Auditory brainstem evoked responses and temperature monitoring during pediatric cardiopulmonary bypass

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Purpose: To examine the effects of temperature on auditory brainstem responses (ABRs) in infants during hypothermic cardiopulmonary bypass for total circulatory arrest (TCA). The relationship between ABRs (as a surrogate measure of core-brain temperature) and body temperature as measured at several temperature monitoring sites was determined.

Methods: In a prospective, observational study, ABRs were recorded non-invasively at normothermia and at every 1 or 2°C change in ear-canal temperature during cooling and rewarming in 15 infants (ages: 2 days to 14 months) that required TCA. The ABR latencies and amplitudes and the lowest temperatures at which an ABR was identified (the threshold) were measured during both cooling and rewarming. Temperatures from four standard temperature monitoring sites were simultaneously recorded.

Results: The latencies of ABRs increased and amplitudes decreased with cooling ($P < 0.01$), but rewarming reversed these effects. The ABR threshold temperature as related to each monitoring site (ear-canal, nasopharynx, esophagus and bladder) was respectively determined as 23 ± 2.2°C, 20.8 ± 1.7°C, 14.6 ± 3.4°C, and 21.5 ± 3.8°C during cooling and 21.8 ± 1.6°C, 22.4 ± 2.0°C, 27.6 ± 3.6°C, and 23.0 ± 2.4°C during rewarming. The rewarming latencies were shorter and Q_{10} latencies smaller than the corresponding cooling values ($P < 0.01$). Esophageal and bladder sites were more susceptible to temperature variations as compared with the ear-canal and nasopharynx.

Conclusion: No temperature site reliably predicted an electrophysiological threshold. A faster latency recovery during rewarming suggests that body temperature monitoring underestimates the effects of rewarming in the core-brain. ABRs may be helpful to monitor the effects of cooling and rewarming on the core-brain during pediatric cardiopulmonary bypass.

Objectif : Examiner les effets de la température sur les réponses du tronc cérébral à des stimuli auditifs chez des enfants pendant la circulation extracorporelle hypothermique dans le cas d'un arrêt circulatoire total (ACT). La relation entre les réponses du tronc cérébral (en tant que mesure substitutive de la température cérébrale centrale) et la température du corps (mesurée à différents points d'enregistrement) a été déterminée.

Méthode : Lors d'une étude prospective d'observation, on a enregistré les réponses du tronc cérébral à des stimuli auditifs, de manière non effractive, à la température normale et à chaque changement de température de 1 ou 2 °C du canal auditif pendant le refroidissement et le réchauffement de 15 enfants (âgés de 2 jours à 14 mois) qui ont eu besoin d'ACT. Les temps de latence et les amplitudes des réponses aux températures les plus basses auxquelles une réponse a été perçue (le seuil) ont été mesurés pendant le refroidissement et le réchauffement. Les températures de quatre points d'enregistrement standards ont été notées simultanément.

Résultats : Les temps de latence des réponses ont augmenté et les amplitudes ont diminué pendant le refroidissement ($P < 0,01$), mais le réchauffement a renversé ces effets. La température du seuil de réponse au canal auditif, au nasopharynx, à l'oesophage et à la vessie a été respectivement déterminée : 23 ± 2,2 °C, 20,8 ± 1,7 °C, 14,6 ± 3,4 °C, et 21,5 ± 3,8 °C pendant le refroidissement et 21,8 ± 1,6 °C, 22,4 ± 2,0 °C, 27,6 ± 3,6 °C, et 23,0 ± 2,4 °C pendant le réchauffement. Les temps de latence du réchauffement ont été plus courts et les temps de latence de Q_{10} plus faibles que les valeurs correspondantes du refroidissement ($P < 0,01$). L'oesophage et la vessie sont des points plus susceptibles aux changements de température en comparaison avec le canal auditif et la nasopharynx.

Conclusion : En aucun point d'enregistrement de la température on n'a pu prédire fidèlement un seuil électrophysiologique. Une récupération plus rapide du temps de latence pendant le réchauffement laisse croire que l'enregistrement de la température corporelle sous-évalue les effets du réchauffement central du cerveau. Les réponses du tronc cérébral aux stimuli auditifs peuvent servir à enregistrer les effets du refroidissement et du réchauffement central du cerveau pendant la circulation extracorporelle chez des enfants.

