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ASSOCIATIONS BETWEEN MELATONIN EXCRETION AND MOODS IN ADOLESCENT BOYS AND GIRLS.

Jill B. Becker¹, Christy M. Buchanan², Jacquelynne S. Eccles^{1,3}, Josephine Arendt⁴, and David C. Klein⁵

¹The University of Michigan, Department of Psychology, Ann Arbor, MI
²Stanford University, The Stanford Center for the Study of Families, Children and Youth,
Palo Alto, CA

³The University of Colorado, Dept. Psychology, Boulder, CO
 ⁴The University of Surrey, Department of Biochemistry, Guildford Surrey, U.K.

and

⁵National Institute of Child Health and Human Development, Section on Neuroendocrinology, Bethesda, MD

Correspondence should be addressed to: Dr. J. B. Becker The Unversity of Michigan Neuroscience Laboratory Building 1103 E. Huron St. Ann Arbor, MI USA 48104-1687 313-763-4363 FAX: 313-936-2690

e-mail: GDFL@UMICHUM.BITnet

ABSTRACT

Self-reports of mood and behaviors were studied in adolescent boys and girls. Morning urine concentrations of the melatonin metabolite, 6-hydroxymelatonin, were found to show specific relations with these behaviors. The relations were different for boys and girls. In girls, increased 6-hydroxymelatonin preceded decreased "self-esteem". In boys, increased affection preceded increased 6-hydroxymelatonin. On measures thought to reflect personality and cognitive style characteristics, melatonin excretion was negatively correlated with traits of "outgoing and friendly", "not depressed", "communal" and "involved" in girls. Boys with higher 6-hydroxymelatonin tended to be less "self-conscious" and to report that their parents were "more strict".

INTRODUCTION

There has been considerable interest recently in a possible role for melatonin in affective disorders (Rosenthal, et al., 1984; Rosenthal, et al., 1986; Souetre, et al., 1989; Thompson, Franey, Arendt, & Checkley, 1988; Winton, et al., 1989)). Small doses of melatonin have been reported to induce fatigue, drowsiness, a decrease in self-reported alertness, and slowed reaction times on at least two different tasks (Arendt, Borbely, Franey, & Wright, 1984; Lieberman, Waldhauser, Garfield, Lynch, & Wurtman, 1984; Sherer, Weingartner, James, & Rosenthal, 1985). During development in humans, melatonin concentrations in serum continuously decline from infancy into adulthood (Waldhauser, et al., 1988) and there are changes in the neural response to melatonin associated with puberty (Mauri, et al., 1985; Norman, & Liwack, 1987). Research from non-human animals suggests that melatonin is involved in the timing of puberty (Foster, Karsch, Olster, Ryan, & Yellon, 1986; Yellon, & Foster, 1986).

Due to reports of melatonin influences on affective behavior and the possible changes in melatonin reported to occur during puberty, we decided to examine whether mood and affect are correlated with production of this hormone in girls 9-10 years old and boys 11-12 years old. This study is a preliminary report of some of our initial findings from a study in which 6-

hydroxymelatonin (the primary melatonin metabolite in urine) and behavior were repeatedly sampled over a one month period of time.

METHODS

Urine samples were obtained on rising for 3 days a week (Monday, Tuesday, Wednesday) for four consecutive weeks from girls 9-10 years old (N=36) and boys 11-12 years old (N=49). Daily questionaires requiring individuals to report their moods and behaviors were filled out three evenings each of the four weeks (Sunday, Monday, and Tuesday). If a day was missed, samples and questionaires were also collected on Thursday and Wednesday, respectively. Some of the items from the daily questionaire that contributed to mood composites are listed in Table 1.

At the end of the month, the child was interviewed by one of the experimenters for more general information about mood, affective behaviors and attitudes (End-of-Month questionaire). At this time the child was also weighed. Some of the questions that were used to generate mood composites from the end of month responses are listed in Table 2.

