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Running Head: Benefit of Melatonin Supplements?

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2006/2007 No. 1

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The Effects of Melatonin Supplements on Improving Worker Performance: A Placebo-Controlled Experiment

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Abstract

This exploratory study is the first to examine the effects of melatonin supplements in an occupational setting. Using a randomized pretest-posttest design, participations received a daily supplement of melatonin or a placebo for 30 days. Participants receiving melatonin, relative to those receiving the placebo, had improved work-related performance and longer sleep hours. The improvement in sleep hours partially mediated the effects of the melatonin intervention on performance. These effects were stronger in older workers than younger workers.

Keywords: Fatigue, Occupational, Industrial
Introduction

The occupational and health-related literature addresses the effects of physiological and environmental factors on melatonin levels in the human body (e.g. Baskett et al., 2001). Many of these studies focus on the effects of reduced melatonin levels found in electrical workers and others who are routinely exposed to strong Electromagnetic Fields (EMF) (e.g. van Wijngaarden et al., 2000; Tynes et al., 2003). Other studies focus on the effects of reduced melatonin levels in shift workers (e.g. Benhaberou-Brun et al., 1999; Lamond et al., 2003; Zhu et al., 2003). This issue is important because evidence suggests that lower melatonin levels are linked to increases in sleep disorders and depression (which ultimately affect job performance), suicide rates, and cancer rates among workers in these industries (Villeneuve et al., 2000; Lamond et al., 2003). Despite the interest in this area, experiments on the effect of melatonin supplements on worker performance are non-existent in the occupational literature. Effects of melatonin supplements on sleep disorders are only moderately addressed in the health-related literature. Therefore, we reviewed the health-related literature to suggest how and why melatonin supplements may improve worker performance in an occupational setting.

The first experiment of melatonin on human subjects was conducted by Aaron Lerner in 1962. He found that the hormone provided a slight sedative effect when applied intravenously (Zhdanova and Wurtman, 1997). First thought to be secreted only by the pineal gland, recent research found that melatonin is also synthesized in other organs such as retinas, bone marrow, and bile (Reiter et al., 2000). Characterized as the 'sleep-promoting' or 'sleep hormone' (e.g. Zhdanova et al., 1997; Rose and Kahan, 2001)
melatonin was first shown to regulate the wake-sleep cycles (synchronize circadian rhythms) in humans (Armstrong et al., 1986; Sack et al., 1992; Zhdanova et al., 1997). Melatonin production is activated by the onset of darkness – with increased levels of the hormone in the body associated with high degrees of darkness (Cagnacci, 1996). As light is introduced, the hormone level in the human body radically drops until it becomes negligible. Introduced as a dietary supplement in health food stores, melatonin became a popular treatment to assist shift-workers in regulating their circadian rhythm, or to reduce jet-lag in air travelers who crossed multiple time zones (Dawson et al., 1995; Hughes and Badia, 1997; Edwards et al., 2000). Taking the supplement by mouth prior to bedtime resets the sleep cycle to begin approximately 30 minutes to two hours after ingestion. In most studies, a single dose was sufficient to counteract the disruptive effects of mild sleep disorders (i.e. jet-lag, and the so-called Monday morning blues) (Lewy, 2001; Herxheimer and Petrie, 2001; Yang et al., 2001). Despite numerous articles on the positive effects of melatonin on health, we found no study which tested the hormone in an occupational setting. In other words, the use of melatonin supplements to alleviate common work-related problems, such as end-of-shift fatigue, that could be induced by inadequate sleep.