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HYPOTHERMIA is critical to adequate brain protection in children undergoing total circulatory arrest (TCA) or low-flow procedures.[1] During active body temperature changes, the non-cerebral sites of temperature monitoring have been found susceptible to thermal variations.[2,3] Consequently, inaccurate interpretations may result when these temperature measurements are used as an approximation of the brain temperature.[4] A reliable and non- invasive indicator of the cerebral effects of temperature is, therefore, useful in determining the optimal temperature for brain protection during cardiopulmonary bypass (CPB).

Auditory brainstem evoked responses (ABRs) represent the electrical activation of the subcortical auditory pathway within the first 10 msec following an acoustic stimulus.[5] Their late components, waves III and V, generated by the neural activity between the cochlear nucleus and the inferior colliculus[6] are sensitive to temperature changes in both children and adults.[7-10] Consequently, rather than measuring body temperature, ABRs may reflect more consistently the effects of temperature on the core-brain in children.

The objective of this study was threefold. The first purpose was to evaluate the effects of temperature changes on the latency and amplitude of ABRs in a group of infants undergoing hypothermic CPB and TCA. The second goal was to determine the lowest temperature at which an identifiable ABR was detected during cooling and rewarming (the threshold). Third, ABRs were used to assess the variability of several non-cerebral sites of temperature monitoring currently used during pediatric cardiac surgery.

Methods

After approval by the Human Studies Committee in our institution, ABRs and temperature from four monitoring locations (left ear canal, nasopharynx, esophagus and bladder) were simultaneously recorded in 15 infants (ages: 2 days to 14 months) undergoing CPB and profoundly hypothermic TCA.

Temperature monitoring

Non-cerebral body temperatures were measured by sterile, disposable thermo-couple sensors (Mon-a-therm, Mallinckrodt, St. Louis MO) as follows: in the left ear canal close to the tympanic membrane; in the nasopharynx at the level of the soft palate in contact with the posterior wall, in the esophagus at the level of clearly identifiable cardiac sounds, and in the bladder using a Foley catheter with a thermistor (Smith Industries, Irvine CA). The position of the nasopharyngeal probe was verified by laryngoscopy when necessary. The child's ear canal was inspected for excess cerumen at the time of positioning the probes. No hearing testing was performed prior to surgery. Since the ear canal temperature had been our primary monitoring temperature site for TCA, ABR recordings during temperature variations were primarily related to changes in this temperature.

Auditory brainstem evoked responses

During CPB, ABRs were recorded at normothermia (36.1 ± 0.2°C) and at every 1 or 2°C of change in ear canal temperature from the beginning of cooling (35.7 ± 0.8°C) to the lowest temperature prior to TCA (18.2 ± 0.2°C); and from initial rewarming (19.1 ± 0.3°C) until return to normothermia (35.8 ± 0.4°C).

The ABRs were elicited by monaural clicks (100 μsec) of alternate polarity at intensities of 85 dB nHL (relative to a normal adult group) and stimulus rates of 23.1 per sec. An insert earphone (Etymotic Research, Elk Grove Village, IL) was used to deliver acoustic stimuli to the right ear. The electrical responses from A_1 and A_2 referred to Fz grounded to the forehead were filtered (100-3000 Hz) and digitized (8 bits, maximum sampling rate of 66 KHz per channel) by a Quantum 84 Clinical Averager (Cadwell Laboratories, Kennewick, WA). A 20 msec analysis-time was used and the number of averaged samples for each recording (800-1500 samples) was adjusted to the 1 or 2°C change in ear canal temperature. The final temperature at the end of each ABR recording was documented and traces were stored on disk for off-line analyses. The lowest temperatures with an identifiable wave III during cooling and rewarming were considered as their respective ABR thresholds. No wave III or V was detected between the time cooling was completed and rewarming began.