In our first analyses we chose to assay one sample per week. In order to minimize variation due to the weekend, Tuesday was selected. Only children who had given urine samples on Tuesday morning of all 4 weeks were included in this analysis. Urine was analyzed for 6-hydroxy-melatonin (6-OH-MEL) according to previously published methods (Arendt, Bojkowski, Franey, Wright, & Marks, 1985). 6-OH-Mel concentrations were adjusted for urinary creatinine and body weight. This allows metabolic and body weight influences on excretion of 6-OH-MEL to be minimized.

Daily and End of Month questionaire responses were analyzed by factor analysis and mood composites were generated. For each composite, the mean value was used for the subsequent analyses. Comparisons between mood composites and 6-OH-MEL were analyzed using Spearman's Ranked Correlation Coefficient analysis for non-parametric analyses.

RESULTS

<u>Urinary 6-OH-MEL</u>. There was a significant sex difference in urinary concentrations of 6-OH-MEL. Females had significantly higher concentrations of the melatonin metabolite 6-OH-MEL ((ng 6-OH-MEL/ml urine)/(ng creatinine/ml)/body weight)) than did males (females: 0.562±0.78 vs. males: 0.321±0.027; mean±SEM; p=0.0017).

Daily Measures.

Analyses were carried out both with means of daily moods obtained for each child during the month and mean 6-OH-MEL concentration, as well as with the day to day concurrence between 6-OH-MEL and behavior.

Girls. The mean 6-OH-MEL in girls (N=36) was negatively correlated with average composites of "self esteem" (rho=-0.282, p<0.05) and "aggression" (rho=-0.327, p<0.02). As is shown in Table 3, other measures of moods also tended to be correlated with the mean 6-OH-Mel in girls, but did not reach statistical significance. When the daily excretion of 6-OH-MEL was compared with daily reports of moods, consistent correlations were found only for "self-esteem" in females. High concentrations of 6-OH-Mel in the Tuesday morning urine specimen were correlated with low self-esteem on the questionaire Tuesday night (rho=-0.255, p<0.01). Daily self-reports of aggression and happy were not consistently correlated with the daily variation in 6-OH-Mel (Table 3). No composites obtained the preceeding evening (i.e. Monday evening) were correlated with urinary 6-OH-MEL the following morning.

Boys. In boys (N=49), "affection" was positively correlated with 6-OH-MEL (rho=0.390, p<0.01). No other measure was significantly correlated with boys' daily responses (Table 4). Affection was correlated with daily changes in 6-OH-Mel (rho=0.315, p<0.01). However, in this case increased self-report of affectionate behavior on Monday night's questionaire preceded an increase in 6-OH-MEL Tuesday morning (Table 4). There were no correlations between 6-OH-MEL and Tuesday evening self report of moods.

End of Month responses. The monthly average (mean) of urinary 6-OH-MEL for each child was compared with the child's responses on the End of Month questionaire. Results from boys and girls were analyzed separately.

<u>Girls</u>. Melatonin excretion was negatively correlated with four related mood composites from the end of month questionaire. Girls with a low mean 6-OH-MEL rated themselves higher on these traits: "outgoing and friendly", "communal", "involved", and "not depressed". These four traits were also positively correlated with each other. "Body image" tended to be positively correlated with 6-OH-MEL as well, but this trait did not reach statistical significance (Table 5). Some items are included on Table 4 so that the reader can make comparisons with the results from boys (Table 5).

Boys Two items were correlated with urinary 6-OH-MEL in boys. Boys with higher 6-OH-MEL tended to be less "self-conscious" (Rosenberg, 1979) about what other people thought of them than those with lower 6-OH-MEL (Table 5). Boys with high 6-OH-MEL also tended to report that their parents were "more strict" with them than did boys with lower 6-OH-MEL. 6-OH-MEL in boys was not related to "involved" or "communal" or other items on which girls showed a strong negative correlation. In fact, as is shown in Table 5, there was a tendancy for a positive correlation between these items and 6-OH-MEL.

