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Neurological Status of Low-risk Vietnamese Newborns: A Comparison with a British Newborn Cohort

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ABSTRACT

A shortened version of the Dubowitz newborn neurological examination, recently re-assessed in rural Thailand, was applied to a group of 58 Vietnamese newborns. The aim was to establish the neurological status of newborns in this population for use in further studies and to compare with groups previously studied. Compared to the original British cohort, the Vietnamese newborns showed significantly lower scores in 10 of 25 items, including several related to truncal tone. Evidence was sought of thiamine and long-chain fatty acid deficiency as a possible cause for these findings, but no correlation was found between the neurological status and the maternal or infant blood levels of these nutritional indicators. The findings suggest that the neurological status of low-risk Vietnamese newborns appears to lie between that of British newborns and those ethnic minority Karen newborns in refugee camps on the Thai-Burmese border tested previously. Although no specific nutritional cause has been identified in the study, the findings may still reflect sub-optimal intake of some important nutrients.

Key words: Neurological examination; Infant nutrition; Nutrients; Thiamine; Fatty acids; Infant nutritional status; Apgar score; Viet Nam

INTRODUCTION

A shortened and modified version of the method for the neurological assessment of full-term and premature infants, originally developed in 1981 (1), has recently been re-assessed and further developed in rural Thailand. It was shown to be reproducible when administered by local health workers (2). The test uses a proforma with drawings of stick figures to facilitate recording of findings. A series of observations and manoevures are carried out on each baby, including assessment of posture, tone, visual responsiveness, and alertness. Findings are recorded by marking the closest stick figure representation on the proforma for each item which has a score of 1 to 5 (some items do not have all scores available). A score of 3 or 4 is usually considered to be 'normal', but this depends on gestational age. Individual item scores can then be totalled. To establish whether this test can detect possible difference in neurological status, it was also applied to three groups of babies: ethnic minority Karen babies in refugee camps on the Thai-Burmese border (referred to as the Karen) and then in two maternity

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hospitals—one in Bangkok and the other one in London. The study has shown that the Thai and British cohorts only differed in performance on a few items. There were marked differences between the British and the Karen cohort, the latter showing poorer scores on a number of items, including those assessing visual responsiveness and truncal tone. Since the study was conducted, the original full test for the neurological examination of newborns has been updated in 1998 (3,4). The latest version of the assessment includes an 'optimality score' for individual items and for the whole examination to facilitate comparison between infants.

Ethnic differences were considered to be a possible reason for the differences between the Karen and the British cohort but were thought to be unlikely as there was no significant neurological difference between the Thai and the British cohort. Nutritional deficiencies in the Karen population were another possibility as their diet has been deemed to be deficient in micronutrients, particularly thiamine. Both thiamine and long-chain fatty acids have been linked to neuronal maturation (5,6). A further setting was sought where similar nutritional factors may pertain to.

The aims of the present study were (a) to perform the shortened neurological examination, applying the recently-developed optimality score system for the full examination to a further Asian cohort with similar nutritional factors in some respects to those found in the Karen refugee camps and establish if similar findings pertain and (b) to see whether there is any evidence of thiamine or long-chain fatty acid deficiency in the above population and also to see whether any correlation between neurological status and blood-level findings in mothers or infants can be found.

MATERIALS AND METHODS

Location and study population

Subjects for the study were recruited during April 1999 at the Hung Vuong Maternity Hospital in Ho Chi Minh City, a large government hospital serving a largely poor urban and semi-rural population. The Medical and Scientific Committee at the Hung Vuong Hospital approved the study. Infants whose mothers had a first trimester ultrasound for estimation of gestational age and who were delivered vaginally at full-term after an uncomplicated pregnancy and labour were included in the study. Infants with abnormal Apgar scores or requiring admission to the neonatal unit for any reason were not considered. After obtaining written consent from the mother, maternal and cord blood samples were taken for transketolase and fatty acid assay. Details of antenatal history, labour, and delivery were obtained from the mother's records.