Anesthetic management

Since previous reports have found no major effects of barbiturates,[5,11] narcotics,[12] ketamine[11] or benzodiazepines[5,11] on the ABR waveforms, anesthetic management was planned as follows: premedication consisted of midazolam *iv*, and patient # 8 received ketamine and midazolam *po* as well. Additional anesthetic management consisted of loading with high-dose, 100-200$\mu g \cdot kg^{-1}$ fentanyl and 0.1-0.2 $mg \cdot kg^{-1}$ midazolam *iv*. Anesthesia was maintained with a constant infusion of 10 $\mu g \cdot kg^{-1} \cdot hr^{-1}$ fentanyl and 50 $\mu g \cdot kg^{-1} \cdot hr^{-1}$ midazolam, except during the period of TCA. Pancuronium and/or vecuronium were used as required for neuromuscular blockade. No volatile anesthetic agents were used.

TABLE I Ages, weights and cardiopulmonary bypass parameters

Case	*Age (days)*	*Weight (kg)*	*Surgical procedure*	*Duration (min) of cooling*	*TCA*	*rewarming*
1	30	3.7	Tetralogy of Fallot repair	23	41	43
2	3	3.7	Arterial switch	24	17	50
3	14*	2.0	Truncus arteriosus repair	21	30	40
4	180*	3.4	PA and valve repair	22	25	45
5	7	3.4	Stage I Norwood	28	59	35
6	52	3.5	VSD and ASD repair	20	36	35
7	19	3.1	VSD, ASD repair	22	43	40
8	362	8.9	Hemifontan procedure	26	45	40
9	3	2.8	Homotopic heart transplant	24	22	35
10	120	5.8	PA reconstr, BDG	29	54	40
11	6	3.4	Arterial switch	30	15	30
12	2	2.6	Stage I Norwood	32	61	40
13	35	4.0	Stage I Norwood	26	56	48
14	60	4.0	VSD repair	20	35	37
15	11	2.5	Truncus arteriosus repair	20	49	40

ASD = atrial septal defect; VSD = ventricular septal defect; PA = pulmonary artery; BDG = bidirectional Glenn shunt, PA = pulmonary artery, reconstr. = reconstruction, * indicates premature gestation (= or < 36 weeks).

TABLE II Individual ABR thresholds, non-cerebral temperature sites and Q_{10} ratios.

	Non-cerebral body temperature (°C)								*Q_{10} wave V latency ratio*	
	ear canal		*nasopharyngeal*		*esophageal*		*bladder*			
Case	*COOL*	*REW*	*COOL*	*REW*	*COOL*	*REW*	*COOL*	*REW*	*COOL*	*REW*
1	25.0	19.3	20.4	23.4	12.0	27.8	26.5	24.1	2.5	1.5
2	21.0	22.5	20.8	20.4	20.0	23.7	21.4	20.0	2.2	1.6
3	24.0	20.2	22.7	20.5	11.9	25.0	21.0	20.5	2.3	1.4
4	22.0	24.0	19.0	24.5	17.0	28.0	16.0	28.4	2.1	2.1
5	25.0	24.0	21.0	25.7	15.5	33.0	22.5	23.9	2.1	1.3
6	23.0	23.5	21.4	24.0	10.8	29.0	19.0	25.0	2.1	1.4
7	19.0	19.0	17.5	20.0	10.4	24.0	19.0	23.3	2.0	1.4
8	26.0	22.0	22.0	22.0	17.6	28.0	23.0	23.0	2.6	1.2
9	26.0	21.9	20.0	22.0	17.0	26.0	20.0	22.0	2.2	1.1
10	24.0	22.7	22.7	20.4	8.9	33.9	14.3	25.4	2.5	1.3
11	21.5	22.8	23.3	20.7	16.0	29.1	22.2	22.3	2.0	1.4
12	25.0	22.0	18.5	26.1	14.1	29.8	30.1	20.6	2.4	1.2
13	22.0	22.0	20.1	23.3	16.7	31.5	23.7	25.1	1.7	1.3
14	20.3	21.0	20.0	20.5	17.0	22.4	21.5	20.0	1.8	1.4
15	21.0	20.1	22.0	22.2	14.2	23.0	22.3	22.0	2.3	1.4
mean	23.0	21.8	20.8	22.4	14.6*	27.6*	21.5	23.0	2.2	1.4†
SD	2.2	1.6	1.7	2.0	3.4	3.6	3.8	1.9	0.3	0.2
MAD	1.9	1.3	1.3	1.7	2.7	2.9*	2.6	1.9		