Despite many reported successes (e.g. Armstrong et al., 1986; Cassone, 1990; Lewy et al., 1992; Attenburrow et al., 1996; Sack et al., 2000; Smits et al., 2003; Wyatt, 2004), the effects of exogenous melatonin administration to correct sleep disorders have been mixed. Some studies show that subjects experienced negative effects of "grogginess and tiredness", upon awaking after melatonin use rather than feeling rested and alert (e.g. Rose and Kahan, 2001). Others experienced modest or no effects of melatonin on sleep
quality or circadian rhythms (e.g. Lushington et al., 1997; Dijk et al., 2001; Singer et al., 2003). Still others found the greatest health benefits are its antioxidant properties for removing toxins from the bloodstream (Gitto et al., 2001). Reasons for these discrepancies have yet to be addressed in the literature; however, after reviewing over 300 scientific articles on melatonin experiments, we find evidence that some of the variance in effects could be explained by variance in dosage size and administration method. Dosage sizes ranged from a low of .1 - .3 mg (e.g., Stone et al., 2000; Zhdanova et al. 2001; Dijk et al., 2001) to a high of 20 mg (Tzischinsky and Lavie, 1994; Stone et al., 2000; Gitto et al., 2001) per day, with little justification for the discrepancy. We also found anecdotal evidence that doses as high as 100 mg have been tried individually, occasionally resulting in death. While higher doses tend to be characterized as 'pharmacological', and lower doses as 'physiological' (Zhdanova et al., 2001), evidence suggests there is no general agreement on what doses are appropriate for treating various sleep disorders or the associated risk factors. Differences in administration include orally – by pill or solution - orally under the tongue, and intravenously - directly into the bloodstream. Since the effects of other dietary supplements are moderated by factors such as the amount of food, drink, or alcohol ingested close to the time of administration, this could explain some of the variance in effect found with melatonin. However, like dosage size, there is no general agreement on the best way to administer melatonin.

In addition to treating temporary, mild sleep disorders (i.e. jet-lag and insomnia) in otherwise healthy adults, melatonin has been used to treat clinical sleep disorders in children (e.g., Zhdanova et al., 1996; Lin-Dyken and Dyken, 2002), sleep disorders in the aged (e.g. Haimov et al., 1995; Lushington et al., 1997; Hughes et al., 1998; Zhdanova et
sleep disorders in patients with Alzheimer's disease (e.g. Singer et al., 2003), fatigue in Chronic Fatigue Syndrome patients (e.g. Teitelbaum et al., 2001), toxicity in septic newborns (e.g. Gitto et al., 2001), sleep disorders in chronic whiplash patients (e.g. van Wieringen et al., 2001), seizures in epileptics (e.g. Peled, 2001), Periodic Limb Movement Disorder (PLMD) (e.g. Kunz and Bes, 2001), and circadian synchronization in the blind (e.g. Lockley et al., 1999; Sack et al., 2000). All but two of these applications were for treating sleep deficiencies. The two exceptions were septic newborns, administered the hormone because of its antioxidant properties to remove blood-born toxins, and epileptics, who were administered the hormone because of its anti-seizure properties. Therefore, there is sufficient evidence to suggest that melatonin may improve sleep quality that is diminished by a plethora of disorders.

In the present study, we expected that administration of melatonin would improve worker performance. We expected the effect to be mediated by improvement in sleep hours, which should reduce fatigue-related performance degradation.

**Method**

**Participants**

Initial baseline data were collected on 366 participants (pre-test sample). Sixty-four participants were excluded (incomplete data) or voluntary dropped out of the study. Post-test measures were collected on 302 participants. After screening the data for univariate and multivariate outliers (Tabachnick & Fidell, 2001; Cohen et al., 2003), 15 participants were excluded. This left a final sample of 287 (M age = 31.87, SD = 13.41; 140 females and 147 males): 119 in the control group (placebo) and 168 in the experimental group (melatonin). Feedback from participants who dropped out of the
placebo group indicated that they experienced little or no effect and viewed the intervention as a waste of time. This created the moderate difference in group sizes. Any bias introduced by selective dropout in the placebo group would likely serve to strengthen any “placebo” effect and minimize differences in criterion measures between the placebo and experimental conditions.