Neurological testing

Two examiners (LD and one local member of staff) examined all babies between 6 and 48 hours of age using the shortened version of the Dubowitz neonatal neurological examination described by McGready *et al.* (2). The findings were recorded and scored on proforma sheets as previously described (2). Gestational age was also assessed clinically using the method published by Dubowitz (7).

Optimality scores

The optimality scores, originally derived from the frequency distribution of neurological findings in a large cohort of British babies, were used for scoring neurological findings. The score was based on the distribution of raw scores for each item in a cohort of low-risk term British infants. Certain items showed a significant change with gestational age, even within term infants, and this was taken into account. A raw score was described as optimal if it was above the 10^{th} percentile for that item, borderline if it fell between the 5^{th} and the 10^{th} centile, and sub-optimal if it fell below the 5^{th} centile. The total optimality scores were calculated by summing individual optimality scores in infants with scores for all 25 items.

Transketolase method

Blood samples were separated immediately after collection, and erythrocytes were washed and stored at -7 °C. The measurement of erythrocyte transketolase activity with co-enzyme stimulation was done on a Roche Cobas Fara centrifugal analyzer (Brownes, Reading, UK) by the method of Mount (8). The activation coefficient (α) was calculated as the ratio of red cell transketolase activity after exogenous thiamine had been added to activity before addition of thiamine. Higher values of α indicate greater transketolase stimulation in response to thiamine and, therefore, pre-existing thiamine deficiency. Thiamine deficiency was defined as an α value greater than 1.19 and serious deficiency as an α value greater than 1.25 (9).

Measurements of fatty acids

Total plasma lipids were extracted by the method of Folch *et al.* (10) by homogenizing the samples in chloroform and methanol (2:1 v/v) containing 0.01% butylated hydroxytoluene under nitrogen. Choline phosphoglycerides were separated by thin-layer chromatography on silica plates using the developing solvents—chloroform:methanol:water (60:30:4)—containing 0.01% butylated hydroxytoluene. Bands were detected by spraying with 2,7-dichlorofluorescein and visualized under ultraviolet light. Fatty acid methyl esters were prepared by heating the lipid extract with 4 mL of 15% acetyl chloride in methanol in a sealed tube at 70 °C for three hours under nitrogen. Fatty acid methyl esters were separated by a gas-chromatograph (HRGC MEGA 2 series, Fisons Instruments, Milan, Italy) fitted with a capillary column (25 m x 0.32 mm ID, 0.25 μ film, BP 20). Hydrogen was used as a carrier gas, and the injector, oven and detector temperatures were 235, 210 and 260 °C respectively. The fatty acid methyl esters were identified by comparing retention time with authentic standards (Sigma-Aldrich Co. Ltd., UK) and calculation of equivalent chain-length values. Peak areas were quantified by a computer chromatography data system (EZChrom Chromatography Data System, Scientific Software Inc., San Ramon, CA).

Statistical analysis

Fisher's exact test was used for comparing the distribution of each neurological item between the Vietnamese and the British cohort.

The distribution of total optimality scores was compared between the two cohorts using the Mann-Whitney U test. Pearson's product moment correlation coefficient was calculated to measure the association between the maternal and infant transketolase α values and the fatty acid levels. The maternal and infant transketolase and fatty acid levels were compared between optimal and non-optimal infants using the unpaired *t*-test. The transketolase levels in Vietnamese, British and Karen cohorts were compared using the chi-squared test.

Data were analyzed using the SPSS for Windows, version 9 (SPSS Inc., Chicago, IL), and any p value of <0.05 was considered to be statistically significant.

RESULTS

Fifty-eight Vietnamese babies were examined. Their mean age was 25 (range 17-48) hours with a mean gestational age of 39.9 (range 38.1-41.8; standard deviation [SD] 0.8) weeks. Characteristics of mothers and babies are shown in Table 1.

Gestational age

The clinical method showed a good correlation to the antenatal ultrasound assessment (data not shown) and was, thus, used for this study for allowing for the possibility of comparing these results with future rural cohorts.