ABR = Auditory brainstem evoked responses, COOL = Cooling, REW = rewarming, MAD = mean absolute deviations from the mean in °C; SD = standard deviation, * $P < 0.05$ relative to ear canal temperature within the same phase of temperature variation, † $P < 0.05$ relative to the Q_{10} wave V latency ratio during cooling

Method of cooling and rewarming

Hypothermia was attained by core cooling using cooled perfusates delivered via the CPB machine. Temperature of the perfusate was reduced to a minimum of 4°C and cooling was stopped when ear canal temperature reached 18°C. This was complimented by surface cooling using reduced air temperature on the room, a cooling blanket, and ice bags around the patient's head. Ice bags were carefully positioned to preclude contact with the nasopharyngeal or ear canal probes. The time of cooling was defined as the period from the beginning of cooling until the ear canal temperature first reached 18°C (24.5 min ± 4 min). No cooling time was < 20 min (Table I).

Rewarming began immediately with reperfusion. Surface cooling measures were reversed and the water temperature of the heat exchanger was maintained at 5 to 10°C above the patient's ear canal temperature until a maximum perfusate temperature of 39°C was reached. The time of rewarming was calculated from initial rewarming to the time that ear canal temperature reached 35.5°C (40 min ± 5 min; Table I).

Cardiopulmonary bypass

Extracorporeal circulation was achieved using a non-pulsatile pump flow (Sarns model 9000, Ann Arbor MI) with a membrane oxygenator (COBE VPCML plus, Arvada, CO). The $PaCO_2$ during CPB was maintained between 30 and 40 mm Hg uncorrected for body temperature (i.e. alpha-stat). "Full" pump flow typically varied from 140 to 160 $ml \cdot kg^{-1} \cdot min^{-1}$ at normothermia, to 100-120 $ml \cdot kg^{-1} \cdot min^{-1}$ at moderate hypothermia (27 to 28°C) or 50-70 $ml \cdot kg^{-1} \cdot min^{-1}$ during profound hypothermia (< 22°C).

Clinical evolution

The patients were observed in the intensive care unit for seizures, prolonged unconsciousness or motor abnormalities. In case of any abnormal neurological event, this was also documented by electroencephalography (EEG).

Data analysis

Threshold identification was made visually by one of the investigators (RAR). This process was achieved by reviewing the sequence of the stored traces during both cooling and rewarming. In addition, the absolute peak latencies and peak-to-peak amplitudes for waves III and V were measured with an automatic cursor. The amplitude of wave III was calculated between its peak and the preceding negativity. Wave V amplitude was determined between its peak and the following maximum negativity.

Latencies and amplitudes for waves V and III were calculated at the following ear canal temperatures: 36°, 35°, 33°, 30°, 28°, 27°, 26° and 25°C during cooling and rewarming. Since wave V represents the electrical response at the level of the inferior colliculus, a Q_{10} wave V latency ratio was derived from these results by dividing the latency of wave V at ear canal temperatures of 25-26°C by the latency at 35-36° C.[13] This ratio indicates the magnitude of change in latency with a 10°C variation in a non-cerebral temperature.

Statistical methods

Values are expressed as mean ± SD. The threshold temperature was compared across several temperature sites using one-way analysis of variance (ANOVA) with repeated measures followed by comparison of the means by the Scheffé test. The latencies and amplitudes at ear canal temperatures of 35°, 33° and 30°C or the Q_{10} latency ratios between cooling and rewarming were compared by Student t tests. Pearson's correlation coefficients determined the association between two parameters. In addition to the standard deviation, variability of each monitoring temperature site at the threshold was evaluated by the mean absolute deviations (MAD) from the mean. A P value < 0.05 was considered significant.

Results

Table I shows age, weight, cooling, rewarming, CPB and TCA durations for all patients. Neurological complication was documented in three patients who showed seizures and abnormal EEG activity. Two of these infants were discharged with no seizure activity and one died four days after surgery.