Discussion

The daily variation in self report in boys and girls of behaviors and moods was correlated with daily variation in morning concentrations of 6-OH-MEL in urine. Monthly means for "aggression" and "self esteem" in girls were both negatively correlated with the mean concentration of 6-OH-MEL. When day to day variation was analyzed, however, only "self esteem" in girls showed a specific relationship in which the morning concentrations of 6-OH-MEL were predictive of the evening report of self-esteem. In this case, high melatonin predicted low self-esteem. In boys, the mean self-report of "affection" in boys showed a positive correlation with the mean 6-OH-MEL. When day to day variation was analyzed, high self-report of affection preceded

increased 6-OH-MEL the following morning. These data suggest that there are sex differences in how 6-OH-MEL influences affective behavior in adolescence.

The value of multiple samples of both hormones and behavior should be apparent from the analyses of these data. When both hormones and behavior are collected at multiple time points, it is possible to consider whether there are specific temporal constraints associated with hormone-behavior relations. Analyses of these temporal relations in our data indicate that there are very different associations for boys and girls. We saw that low nocturnal 6-OH-MEL predicted greater "self esteem" that evening in girls (i.e. hormone -> behavior). In contrast, in boys self report of "affection" preceded an increase in urinary 6-OH-MEL the following morning (i.e. behavior -> hormone). Only with repeated sampling procedures can such relations be examined.

We began these experiments expecting to find an association between melatonin production and affective behavior. This hypothesis was not born out specifically by our data. However, the idea that high melatonin secretion may be associated with reduced energy level and fatigue (Arendt, et al., 1984; Lieberman, et al., 1984; Sherer, et al., 1985) is supported by the hormone behavior relations found in girls. High concentrations of 6-OH-MEL in girls were correlated with low self-reported indices of active childhood activities (i.e. "involved", "not depressed", outgoing and friendly" and "communal"). Since there have been reports that girls experiencing precocious puberty and normal boys and girls in later stages of puberty are more likely to report tiredness (Sonis, et al., 1985; Susman, Nottleman, & Blue, 1983), there may be interactions between melatonin secretion and energy levels during puberty that are reflected in self-report of activities.

Given the different ages of our boys and girls direct comparisons between the two sexes were not conducted. However, the finding that hormone-behavior relations in boys are very different than those in girls is quite interesting. Whether this reflects a developmental difference or a gender difference remains to be determined. Nevertheless, the data from the daily measures from the boys and girls illustrates very well that correlations between hormones and behavior may be in either direction. Behavior may modulate hormonal secretions as well as hormones modulating behavior. Only temporal analyses of the relations can determine the direction of such an association.

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Table 1. Mood Composites from Daily Measures.

1. "Affection"

- How often today did you

(Response: never, once, twice, three or more times)

- tell someone you like them
- give someone a hug because you like them
- help a friend, brother or sister
- help your mother or father
- do something nice for a friend

2. "Aggression"

- How often today did you

(Response: never, once, twice, three or more times)

- yell at a friend
- hit or push someone
- 3. "Self esteem" scale: 1=not at all 5=very
- how much did you like yourself today
- today I felt proud
- today I felt confident
- 4. "Happy" scale: 1=not at all 5=very
- right now I feel happy
- today I felt happy
- today I felt friendly
- today I felt excited
- **5.** "Nervous" scale: 1=not at all 5=very
- right now I feel nervous
- today I felt nervous

TABLE 2. Mood composites from End of Month Questionaire items.