Individual item optimality scores

Table 2 shows the optimality scores (i.e. 1=optimal, 0.5=borderline, 0=sub-optimal) given to the corresponding raw scores of each neurological item. Table 3 shows the comparison of the optimality scores where significant differences were found between the Vietnamese and the British cohort. Five of 10 items where significant differences were found related to truncal tone, posture, head control 1 and 2, head lag, and ventral suspension. There were also significant differences in some other items, namely spontaneous movement, startle, visual alertness, moro response, and placing response. In most instances, the percentage of optimal scores did not reduce because of an increase in sub-optimal scores but due to a greater percentage of borderline scores.

Total optimality scores

The total optimality score was significantly ($p<0.001$) lower for the Vietnamese babies compared to the British babies. Only 50% of the Vietnamese babies had a total optimality score of ≥22.5, that is the 10^{th} percentile of the British babies.

Table 1. Characteristics of Vietnamese mothers and infants (n=58)

Characteristics	Mean (SD)	Range
Age (years) of mother	26 (5.4)	19-39
Weight (kg) of mother	56 (6.2)	44-78
Height (cm) of mother	155 (4.6)	145-168
Number of years of education of mother	8 (3.1)	3-15
Birth-weight (g) of infant	3,061 (350)	2,400-3,800
Head circumference (cm)	32 (1.3)	28-34
Time cord-blood taken (minutes) median	0	0-80
Time maternal blood taken (hours)	23 (10)	3-43
	No.	%
Sex: male	34	59
Live in Ho Chi Minh City	29	50
Live in rural province	29	50
Baby born following spontaneous labour	57	98
Analgesia needed by mother at delivery	3	5
Mode of delivery		
Vaginal	51	88
Vacuum extraction	5	9
Forceps	2	3

SD=Standard deviation

Table 2. Optimality scores derived from raw scores*

Neurological item	Gestational age (weeks)	Optimality score		
		1	0.5	0
		Raw score		
Posture	37-38	4; 3		<3; 5
	39-40	4	3.5; 3	<3; 5
	41-42	4	3.5	<3.5; 5
Arm recoil	37-38	4; 3	2.5	<2.5; 5
	39-40	4; 3	2.5	<2.5; 5
	41-42	4; 3		<3; 5
Arm traction	37-38	4; 3		<3; 5
	39-40	4; 3		<3; 5
	41-42	4; 3		<3; 5
Leg recoil	37-38	4; 3		<3; 5
	39-40	4; 3.5	3	<3; 5
	41-42	4; 3.5	3	<3; 5
Leg traction	37-38	4; 3		<3; 5
	39-40	4; 3		<3; 5
	41-42	4; 3.5	3	<3; 5
Popliteal angle	37-38	4; 3	2.5; 2	<2; 5
	39-40	4; 3		<3; 5
	41-42	4; 3		<3; 5
Head control 1	37-38	4; 3		<3; 5
	39-40	4; 3		<3; 5
	41-42	4; 3		<3; 5
Head control 2	37-38	4; 3		<3; 5
	39-40	4; 3		<3; 5
	41-42	4; 3		<3; 5
Head lag	37-38	4; 3; 2		<2; 5
	39-40	4; 3; 2.5	2	<2; 5
	41-42	4; 3	2.5	<2.5; 5
Ventral suspension	37-38	4; 3	2.5	<2.5; 5
	39-40	4; 3	2.5	<2.5; 5
	41-42	4; 3		<3; 5
Spontaneous movement		4	3	<3; 5
Tremor		3; 2; 1		>3
Startle		1; 2	3	>3
Auditory orientation		4; 3; 2		<2; 5
Visual red wool		4; 3	2	<2; 5
Alert red wool		4; 3	2	<2; 5
Peak excitement		2; 3	1	>3
Consolability		3; 2	4	<2; 5
Hand posture		2; 1		>2
Sucking		3	2	1; 4
Palmar grasp		4; 3	2	<2; 5
Plantar grasp		3		<3
Moro	37-38	4; 3		<3; 5
	39-40	4	3; 3.5	<3; 5
	41-42	4	3.5	<3.5; 5
Placing		3	2	<2
Eye orientation		1; 2		3