Figure 1 illustrates ABR latencies relative to ear canal temperatures. Figure 2 shows typical ABR recordings in a five-week old infant during active temperature changes for TCA. During hypothermia, ABR latencies increased and their amplitudes decreased. All ABR waves were present at ear canal temperatures above 26°C (nasopharynx: 23°C). A 10°C reduction in ear canal temperature from normothermia decreased the amplitude of waves V and III by 30% and 25% respectively. As body temperature continued to decrease and ear canal temperatures reached 23°C, waves V and III were identified in 20% and 53% of our cases respectively. The site-specific ABR group mean thresholds during cooling were 23.0°C ± 2.2 (ear canal), 20.8°C ± 1.7 (nasopharynx), 14.6°C ± 3.4 (esophagus), and 21.5°C ± 3.8 (bladder). One patient did not achieve electrical silence as determined by ABR until nasopharyngeal temperature reached 17.5°C and ear canal temperature was at 19°C. Following reperfusion and during rewarming, the site-specific ABR thresholds were 21.8°C ± 1.6 (ear canal), 22.4°C ± 2.0 (nasopharynx), 27.6°C ± 3.6 (esophagus), and 23.0°C ± 2.4 (bladder) (Table II). When ear canal temperatures reached 23°C, waves III and V had been identified in 67% of our cases, but all components of the ABR waveform were present in all patients when ear canal temperature reached 25°C (nasopharynx: 26.5°C). At this stage, amplitudes of the waves V and III were comparable with 80% and 85% of their respective pre-cooling values. The largest variability of temperature monitoring at the threshold was found for the esophageal temperature followed by the bladder, ear canal and nasopharynx.

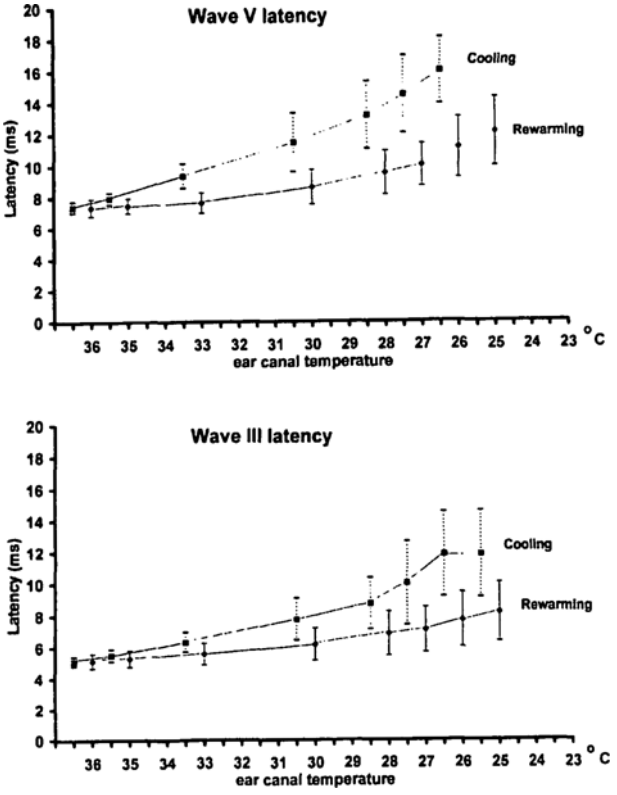

FIGURE 1 Latency changes of waves III and V with variations in ear canal temperature during cooling and rewarming. Latencies doubled at temperatures of 25-26°C compared with initial cooling (35-36°C). Latency variability was greater at lower temperatures during both cooling and rewarming. Latencies during rewarming were shorter than their respective cooling values at similar temperatures. Latency values are indicated as mean ± SD. The horizontal axis offset (0.5°C) between "cooling" and "rewarming" was used to enhance legibility of data.
ms = milliseconds.

