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Mörelius, E., Ivars, K., Gustafsson, P., Theodorsson, E., Nelson Follin, N., (2017), Salivary cortisol circadian rhythm in infants at psychosocial risk showed more variations than previous studies of healthy full-term infants, *Acta Paediatrica*, 106(12), 2060-2061. <https://doi.org/10.1111/apa.14023>

Original publication available at:

<https://doi.org/10.1111/apa.14023>

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Salivary cortisol circadian rhythm in infants at psychosocial risk showed more variations than previous studies of healthy full-term infants

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Healthy infants establish a salivary cortisol circadian rhythm (SCCR) at one month of age (1). This study investigated the development of SCCR in infants at high psychosocial risk, by measuring salivary cortisol levels during their first year of life and evaluating whether those were related to behavioural regularity.

This longitudinal study comprised 25 infants (52% girls) from 17 families with psychiatric problems and eight with social problems. The infants were born at a mean (range) gestational age of 39+3 (34+6 to 42+1) weeks and were consecutively recruited when the families enrolled in a six-week daycare programme, for three days a week, which aimed to improve parent-child interaction (2).

The study began during the infants' first week at daycare, when they were 1-9 months, and ended when they were 12 months old. The majority of the infants ($n=20$) had been enrolled by the age of three months, with a further two at four months and one each at five, six and nine months. The number of samples rose and fell throughout the study period, ranging from one infant at one month to 21 infants at 12 months (Table 1). Saliva samples were obtained at home, on two consecutive weekdays each month, at least one hour after the infant slept, cried, travelled by car or was fed. Sampling was conducted between 7.30am-9.30am, 10.00-12.00pm and 19.30-21.30pm. A competitive radioimmunoassay was used to analyse duplicate samples for cortisol concentrations and the inter-assay coefficients of variation were 12% at 2.0 nmol/L and 6% at 10.0 nmol/L. Prior to the non-parametric statistical analysis, the averages for the morning and evening concentrations from the two consecutive weekdays were calculated for each infant per month. To avoid weighting certain individuals higher because of large inter-individual differences in absolute cortisol concentrations, an evening and morning cortisol index was calculated for each individual by dividing the evening cortisol value by the morning cortisol value on that particular day, with higher values indicating less established SCCR. SCCR was defined as a 20% drop in the ratio between evening and morning cortisol levels. Behavioral regularity was studied monthly using six

items from the Baby Behavior Questionnaire (4). The regional ethical board at Linköping University approved the study (number M196-06).

We collected 1,204 (80%) out of a possible 1,506 saliva samples and these showed that the 12 infants who had been recruited in months one and two had established SCCR by the first measurement in month two and that this persisted throughout the year (Table 1). Behavioral regularity increased between months 3-6 ($p < 0.05$), but not between months 6-12. A non-significant correlation was found between SCCR development and behavioural regularity. Table 1 presents the cortisol concentrations and evening and morning indices as well as previous data for healthy full-term infants (1). Further analyses showed that the evening and morning indices were higher if mothers were referred for social problems (0.03, 5.1%) than those with psychiatric problems ($p < 0.05$), higher if they received psychological counselling during pregnancy (0.14, 26.6%) than those that did not ($p < 0.05$) and higher in the three that had smoking mothers (3.2, 603.9%) than those that did not ($p < 0.05$).

The four families that dropped out early due to difficulties completing forms and following instructions were probably those with the heaviest psychosocial burdens. This could have provided a selection bias if the most vulnerable infants had been excluded. Despite that, we were still able to show that infants at high psychosocial risk had established SCCR by the time of their study inclusion, albeit with higher variability than previously seen in healthy full-term infants (1), which could be explained by the environment these infants live in (2,5).

Abbreviations

SCCR, salivary cortisol circadian rhythm.

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Acknowledgements

We would like to thank the infants and parents who took part, psychologist Lena Blom, family counsellors Catharina Gustavsson, and Gunilla Hellström, research nurse Christina Fuxin, laboratory technicians Lisbeth Hjärle and Anna Pfister and Mats Fredrikson, PhD for statistical support.

Funding

The study was supported by Region Östergötland, Sweden.

Conflict of interest

No conflict of interests to declare.

Table 1 Salivary cortisol values and evening/morning cortisol indices in infants at high psychosocial risk

Age		Morning values		Morning values healthy full-term infants (1)		Noon values		Noon values healthy full-term infants (1)		Evening values		Evening values healthy full-term infants (1)		Evening and morning mean cortisol index	P-value Evening and morning index
Month	n	Median	Q1-Q3	Median	Q1-Q3	Median	Q1-Q3	Median	Q1-Q3	Median	Q1-Q3	Median	Q1-Q3		
2	12	9.9	4.6-13.5	6.1	3.9-9.8	4.4	3.7-6.5	5.2	3.4-7.3	3.0	1.7-4.6	2.7	1.7-4.9	0.30	0.010
3	19	8.9	6.1-16.2	7.5	4.2-11.9	5.3	3.6-9.1	5.9	4.1-8.5	2.2	1.5-3.4	3.3	1.9-5.9	0.25	0.0001
4	16	8.4	6.5-12.2	8.0	5.7-13.5	7.5	3.6-9.2	6.2	3.7-9.0	2.0	1.4-3.0	2.5	1.5-4.4	0.24	0.001
5	18	12.5	8.6-20.0	8.3	5.0-13.8	8.3	5.5-11.7	5.9	3.5-8.6	2.8	1.7-5.6	3.1	1.3-6.2	0.22	0.039
6	20	7.2	4.5-11.3	8.9	6.2-14.9	8.4	6.3-11.8	5.4	3.9-8.8	2.4	1.5-3.8	2.3	1.3-5.0	0.33	0.006
7	20	7.0	5.5-9.8	7.7	5.0-14.6	6.9	5.2-7.8	5.1	3.6-8.1	2.1	1.4-3.9	2.3	1.4-4.2	0.30	0.0001
8	17	10.0	6.4-14.6	8.4	5.6-14.2	4.2	3.6-7.7	5.9	3.5-10.6	1.4	1.0-3.2	2.2	1.4-4.3	0.14	0.0001
9	16	8.4	7.2-14.9	8.9	6.0-14.8	4.8	3.2-8.4	5.6	3.6-9.9	1.1	0.8-2.5	2.3	1.2-5.2	0.13	0.007
10	19	10.5	4.6-11.5	10.0	6.1-14.2	5.5	3.6-8.8	5.4	3.7-8.9	1.6	1.0-7.8	2.4	1.3-5.6	0.15	0.010

11	15	8.0	5.5-15.3	10.5	6.9-17.1	4.4	2.8-9.3	5.3	3.4-9.7	1.5	1.1-2.2	2.1	1.2-5.6	0.19	0.012
12	21	11.7	5.4-19.0	10.9	5.9-14.4	4.7	2.9-7.8	5.2	3.1-8.6	1.9	1.2-5.1	2.0	1.1-4.2	0.16	0.001

Monthly median (quartile 1 – quartile 3) salivary cortisol values [nmol/L] at three different sampling times: in the morning (07.30-9.30 am), at noon (10.00-12.00 pm) and in the evening (19.30-21.30pm). n = number of infants in each month. Grey columns show comparable data from healthy full-term infants (1). Last two columns: Evening/Morning mean cortisol index and monthly p-values for difference between evening and morning cortisol on a group concentration using Wilcoxon’s rank-sum test.