*A score is described as optimal (1) if it was above the 10th percentile in the British cohort for that item, borderline (0.5) if it fell between the 5th and the 10th centile, and sub-optimal (0) if it fell below the 5th centile

Transketolase levels

Eleven mothers showed 'serious deficiency,' and nine showed marginal deficiency. Only one infant was 'seriously deficient,' and six were marginally deficient. A positive correlation was found between the maternal and the infant erythrocyte transketolase activity level (r=0.396, p=0.003). No significant difference was found between the erythrocyte transketolase activity levels for Vietnamese mothers and either British (p=0.41) or Karen mothers (p=0.07) tested previously (11). There was no significant difference between the erythrocyte transketolase activity levels for Vietnamese and British cord-blood samples (p=0.42). However, significantly more Karen infants were deficient compared to Vietnamese infants (p=0.003).

Fatty acid levels

The fatty acid levels seen were similar to levels measured in other Asian populations (12). There was a positive correlation between maternal and infant docosahexaenoic acid (r=0.39, p=0.013) and maternal and infant ascorbic acid levels (r=0.325, p=0.041).

Table 3. Comparison of optimality scores for Vietnamese and British cohorts (only including babies with a gestational age between 38.0 and 41.9 weeks)

Neurological item	Optimality score	Vietnamese % (no./total no. tested)	British % (no./total no. tested)
Posture	1	32.8 (19/58)*	94.1(160/170)
	0.5	67.2 (39/58)	4.7 (8/170)
	0	0	1.2 (2/170)
Head control 1	1	82.8 (48/58)*	96.5 (164/170)
	0	17.2 (10/58)	3.5 (6/170)
Head control 2	1	81.0 (47/58)*	96.5 (164/170)
	0	19.0 (11/58)	3.5 (6/170)
Head lag	1	56.9 (33/58)*	94.7 (161/170)
	0.5	31.0 (18/58)	5.3 (9/170)
	0	12.1 (7/58)	0
Ventral suspension	1	75.9 (44/58)*	94.7 (160/169)
	0.5	12.1 (7/58)	3.6 (6/169)
	0	12.1 (7/58)	1.8 (3/169)
Spontaneous movement	1	87.9 (51/58)*	74.3 (124/167)
	0.5	12.1 (7/58)	24.0 (40/167)
	0	0	1.7 (3/167)
Startle	1	75.9 (44/58)*	98.2 (163/166)
	0.5	20.7 (12/58)	1.8 (3/166)
	0	3.4 (2/58)	0
Alertness to red woolly ball	1	64.2 (34/53)*	87.6 (134/153)
	0.5	32.1 (17/53)	10.5 (16/153)
	0	3.7 (2/53)	1.9 (3/153)
Moro	1	44.8 (26/58)*	83.5 (137/164)
	0.5	22.4 (13/58)	11.6 (19/164)
	0	32.8 (19/58)	4.9 (8/164)
Placing	1	70.2 (40/57)*	83.4 (136/163)
	0.5	28.1 (16/57)	15.3 (25/163)
	0	1.7 (1/57)	1.3 (2/163)

P value in Fisher's exact test: *=Significant difference; p<0.05
No significant differences were observed in the remaining items, namely: arm recoil, arm traction, leg recoil, leg traction, popliteal angle, tremor, auditory orientation, visual red wool, peak excitement, consolability, hand posture, sucking, palmar grasp, plantar grasp, and eye orientation

Comparison of neurological findings with transketolase and long-chain fatty acid levels

No significant differences were found in maternal and infant transketolase levels between infants with different total optimality scores and different selected optimality scores for individual items, although a trend was seen in head control 2 where infants with not-optimal head control 2 had higher infant transketolase levels (p=0.056;

Table 4). There were also no significant differences in either docosahexaenoic acid or ascorbic acid levels between infants with different total optimality scores and different optimality scores for individual items (data not shown).

