Significant impact of nocturnal melatonin secretion on obesity-related metabolic disorders in children and adolescents

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Background:
In addition to its function in circadian rhythm melatonin plays an important role in energy metabolism and body weight regulation. In animals pinealectomy induces insulin resistance and administration of melatonin to diabetes prone rats ameliorates their glucose metabolism. Studies of melatonin–insulin interactions in animal models as well as in humans have revealed an inverse relationship between these two hormones. Furthermore loss-of-function mutations of the melatonin receptor gene are associated with insulin resistance and DM II in humans (1,2).

Objective and hypotheses:
So far the effect of melatonin on energy metabolism in childhood remains unclear. As obese adolescents were found to have disturbed and shifted sleep rhythm a link between low melatonin secretion and impaired glucose metabolism was suggested. We therefore aimed to explore the effect of nocturnal melatonin secretion on glucose metabolism in obese children and adolescents.

Methods:
A cross sectional study of 148 obese (>97.percentile) children and adolescences (10-17 ys) was performed. Based on fasting blood samples, insulin resistance was defined as age and sex adjusted HOMA-IR >95. percentile (using Allard percentiles) and correlated with nocturnal Melatonin secretion. Melatonin secretion was measured as its main metabolite 6-sultatoxymelatonin normalized to urinary creatinine (MT6:Cr-ratio) in the first morning urinary void.
Differences in medians were tested using non-parametric tests (Mann-Whitney-U-test, Kruskal-Wallis-test). To analyse the influence of the independent variables age, sex and Tanner status a multiple linear regression analysis was done.
Statistical analyses were performed using statistical package SPSS 22.

Results:

Table 1: sample characteristics	
***sample** (n)*	148
***age** [mean ± sd]*	14.6 ± 2.1
male sex	49 %
***BMI** (kg/m²) [mean ± sd]*	33.5 ± 5.5
***BMI-SDS** [mean ± sd]*	2,7 ± 0,6
Pubertal status	
infantile	9.3 %
pubertal	19.3 %
postpubertal	71 %

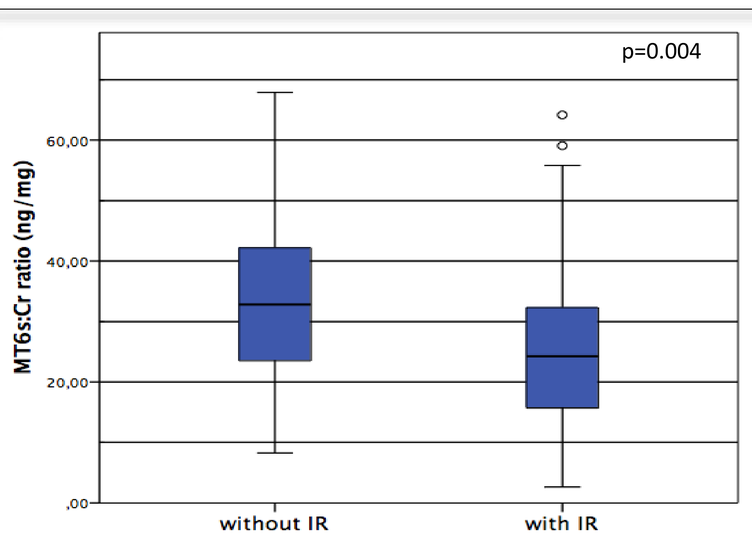

Figure 1: Correlation of melatonin secretion and insulin resistence (IR): Subjects with IR (n=101) showed significant lower nocturnal melatonin levels (p=0.004). The median MT6:Cr ratio was 24.3 ng/mg (1st quartille: 15.7 ng/mg; 3rd quartile: 33.0 ng/mg) among subjects with IR vs. 32.8 ng/mg (1st quartile: 23.1 ng/mg; 3rd quartile: 42.7 ng/mg) among those with unimpaired insulin secretion. Adjusted for age, sex and Tanner status the effect remained significant.

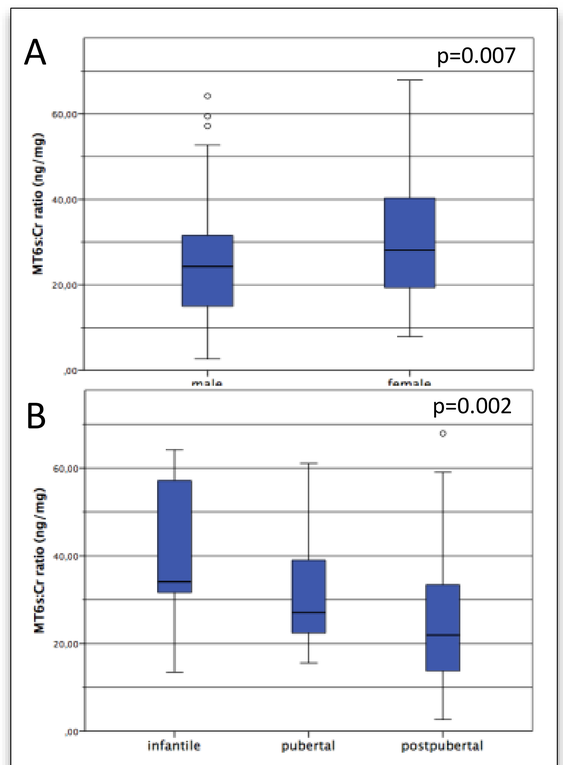

Figure 2: Influence of sex (A) and pubertal status (B) on melatonin secretion.

Conclusion:
We found a strong association of lower nocturnal melatonin secretion and insulin resistance in obese children. To increase melatonin levels – either endogenously by prolonged nighttime darkness or exogenously by supplementation – might be one future strategy in management of obesity -induced morbidity.

References:

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