011$] as a consequence of an earlier awakening [26 (42) min, $t_{25} = 3.139$, $P = 0.004$], whereas active sleep duration increased [reference: 62 (10)% versus cool: 69 (14)%; $t_{25} = 2.58$; $P = 0.016$] at the expense of quiet sleep [reference: 24(10)% versus cool: 18 (10)%; $t_{25} = 2.95$; $P = 0.007$]. These results are presented in Table 3.

Table 2 Mean (SD) values of incubator air temperature (T_{inc}, °C), oesophageal temperature (T_{es}, °C), mean skin temperatures ($\bar{T}_{sk}$, °C) and oxygen consumption ($\dot{V}O_2$, ml min^{-1} kg^{-1}) during reference and cool conditions (calculated over the whole experiment duration). Statistical results of comparisons between reference and cool conditions are indicated (*t*-values, degrees of freedom and probability)

Parameter	Reference	Cool	Reference versus cool comparisons
T_{inc}	33.22 (0.69)	31.72 (0.57)	$t_{24} = 9.49$ $P < 0.001$
T_{es}	37.05 (0.26)	36.90 (0.19)	$t_{24} = 3.07$ $P = 0.005$
$\bar{T}_{sk}$	36.78 (0.32)	36.45 (0.41)	$t_{21} = 4.78$ $P < 0.001$
$\dot{V}O_2$	6.88 (1.64)	6.55 (1.75)	$t_{24} = 0.28$ NS

Analysis of individual data

The average $\dot{V}O_2$ versus body temperature relationship was investigated further by analyses performed on the individual data (Fig. 2). According to the slopes of the $\dot{V}O_2$ versus T_{es} and $\dot{V}O_2$ versus $\bar{T}_{sk}$ relationships, three groups of neonates (A–C) can be identified. In group A (nine neonates), the slopes were always negative (correlation coefficient, *r*, between −0.45 and −0.90 for T_{es}, and −0.34 and −0.89 for $\bar{T}_{sk}$). In group B (13 neonates), the slopes were always positive (*r* between 0.59 and 0.89 for T_{es}, and between 0.46 and 0.91 for $\bar{T}_{sk}$). In group C (four neonates), the slopes were positive for T_{es} but negative for $\bar{T}_{sk}$ (*r* between 0.80 and 0.91 for T_{es}, and between −0.44 and −0.71 for $\bar{T}_{sk}$). The interindividual differences in response to cool exposure cannot be related to morphometric variables (e.g. gestational age, postnatal age, body mass, height, body surface area or cranial perimeter; Table 4), to T_{inc} or to a gender difference.

In the reference condition (Fig. 3), group B showed higher T_{es} and $\bar{T}_{sk}$ values than the other groups (interactions group × thermal condition: $P < 0.047$). The cool influence was more pronounced in this group since it decreased T_{es}, $\bar{T}_{sk}$ and $\dot{V}O_2$ ($P < 0.035$), unlike the other groups (only one significant result: $\bar{T}_{sk}$ of group A: $t_8 = 2.790$, $P = 0.024$).

In the reference condition, the thermoneutrality criteria of Sauer et al. (1984) were fulfilled for body temperatures and T_{inc} for each group of neonates, with the exception of group B, in which T_{es} was not significantly lower than 37.3 °C [37.21 (0.26) °C, $t_{12} = 1.242$, $P = 0.238$]. As expected, the cool exposure did not fulfil these thermoneutrality conditions for any of the groups.

The cool influence increased body activity whatever the group of neonates [+6 (6)% of total sleep time, $t_{24} = 5.258$, $P < 0.001$]. It tended to decrease total sleep time (Fig. 4, $t_8 = 2.144$, $P = 0.064$) and quiet sleep duration ($t_8 = 2.141$, $P = 0.065$) in group A and increased active sleep duration in group B ($t_{12} = 2.345$, $P = 0.037$). Sleep pattern was not affected in group C. In the reference condition, when the three groups are compared, group B differed from the other groups, with its lower total sleep time (versus group A: $t_{20} = 1.838$, $P = 0.081$; versus group C: $t_{15} = 2.329$, $P = 0.034$). The longest quiet sleep episode did not differ between the three groups of subjects and was not modified by the cool condition.