**Study Design**

The study design was a placebo-controlled, randomized, double-blind experiment where baseline data were collected prior to administration of the melatonin and after 30 days of continuous melatonin use. Participants received either melatonin or a placebo. Melatonin (or placebo) was administered orally by the participant 30 minutes prior to their normal bedtime. A dosage of 1 mg. of melatonin was chosen by the company physician based on Attenburrow, et. al. (1996) and consultation with several colleagues who suggested a low dose range of .3 to 3 mg. One week's worth of the hormone or placebo (7 tablets) was given to each worker on Monday's. Participants were asked to maintain a daily record of their sleep hours. For the first few days of the study, plant meetings were held to ensure sleep records were being completed and the hormone/placebo was being administered properly.

**Measures**

In addition to demographic data, (gender, age, job type), data were collected on, average sleep hours per 24 hour period four weeks prior to and during the 30 day intervention period, and a performance measure assessed just prior to the intervention and again at the end of the 30 day intervention. The measure of pre-intervention sleep was the per-day average over the four week pre-intervention period and the post-intervention
measure was the per-day average during the 30 day intervention period. This measure is not ideal but is a conservative estimate of pre-post differences in sleep hours. Additionally, participants rated their own change in performance since the beginning of the intervention. After 30 days, they were asked to rate their perceived change in performance, due to the intervention, as either 'unchanged', 'improved', or 'reduced'.

The performance measure used was based on the company’s job analysis. Workers are expected to remember part specifications and new product details and visually detect defects. In order to visually detect defects, workers must remember new product details. The performance measure assessed memory and visual detection of defective parts. The measure included a simple digit span, recall of part specifications after being shown a series of common specifications for 1 minute, and detection of defects after being shown specifications. There were a total of 20 items (worth 5 points each) which summed to total score of 100. In order to minimize carry-over effects from the pre-intervention to the post-intervention assessment of performance, the specific specifications and defects were altered for the second administration. The correlation between the first and second administration 30 days later was .63.

Results

Descriptive statistics for each variable are shown in Table I. Regression-adjusted change (Cohen et al., 2003) in performance was the primary outcome measure. The pre-intervention performance served as a control variable and the experimental manipulation (placebo vs. melatonin, dummy coded) served as the predictor variable (table I).

The test of the effect of the melatonin intervention on regression adjusted change in performance was significant, $B = 7.03$, $t(284) = 7.37$, with a partial $r$-square (effect
size controlling for pre-intervention performance) of .16. The performance of workers receiving melatonin improved by over 7 points more than the performance of workers receiving the placebo.

We examined potential moderators of the effect of the melatonin intervention on performance. Neither gender nor job type interacted significantly with the intervention. A small but significant moderating effect of age was found, $B = -.21, t(282) = -3.03, p < .005$, partial r-square = .03. An analysis of simple slopes indicated that the melatonin intervention improved the performance of older workers more than younger workers. The performance of older workers [mean of age (31.87) plus 1 SD (13.41)] improved as a result of the intervention by almost 10 points (9.81) relative to the placebo group while the performance of younger workers (mean of age minus 1 SD) improved by just over 4 points (4.12) relative to the placebo group.

Next, we tested the hypothesis that the improvement in performance for workers receiving melatonin was mediated by an increase in sleep hours. In other words, some, or all, of the effect of the melatonin intervention on change in performance may be due to an increase in sleep hours as a result of using melatonin. Testing this hypothesis requires testing the effect of the intervention on the change in sleep hours, testing the effect of the intervention on change in performance, and testing the partial effect of the intervention (controlling for change in sleep hours) and the partial effect of the change in sleep hours (controlling for the intervention) on the change in performance (Judd & Kenny, 1981; Sobel, 1982; MacKinnon et al., 2002). The mediating, or indirect, effect is assessed by the difference between the total effect of the intervention on change in performance (change in performance regressed only on the intervention) and the partial effect of the
intervention on change of performance (controlling for change in sleep hours).

