Saliva cortisol as a criterion for pain assessment in children with severe neurological impairment.

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BACKGROUND. Median unstimulated saliva cortisol concentrations in the region of 8 to 11 nmol/L have been reported for healthy children. Serum and saliva cortisol are expected to increase under conditions of stress and have been shown to increase in infants and children with acute pain. Only one previous study has examined saliva cortisol in children with neurological impairments (1). In that study the diurnal rhythm characteristic of cortisol release was found to be absent in several children both with and without impairments.

AIMS. The study reported formed part of the validation process of the Paediatric Pain Profile (PPP), a 20-item behaviour rating scale designed to assess pain in children with severe to profound neurological disability (2).

In order to support the scale's validity, the hypotheses were that both PPP score and saliva cortisol concentration would 1) be higher in children with 'high pain' than 'low pain' and 2) saliva cortisol concentration would positively correlate with the total PPP score.

METHODS. Two groups of children were identified from an earlier parental survey, 19 reported to have daily pain of at least moderate severity ('high pain' group) and 10 reported to have no or minimal pain ('low pain' group).

Children (mean age 9.7 ± 5.5) were filmed undergoing five everyday morning activities and unstimulated samples of saliva were collected using the Salivette™. Saliva samples were also collected on a demonstration day and by parents on a reference day in the absence of the investigators. Saliva samples were analysed for cortisol by radioimmunoassay. Five three-minute episodes of film were scored independently by three raters using the PPP and associations between saliva cortisol and PPP score explored. During filming, children were assessed for hip dislocation and spinal curvature and their motor skills and function assessed using the Gross Motor Function Measure (GMFM).

RESULTS.

Table 1. Population characteristics for total population and by pain group.

Pain groups	All	High pain	Low pain	P†
N	29	19	10	
Age (years)	9.7 ± 5.0	9.9 ± 4.5	9.6 ± 5.8	0.859
GMFM	13.4 ± 18.8	9.4 ± 14.7	20.9 ± 23.9	0.056
Pain history (Y:N)	22:4	16:0	6:4	0.014
History of hospitalisations (Y:N)	14:12	11:5	3:7	0.105
History of significant surgery (Y:N)	18:8	15:3	1:7	0.001
Dislocated hip (Y:N)	12:17	10:9	2:8	0.126
Scoliosis (Y:N)	18:11	15:4	3:7	0.017
Kyphosis (Y:N)	8:21	8:11	0:10	0.027

† Statistics calculated are the independent samples t-test and Fisher's Exact test.

Table 2. Median saliva cortisol concentration for total population and by pain group.

Saliva cortisol concentration (nmol/L)	N Groups (H:L)	All Median	High pain Median	Low pain Median	P†
Morning samples					
Control day	22 (14:8)	5.08	5.75	3.08	0.267
Filming	25 (15:10)	5.60	7.90	4.56	0.008
Afternoon samples					
Control day	20 (13:7)	1.90	2.30	1.55	0.183
Demonstration day	24 (17:7)	2.80	3.00	1.70	0.166

† Statistics calculated are the Mann-Whitney test.

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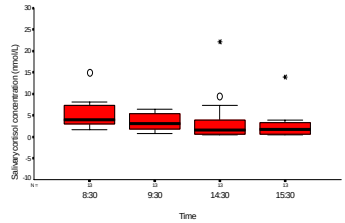
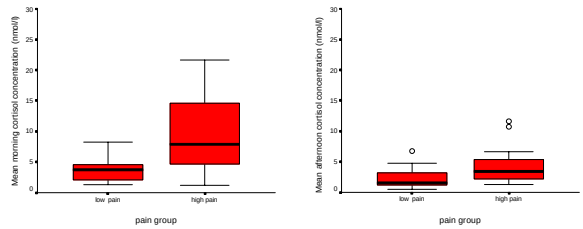
Figure 1. Boxplots of saliva cortisol concentration (nmol/L) collected on reference day (times approximate).



Circadian rhythm was apparent in all but three children. In two of these, higher afternoon concentrations were associated with afternoon behaviour suggestive of pain.

With data from demonstration, reference and video days aggregated, median morning cortisol concentration was 5.3 nmol/l (90% between range 1.2, 20.5) and afternoon 2.8 nmol/l (90% between range 0.5, 11.2). Children in the high pain group had significantly higher salivary cortisol both in the morning (median 7.9 vs 3.7 nmol/l. MW test p=0.010) and the afternoon (median 3.3 vs 1.5 nmol/. MW test p=0.031). **(Figures 2 and 3).**

Figures 2 & 3. Boxplots of aggregated morning and afternoon saliva cortisol concentrations (nmol/L).



Depending upon video-rater, correlation between PPP score (mean during five morning activities) and saliva cortisol concentration was moderate at from 0.378 to 0.451(R_S). PPP scores of each rater differentiated between high and low pain groups (MW test 0.011 to 0.033).

In a stepwise regression analysis with area under the curve (AUC) for saliva cortisol on the reference day as the dependent variable and age, sex, pain group and receiving budesonide or not as independent variables, administration of budesonide explained 22% of the variance in AUC (F= 4.66, P=0.047). No other variable was a contributing factor. On the morning of filming, pain group explained 22% of the variance (F = 6.33, P=0.019). When the variable 'pain group' was replaced in the analysis by the PPP score this explained 27% of the variance in saliva cortisol concentrations (F=8.51, P= 0.008).

CONCLUSION. The results support the concurrent validity of the Paediatric Pain Profile. Whilst saliva cortisol was higher in a high than a low pain group and correlated with pain behaviour, concentrations of cortisol overall appear lower than those reported elsewhere. Medication may be an interacting factor, but there are other possibilities such as early exposure to adverse or nociceptive events, prolonged pain history or the central nervous system disease itself. Further investigation is warranted.

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2. Hunt AM. Towards an understanding of pain in the child with severe neurological impairment