Discussion

Analysis of the pooled data from all 26 neonates revealed that the cool condition induced lower body temperatures, greater motor activity and sleep changes,

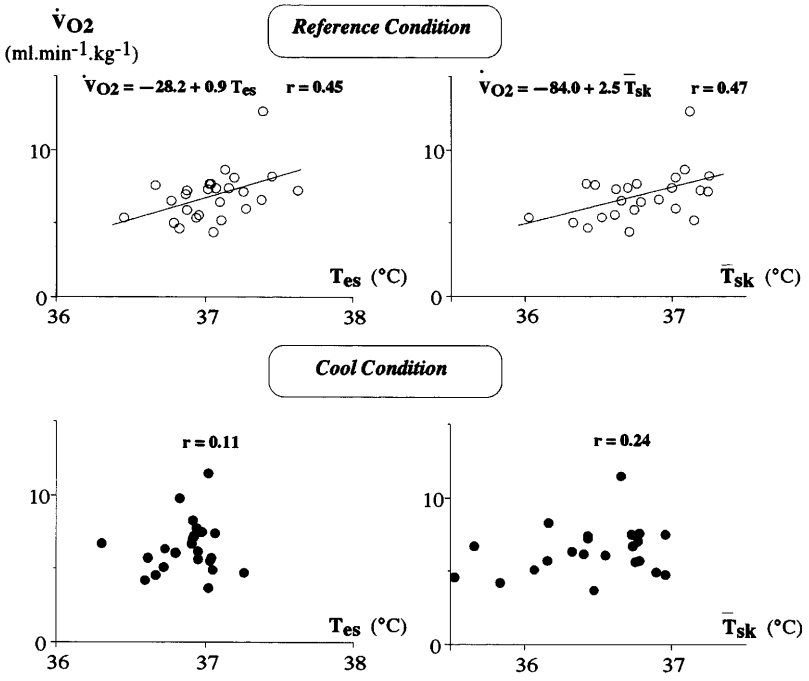

Fig. 1 Oxygen consumption ($\dot{V}O_2$, ml min^{-1} kg^{-1}) as a function of oesophageal (T_{es}, °C) or mean skin temperature ($\bar{T}_{sk}$, °C) in reference (*open circles*, *upper plots*) and cool conditions (*closed circles*, *lower plots*)

Table 3 Sleep parameters in reference and cool conditions. Sleep stages are given as a percentage of total sleep time (or, for wakefulness after sleep onset, as a percentage of global sleep duration). Comparisons (degrees of freedom: 25) between reference and cool thermal conditions are also reported (*t*-test). (*TST* Total sleep time, *WASO* wakefulness after sleep onset, *FSSC* frequency of sleep stage changes)

Parameter	Reference	Cool	Cool versus reference comparisons	
			t_{25}	P
TST (min)	118.0 (34.0)	95.4 (40.1)	2.74	0.011
Active sleep	62 (10)	69 (14)	2.58	0.016
Intermediate sleep	14 (10)	13 (10)	0.43	NS
Quiet sleep	24 (10)	18 (10)	2.95	0.007
WASO	6 (7)	9 (14)	1.22	NS
FSSC (min^{-1})	0.074 (0.027)	0.077 (0.030)	0.58	NS

suggesting that $\dot{V}O_2$, which was not changed, is not the most appropriate criterion for defining thermoneutrality. In most studies performed on neonates, $\dot{V}O_2$ is related to air temperature. From pooled (Adamsons et al. 1965; Hey 1969, 1975; Hey and O'Connell 1970) or from individual data (Grausz 1968; Hey and Katz 1969; Hill and Rahimtulla 1965; Hull and Smales 1978; Mestyan et al. 1964b), authors have reported a negative relationship between $\dot{V}O_2$ and T_{inc}. This temperature, however, in contrast to internal or T_{sk}, is not the thermal input of the thermoregulatory central controller.