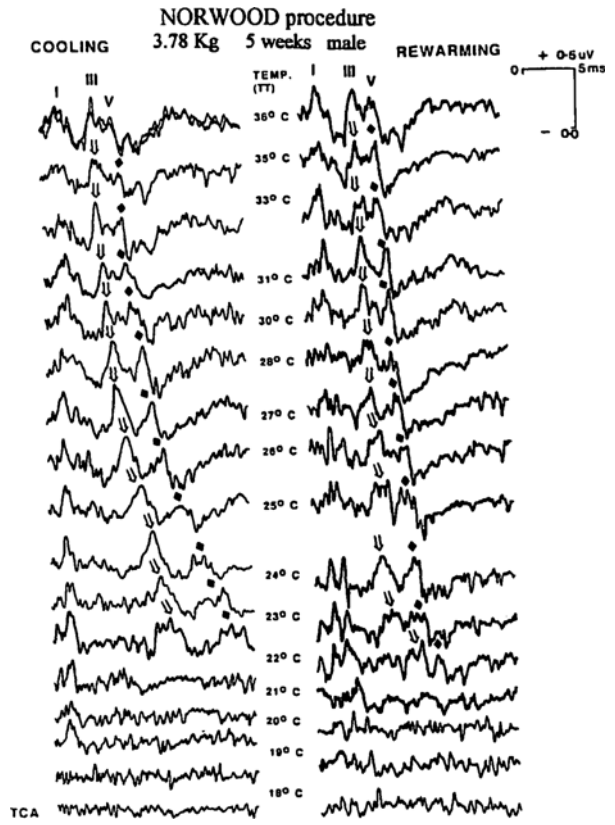

FIGURE 2 Auditory brainstem evoked responses recorded in a five-week old infant (case 13) during hypothermic cardiopulmonary bypass for total circulatory arrest (TCA). In this patient, waves V (♦) and III (⇓) were reliably recorded down to ear canal temperatures of 22°C, which was equivalent to 20.1°C, 16.7°C and 23.7°C measured respectively at the nasopharynx, esophagus and bladder. These temperatures were considered as the cooling ABR threshold. As body temperature continued to decrease, a positive deflection peaking at 2.0 msec was the only detected evoked potential during profound hypothermia. This component disappeared under TCA. During rewarming following TCA, waves III and V were initially detected when ear canal temperatures reached 22°C or 23.3°C, 31.5°C, and 25.1°C recorded respectively in the nasopharynx, esophagus and bladder (rewarming ABR threshold). At the end of rewarming, wave V latency for this patient was 0.3 ms shorter than its counterpart value obtained prior to cooling. ms = milliseconds; μV = microvolts.
TCA = total circulatory arrest, TT: ear canal temperature.

The wave V latencies at 35°C, 33°C and 30°C were shorter during rewarming than during cooling ($P < 0.01$). Consequently, the Q_{10} latency ratios were smaller during rewarming (1.4 ± 0.2) than during cooling (2.2 ± 0.3) ($P < 0.001$). No differences were found between cooling and rewarming ABR amplitudes ($P > 0.10$). In three cases the wave V latency did not return to pre-cooling values (delay: 0.1 to 0.3 msec) at the end of rewarming, but only one patient (case # 12) showed a persistently prolonged wave V latency (0.3 msec) up to the end of CPB. This patient had the longest TCA period, and, during the postoperative follow-up, clinical seizures and abnormal EEG activity were detected. Although his ABR latencies during the initial rewarming were shorter than cooling values, latency delay became apparent toward the end of rewarming. The ABR latencies for the other two cases returned to pre-cooling values at the end of CPB and these patients did not show any adverse clinical neurological signs. No correlations were found among durations of cooling, rewarming or TCA durations and Q_{10} ratios or ABR threshold temperatures.

Discussion

As in previous reports,[7–10] we found that ABR latencies consistently increased and amplitudes decreased when body temperature was reduced. With increases in body temperature by rewarming, the opposite effect was observed. In our study, the lowest temperature where the subcortical auditory electrical activity was detected (wave III) differed between cooling and rewarming, depending on the site of temperature monitoring. Our findings suggest that no temperature site consistently predicts ABR thresholds in infants during active body temperature changes. The esophageal and bladder sites were more susceptible to temperature variations than were nasopharyngeal and ear canal locations. Esophageal temperature, lying in close approximation to the descending aorta, often changed rapidly with CPB perfusate temperature.[4] Bladder temperature tended to respond more slowly,[4] reflecting this being a more "vessel poor" bed than that monitored by the ear canal[14] or nasopharyngeal probes.[2] This is consistent with previous reports[3,4,15] that temperatures measured at different non-cerebral sites vary widely and may not accurately predict brain temperature. Unfortunately, even ear canal or nasopharynx temperatures failed to predict the electrical events in the brain closely, as reflected by ABRs (Table II).