1. "Involved" (alpha=0.70)

How have you felt over the past month? Rating scale: 1=never 7=a lot

- looked forward to things

- liked talking with my family

- enjoyed things I did

- was easy to cheer up

2. "Not Depressed (physiological)" (alpha=0.65)

How have you felt over the past month? Rating scale: 1=never 7=a lot

- slept very well

- liked to go out to play

- had lots of energy

3. "Outgoing and Friendly" (alpha=0.74)

Rate yourself on the following scales. How would you decribe yourself as a person? 1=not at all 5=verv

- friendly

- funny

- smart

- competetive

- warm

- outgoing

- confident

- happy

4. "Communal" (alpha=0.66)

Rate yourself on the following scales. How would you decribe yourself as a person?

1=not at all 5=very

- trusting

- kind

- confident

5. "Body Image" (Peterson Self Concept Scale; alpha=0.53)

1=describes me very well, 2=well, 4=not quite, 6=not at all

- I am happy with my weight

- I am proud of my body

- Most of the time I am happy with the way I look

- I wish I were in better condition (scale reversed for analysis)

- I am not comfortable with the way my body is developing (scale reversed)

- I am happy with my height

- I feel strong and healthy

- My body is growing about as quickly as I would like

6. "Self-consciousness" (Rosenberg items; alpha=0.63)

In front of the class talking about your summer, would you be

1= not at all 7=very

- nervous

- embarased

If you wore wrong clothes to a party, how much would it bother you?

How nervous do you get when someone watches you?

7. "Strict Parents" (alpha=0.70)

scale: 1=very strict 2=strict 3=a little strict 4=not at all strict

- My parents are:

- My parents should be:

Table 3. Correlation Coefficients for Relations in Girls Between Tuesday morning 6-OH-MEL and Daily Mood Composites.

		CORRELATION COEFFICIENT ¹	
MOOD COMPOSITE	AVG. MONTH	ALL MONDAYS	ALL TUESDAYS
"self esteem"	-0.285*	-0.135	-0.255*
"happy"	-0.246	-0.093	-0.176
"aggression"	-0.327*	-0.038	-0.143

^{1.} Spearman Correlation Coefficients were obtained by comparisons between the mean or individual values for 6-OH-MEL and the mean or individual values for mood composites.

Table 4. Correlation Coefficients for Relations in Boys Between Tuesday morning 6-OH-MEL and Daily Mood Composites.

		CORRELATION COEFFICIENT ¹	
MOOD COMPOSITE	AVG. MONTH	ALL MONDAYS	ALL TUESDAYS
"affection"	0.390**	0.315*	-0.006
"happy"	0.225	0.130	-0.011
"nervous"	0.01	0.207	0.126
"aggression"	0.04	0.094	-0.01

^{1.} Spearman Correlation Coefficients were obtained by comparisons between the mean or individual values for 6-OH-MEL and the mean or individual values for mood composites.

^{*} p<0.05

^{*} p<0.05

^{**}p<0.01

Table 5. Correlation Coefficients for Relations in Girls Between 6-OH-MEL and Mood Composites from the End of Month Questionaire.

MOOD COMPOSITE	CORRELATION COEFFICIENT ¹	
"involved"	$r_S = -0.346*$	
"not depressed"	$r_S = -0.365*$	
"outgoing and friendly"	$r_{S} = -0.387*$	
"communal"	$r_{\rm S} = -0.502**$	
"strict parents"	$r_{\rm S} = 0.140$	
"body image"	$r_8 = 0.239$	

1. Spearman Correlation Coefficients were obtained by comparisons between the mean of 4 values for 6-OH-MEL and the mean values for the mood composites described in Table 1.

Table 6. Correlation Coefficients for Relations in Boys Between 6-OH-MEL and Mood Composites from the End of Month Questionaire.

MOOD COMPOSITECORRELATION COEFFICIENT¹"self conscious" $r_s = -0.284*$ "strict parents" $r_s = -0.344**$ "involved" $r_s = 0.219$ "communal" $r_s = 0.129$ "body image" $r_s = -0.221$

^{*} p<0.05 ** p<0.02

^{1.} Spearman Correlation Coefficients were obtained by comparisons between the mean of 4 values for 6-OH-MEL and the mean values for the mood composites described in Table 1.