Under our experimental conditions, the $\dot{V}O_2$ versus body temperature relationships on pooled data did not show the expected negative correlation. This observation joins those recorded on pooled (Adamsons et al. 1965; Pribylova and Znamenacek 1966; Rutter et al. 1978) or individual data (Hill and Rahimtulla 1965). Some authors found a negative correlation with abdominal temperature (Adamsons et al. 1965) or rectal temperature (Pribylova and Znamenacek 1966). Sulyok et al. (1973) pointed out an average positive $\dot{V}O_2$ versus T_{es} relationship, but only on the warm side of the thermoregulatory range.

In the present study, differences in the relationships between $\dot{V}O_2$ and body temperatures under reference (significant slope) and cool conditions (non-significant slope) are consistent with the data presented by Hill and Rahimtulla (1965). While emphasising that individual $\dot{V}O_2$ was not related to the level or the direction of rectal temperature variation, they assumed that the thermoregulatory response at low environmental temperatures, in contrast to thermoneutral ones, can be overcome by the effect of body cooling on metabolic reactions via a Q_{10} effect (according to Van't Hoff's law applied to homeotherms). A Q_{10} effect has been described by Adams et al. (1964) on 2- to 18-day-old pre-term neonates for rectal temperatures ranging between 32 and 38 °C. If we consider that the ratio of the reaction rates at temperatures differing by 10 °C is about 2:3 (Brück 1992), the variation in T_{es} (36.3–37.6 °C) recorded in the present study would be too small to change appreciably the chemical processes involved in the metabolic rate.

Due to the large interindividual $\dot{V}O_2$ variability (Grausz 1968; Hull and Smales 1978; Silverman and Agate 1964), the averaging of relationships may mask individual thermoregulatory responses. Grausz (1968) assumed that the large amount of scatter in metabolic rate may explain why correlations are only significant for wide ranges of ambient temperature. This probably explains why Rutter et al. (1978) did not find any correlation, since most of their recordings were performed