Temperatures from non-cerebral locations during cooling have been found to be higher than actual brain temperatures[2–4,15] but, during rewarming, temperatures commonly underestimate brain temperatures.[4,15] Our results showed shorter ABR latencies and smaller Q_{10} latency ratios during rewarming than during cooling, suggesting that both ear canal and nasopharyngeal temperatures underestimate the rewarming process of the core-brain. These findings might be important as cerebral hyperthermia may occur at the end of rewarming as a result of inaccurate measurements of core body temperature.[16] Thus, ABRs may be a useful monitor during rewarming, where excessive increases in cerebral temperature enhances the susceptibility of the brain to focal ischemic insults[17,18] or to the risk of a dissociated flow/metabolism ratio after TCA.[17]

Hypothermia decreases the brain metabolic activity and slows axonal conduction and synaptic transmission in humans and experimental animals.[19,20] Human neonates[1] usually show Q_{10} metabolic values of 3.7 with hypothermia compared with adult values of 2.8. Our Q_{10} latency ratios averaged 2.2 during cooling, a lower value than expected for brain metabolic suppression induced with 10°C reduction in the infant's body temperature. However, our Q_{10} latency values in young infants, are in agreement with those reported in older children by Kaga *et al.*[8] They suggested that their ABR latencies increased to about 200% with cooling from 36 to 26°C using rectal temperature monitoring.

Study limitations

There is no previous evidence indicating that the ABR threshold correlates with adequate cerebral metabolic suppression prior to TCA. Also, ABRs have not been recorded in cases of excessive rewarming after hypothermic CPB. In order to become clinically applicable, further studies should address the correlation between ABRs and other indicators of brain metabolism[1] or core-brain temperature.[4,15] Furthermore, the small sample size in our study precludes any association with clinical outcome. Interestingly, one patient showed unrecovered wave V latency at the end of CPB and his clinical evolution was followed by postoperative seizures. Although the importance of this finding is unknown, any persistently unrecovered wave V latency at the end of rewarming should alert to the possibility of brainstem dysfunction.

The latency of all ABR components decreases in infants within the first year of life.[5,11] Several factors such as myelination, cochlear maturation, resolution of middle ear abnormalities (fluid, unabsorbed mesenchyme), increased synaptic efficiency and firing synchrony may be responsible for these physiological alterations.[5] Experimental evidence in animals[13] suggests that the immature auditory pathway responds to the effects of cooling with a greater delay in transmitter release and prolonged ABR latencies than does a more mature system. This may indicate an age dependent sensitivity to the effects of brain cooling. In addition, since the temperature of an internal body site is influenced by the rate of blood flow through the site,[2] hemodynamic alterations as a result of the underlying congenital heart disease might account for some variations in the monitoring temperature.

Previous investigations indicate that hypoxic and hypercapnic conditions which depress the electrical activity of the cerebral cortex do not depress ABRs.[21] This seems to suggest that the ABR generating structures are still able to function in the presence of severe deviations from homeostasis. Although ABRs have been used for monitoring brainstem ischemia,[22] cerebral hypoperfusion that quickly results in an isoelectric EEG, does not initially alter the ABRs.[23] This appears to indicate that the brainstem auditory pathway is still capable of generating its electrical response at extremely low levels of blood flow.

The brain structures involved in the generation of ABRs and their resistance to the effects of narcotic-based anesthesia,[11,12] sedatives[11] or nitrous oxide /halothane anesthesia,[5,11] make them useful for moni-

toring the effects of temperature on the core-brain. This pharmacological "resistance" does not extend to enflurane, which has been shown to cause a temperature independent prolongation of the ABR latencies.[24] In experimental animals, cooling temperatures of deep brain structures (e.g. hypothalamus) tend to lag behind cortical cooling by approximately 1.0°C.[14] In humans, Stone *et al.*[4,15] found temperatures 3.6°C higher at deep brain structures relative to the surface, which may be related to the outside brain cooling more rapidly due to the proximity of cerebral arteries.[14] In addition, auditory brainstem regions have the highest levels of glucose utilization[25] indicating that this neural pathway functions at higher levels of local cerebral energy metabolism. Thus, the core brain may still be physiologically active while the cortex has essentially stopped neural activity during cooling. Consequently, in addition to other electrophysiological indicators (e.g. EEG), monitoring ABRs may give another and potentially more conservative guide to determine if brain electrical activity has been adequately suppressed prior to TCA.

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