Table 4. Comparison of maternal and infant ETKA levels with optimality scores for assessed items and total/total tone optimality scores

Neurological item	Maternal ETKA			Infant ETKA		
	No.	Mean (SD)	p value	No.	Mean (SD)	p value
Head control 1						
Optimal	48	1.17 (0.10)	0.651	45	1.10 (0.07)	0.501
Not optimal	10	1.15 (0.07)		9	1.12 (0.05)	
Head control 2						
Optimal	47	1.16 (0.10)	0.599	45	1.09 (0.07)	0.056
Not optimal	11	1.18 (0.07)		9	1.14 (0.06)	
Head lag						
Optimal	33	1.17 (0.10)	0.854	31	1.10 (0.07)	0.954
Not optimal	25	1.16 (0.09)		23	1.10 (0.07)	
Ventral suspension						
Optimal	44	1.16 (0.10)	0.891	42	1.10 (0.07)	0.275
Not optimal	14	1.17 (0.09)		12	1.12 (0.05)	
Visual red wool						
Optimal	40	1.16 (0.10)	0.881	39	1.11 (0.07)	0.242
Not optimal	13	1.16 (0.09)		10	1.08 (0.04)	
Alert red wool						
Optimal	34	1.15 (0.09)	0.356	33	1.11 (0.07)	0.484
Not optimal	19	1.18 (0.11)		16	1.10 (0.07)	
Total optimality score						
<22.5*	24	1.14 (0.10)	0.179	22	1.11 (0.06)	0.800
≥22.5	24	1.17 (0.08)		22	1.11 (0.08)	
Total tone optimality score						
<8.65*	28	1.17 (0.10)	0.918	26	1.11 (0.07)	0.312
≥8.65	30	1.16 (0.10)		28	1.09 (0.07)	

*10th percentile for British cohort
ETKA=Erythrocyte transketolase activity; SD=Standard deviation

DISCUSSION

The shortened neurological examination for term neonates, developed for use in resource-poor settings in Thailand, proved again to be simple and appropriate to administer. We could demonstrate in this population a difference in neurological status compared to the British one. Problems similar but to a lesser degree than those previously observed in a Karen refugee population were observed on tone items and visual alertness.

We also aimed at investigating whether the differences observed in the neurological state of this partly rural and partly urban Vietnamese population might be associated with some specific nutritional deficiencies. We found no deficiencies in long-chain fatty acids that have been linked to neurological abnormalities, particularly to delayed visual maturation in previous studies. As in the Karen population, who had somewhat similar neurological findings, we observed thiamine deficiency in mothers though considerably less severe than found in those of the Karen refugee camps. We did not demonstrate an association between the transketolase levels and the sub-optimal neurological findings. However, the correlation between individual transketolase levels and neurological findings is known to be poor in both adults and children (13). In future studies, it may be worth considering other nutritional deficiencies which it was not possible to measure in this study.

In this study, we applied the gestational age-corrected optimality score as outlined above to the shortened neurological examination. We used both optimality score for individual items and total optimality score. The optimality score has definite advantages when comparing large cohorts where the gestational age of full-term infants might be spread over several weeks. It should, however, be used with caution as it might mask where the neurological differences lie, unless the distribution of the normal, sub-optimal and borderline scores is more closely inspected. This was highlighted in this cohort where most reduction in optimal scores was due to an increase in borderline scores. Severe neurological abnormality is more often associated with a severe shift towards the sub-optimal score in many items. In these situations, it may be helpful to look at the frequency distribution of the raw scores. The optimality scores on British babies have been used here as a reference to allow comparisons between infants in different settings. The British optimality score, however, reflects the optimality of infants in a different ethnic, nutritional and socioeconomic setting and should not, therefore, be used as a gold standard for future studies in this setting. Although the neurological findings were not optimal in terms of a British population, this sample represents a relatively problem-free newborn population in Viet Nam and could be used as a baseline for comparison with infants who might have had an insult in the antenatal and perinatal period or come from even less-privileged surroundings.

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