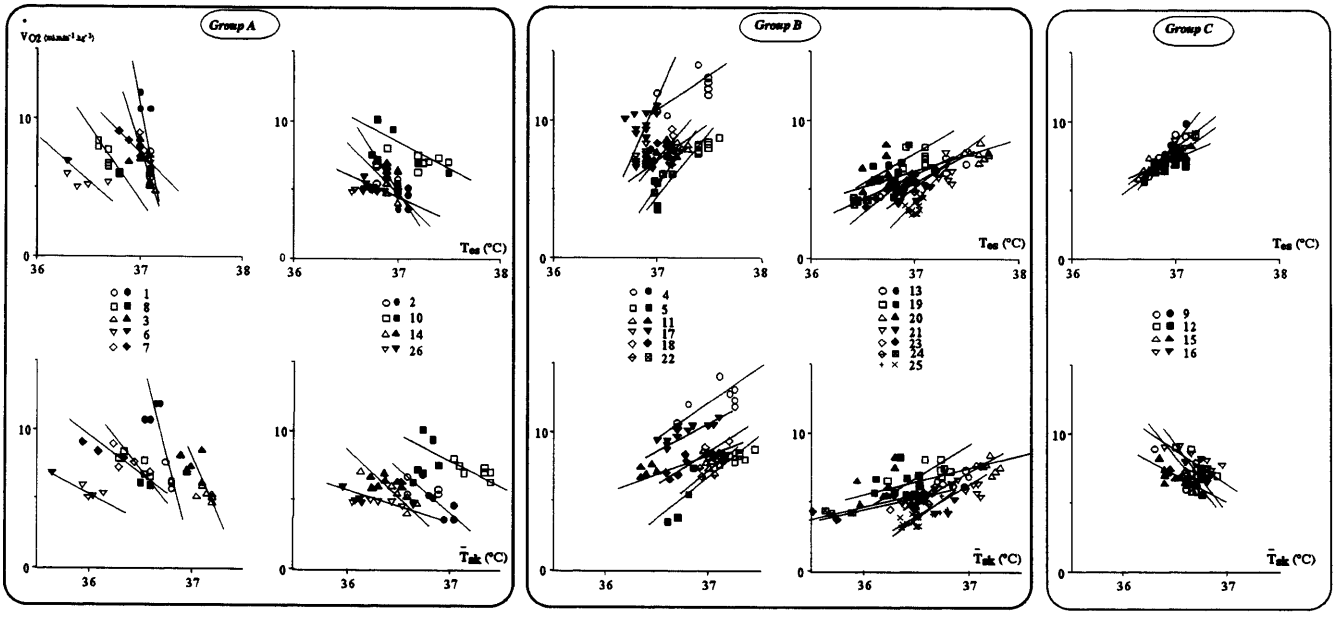

Fig. 2 Individual relationships between mean values of $\dot{V}O_2$ (ml min^{-1} kg^{-1}) and T_{es} (*top*) and between $\dot{V}O_2$ and $\bar{T}_{sk}$ (°C, *bottom*) in the reference (*open symbols*) and cool (*full symbols*) conditions plotted for each "group" of neonates (A, B and C). For clarity, the data recorded from neonates in groups A and B were split into two graphs

at thermoneutrality. In our study, the range of air temperature (30.8–34.4 °C), and therefore of body temperature, was smaller than in most experiments (the largest range, 12–40 °C, was studied by Adamsons et al. (1965).

The results of the present study confirm that there is a considerable variability of thermoregulatory responses among neonates that can mask a possible cool effect when data are pooled, discouraging attempts to make generalisations about neonatal thermoregulatory responses. With respect to thermal and sleep parameters, three strategies can be developed to maintain the body homeothermia.

In group A a peripheral vasoconstriction seems to have occurred, as reflected by changes in body temperatures ($\bar{T}_{sk}$ decreased whereas $T_{es}-\bar{T}_{sk}$ increased). As a result, the convective body heat loss decreased and T_{es} was maintained without any increase in $\dot{V}O_2$. The sleep and motor activity disturbances are in agreement with those reported in the literature (Azaz et al. 1992; Bach et al. 1994; Brück et al. 1962; Fleming et al. 1988; Telliez et al. 1997a).

In group B, the high levels of body temperatures recorded in the reference condition could be attributable to the fact that the air temperature was probably above the thermoneutral zone, as indicated by higher body temperatures than in groups A and C. Hey (1969) and Adamsons et al. (1965) reported that exposure to warm temperatures can increase heat production, but this result remains questionable (Wheldon and Harpin 1982). As a consequence, no vasoconstriction or increase in $\dot{V}O_2$ occurs during the cooler condition. However, the sleep and body movement changes observed are similar to those induced by a cool stimulation. They can therefore no longer be considered as a typical response to cold.

In group C, the cool condition probably still belongs to the thermoneutral zone. Neither increased $\dot{V}O_2$ nor vasoconstriction is necessary since the body's thermal balance is not modified. Although sleep was not altered, body movements increased sharply, suggesting thermal discomfort.

Table 4 Physical parameters of the neonates [mean (SD)] of the three groups of neonates (groups A, B and C) at birth and during the experiments. (*GA* gestational age, *PCA* postconceptional age, *PNA* postnatal age, m_b body mass, *Ht* body height, A_D body surface area, *CrP* cranial perimeter)

Parameter	A		B		C	
	Birth	Experiment	Birth	Experiment	Birth	Experiment
GA (weeks)	34.2 (1.2)	–	33.9 (2.3)	–	33.8 (2.9)	–
PCA (weeks)	–	37.0 (1.1)	–	37.3 (2.0)	–	37.3 (1.3)
PNA (days)	–	20 (7)	–	24 (10)	–	25 (14)
BM (kg)	1.933 (0.317)	2.199 (0.207)	1.778 (0.338)	2.203 (0.229)	1.614 (0.283)	2.029 (0.232)
Ht (cm)	43.3 (2.3)	–	42.6 (2.1)	–	42.9 (2.1)	–
A_D (cm^{-2})	1541 (184)	1665 (113)	1450 (201)	1685 (131)	1354 (172)	1568 (129)
m_b/A_D ($\times 10^{-3}$)	1.25 (0.06)	1.32 (0.03)	1.22 (0.07)	1.31 (0.03)	1.19 (0.06)	1.29 (0.05)
CrP (cm)	30.8 (1.3)	–	30.1 (2.2)	–	30.9 (2.2)	–