^{*} p<0.05 ** p<0.02

REFERENCES

Arendt, J., Bojkowski, C., Franey, C., Wright, J., & Marks, V. (1985). Immunoassay of 6-hydroxymelatonin sulfate in human plasma and urine: abolition of the urinary 24-hour rhythym with atenolol. <u>60</u>, 1166-1173.

Arendt, J., Borbely, A. A., Franey, C., & Wright, J. (1984). The effects of chronic, small doses of melatonin given in the late afternoon on fatigue in man: a preliminary study. <u>45(3)</u>, 317-21.

Foster, D. L., Karsch, F. J., Olster, D. H., Ryan, K. D., & Yellon, S. M. (1986). Determinants of puberty in a seasonal breeder. 42(331), 331-84.

Lieberman, H. R., Waldhauser, F., Garfield, G., Lynch, H. J., & Wurtman, R. J. (1984). Effects of melatonin on human mood and performance. 323(2), 201-7.

Mauri, R., Lissoni, P., Resentini, M., De Medici, C., Morabito, F., Djemal, S., Di Bella, L., & Fraschini, F. (1985). Effects of melatonin on PRL secretion during different photoperiods of the day in prepubertal and pubertal healthy subjects. 8(4), 337-41.

Norman, A. W., & Liwack, G. (1987). Hormones . San Diego: Academic Press.

Rosenberg. (1979).,

Rosenthal, N. E., Sack, D. A., Gillin, J. C., Lewy, A. J., Goodwin, F. K., Davenport, Y., Mueller, P. S., Newsome, D. A., & Wehr, T. A. (1984). Seasonal affective disorder: a

description of the syndrome and preliminary findings with light therapy. <u>Archives of General Psychiatry</u>, 41, 72-80.

Rosenthal, N. E., Sack, D. A., Jacobsen, F. M., James, S. P., Parry, B. L., Arendt, J., Tamarkin, L., & Wehr, T. A. (1986). Melatonin in seasonal affective disorder and phototherapy. 21(257), 257-67.

Sherer, M. A., Weingartner, H., James, S. P., & Rosenthal, N. E. (1985). Effects of melatonin on performance testing in patients with seasonal affective disorder. <u>58</u>(3), 277-82.

Sonis, W., Comite, F., Blue, K., Pescovitz, O. H., Rahn, C. W., Hench, K. D., Cutler, G., Loriaux, D. L., & Klein, R. P. (1985). Behavior problems and social competence in girls with true precocious puberty. <u>106</u>, 156-160.

Souetre, E., Salvati, E., Belugou, J. L., Pringuey, D., Candito, M., Krebs, B., Ardisson, J. L., & Darcourt, G. (1989). Circadian rhythms in depression and recovery: evidence for blunted amplitude as the main chronobiological abnormality. <u>28</u>(3), 263-78.

Susman, E., Nottleman, E. D., & Blue, J. H. (1983). <u>Social competence</u>, <u>psychological states and behavior problems in normal adolescents</u>. Detroit, MI:

Thompson, C., Franey, C., Arendt, J., & Checkley, S. A. (1988). A comparison of melatonin secretion in depressed patients and normal subjects. <u>152</u>(260), 260-5.

Waldhauser, F., Weiszenbacher, G., Tatzer, E., Gisinger, B., Waldhauser, M., Schemper, M., & Frisch, H. (1988). Alterations in nocturnal serum melatonin levels in humans with growth and aging. <u>66(3)</u>, 648-52.

Winton, F., Corn, T., Huson, L. W., Franey, C., Arendt, J., & Checkley, S. A. (1989). Effects of light treatment upon mood and melatonin in patients with seasonal affective disorder. <u>19</u>(3), 585-90.

Yellon, S. M., & Foster, D. L. (1986). Melatonin rhythms time photoperiod-induced puberty in the female lamb. <u>119(1)</u>, 44-9.