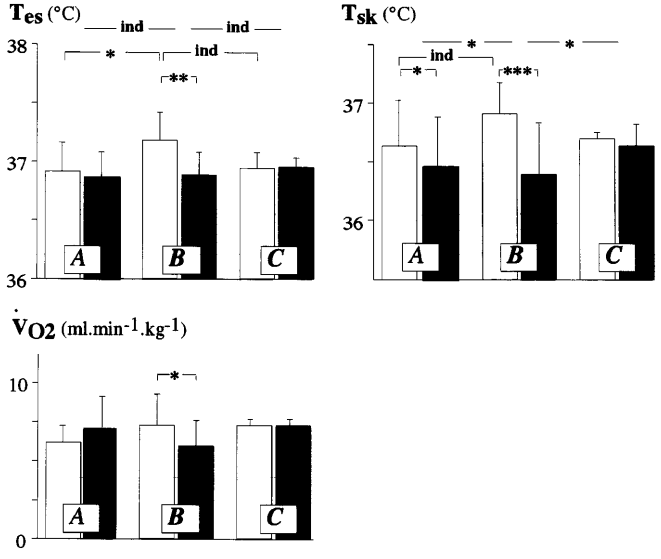

Fig. 3 Thermal and metabolic parameters (means ± SD) as a function of the three groups (A, B and C) and both experimental conditions (reference: *light columns*, cool: *black columns*). The significant (*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$) and indicative (*ind*: $0.05 < P < 0.10$) differences in intra- and intergroup statistical comparisons are shown (below the graph for group differences in one experimental condition, above the graph for group effect on cool response)

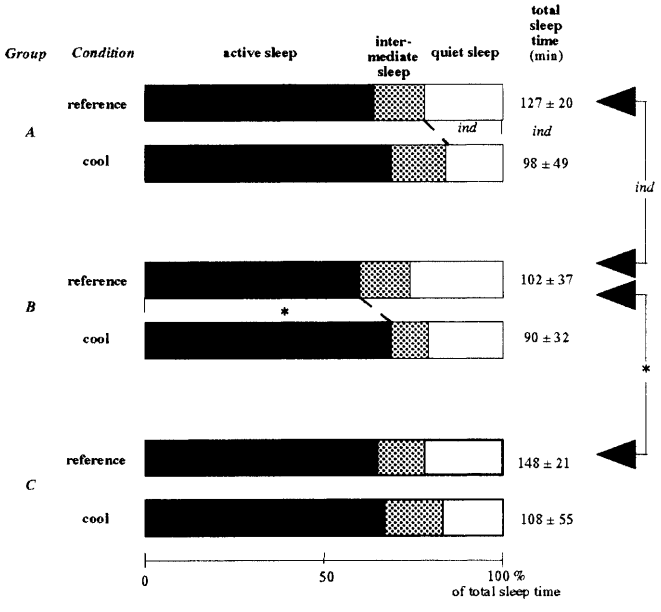

Fig. 4 Sleep parameters (expressed as a percentage of total sleep time) in reference and cool conditions for the three groups of neonates (groups A, B and C). (*IS* Intermediate sleep). *$P < 0.05$; ind: $0.05 < P < 0.10$

Considering the individual thermoregulatory responses, it could be assumed that for air temperature deviations larger than 1.5 °C, the energy cost could be larger in group A than in the two other groups.

Since the longest quiet sleep duration and the morphologic parameters, and their deviation from standards, are considered as indices of maturation, the discrepancy reported above cannot be attributed to a difference in the morphofunctional neural organisation of the central nervous system between the three groups, but rather to the location of the air temperature level according to the thermoneutral zone during the reference experiment. As yet, we have no firm hypothesis on this aspect, which needs further investigations.

In conclusion, in a cool environment, the metabolic cost due to thermoregulatory processes implied in the maintenance of homeothermia should not be evaluated from pooled data. The large variability may mask individual thermoregulatory responses, particularly with small thermal stimulations. Decreases in air temperature as small as 1.5 °C below thermoneutrality have an effect on body temperatures, sleep, and restlessness, although $\dot{V}O_2$ does not generally change. From these results, it can be held that thermoneutrality cannot be defined only on the basis of the thermal parameters, but should also take into account sleep variables, which are criteria that are more sensitive to mild cool exposure than the effector outputs of the thermoregulatory system.

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