Equivalently, the mediating effect can be assessed by the product of the regression coefficient from change in sleep hours regressed on the intervention and the partial regression coefficient for change in sleep hours when change in performance is regressed on both the intervention and change in sleep hours. To simplify the mediation analysis, regression adjusted change scores were created for sleep hours and performance by regressing the respective post-intervention scores on the respective pre-intervention scores. The resulting residual for sleep hours is the regression adjusted change in sleep hours and the resulting residual for performance is the regression adjusted change in performance (Cohen et al. 2003).

First, we estimated the effect of the intervention on change in sleep hours, $B = 0.82$, $t(285) = 6.83$, $p < .001$, $r^2 = 0.14$. Workers receiving melatonin slept almost an hour more (50 minutes) per day than workers receiving the placebo. Second, the effect of the intervention on change in performance was estimated, $B = 6.97$, $t(285) = 7.34$, $p < .001$, $r^2 = 0.16$. Of course, this effect is essentially identical to the effect of the intervention on performance reported above (the slight difference is due to the small difference on the pre-intervention measure of performance between the placebo and melatonin groups). Lastly we estimated the partial effect of the intervention on performance, $B = 5.34$, $t(284) = 5.38$, $p < .001$, partial $r^2 = 0.09$, and of the partial effect of change is sleep hours on performance, $B = 1.99$, $t(284) = 4.37$, $p < .001$, partial $r^2 = 0.06$. The mediating, or indirect, effect of change in sleep hours on change in performance becomes $1.63$ ($6.97-5.34$ or, alternatively, $0.82 \times 1.99$). This coefficient for the mediating effect can be tested for significance (Sobel, 1982). The mediating effect of
change is sleep hours on change in performance is highly significant, $z = 3.69, p < .001$. Thus, the indirect effect of the intervention, through the increase in sleep hours, represents about 23% of the total effect of the intervention on the change in performance ($1.63/6.97$).

Again, a moderating effect was found for age. When change in performance was regressed on the intervention, change in sleep hours, age, and the interaction of change in sleep hours and age, the interaction was significant, $B = 0.91, t(282) = 2.90, p < .005$, partial r-square = .03. Simple slopes indicated that the effect of change in sleep hours on change in performance was stronger for older workers ($B = 3.11$) than for younger workers ($B = 0.67$).

Lastly, we examined participants’ perceptions of improved performance over the 30-day period. Participants’ perceptions of improved performance were significantly correlated with actual change in performance, $r(285) = .28, p < .001$. Participants in the melatonin condition rated their performance as significantly more improved ($M = 2.33$) than participants in the placebo condition ($M = 1.91$), $F(1,185) = 35.52, p < .001$, $eta^2 = .11$. This effect was not moderated by age. However, age was positively correlated with perceptions of improved performance, $r(285) = .18, p < .005$.

Discussion

This study found that melatonin improved worker performance in an industrial setting. The improvement was found using pre-post measure of job-related performance and validated by the perceptions of employees concerning their individual performance. The effect varied by worker age, and was partially mediated by an increase in sleep
hours. These effects were found using a low dosage and oral administration of melatonin.

The results indicate that older workers benefited more from the intervention than younger workers. This effect was found despite the disproportionate number of younger workers in the sample (70% under the age of 40). The greater benefits to older workers possibly occurred because melatonin increased the average number of sleep hours, which diminish with age (MacGibbon et al. 2001). The increase in sleep hours was linked to improved performance. Improvement in older workers could also be explained by reduction in sleep interruption and blood-born toxins, which melatonin has been found to reduce in other studies (Lavie, 2001).

This study suggests that the mixed results of melatonin benefits found in previous studies may be due to dosage size and administration method. While recommended oral dosages ranged from .3 to 3 mg, we found that dosages as high as 10 - 30 mg in the literature. In addition, the literature also varied in administration method - with several variations of oral and intravenous methods. Anecdotal evidence suggests that higher doses may interrupt sleep rather than enhance it. This was reported in workers who tried higher levels of melatonin after completion of the study. Intravenous methods may affect sleep benefits because a greater percentage of melatonin reaches the blood-stream much faster than that found with oral administration.

The post-test of performance was a single administration – on the 30th day of continuous melatonin usage. This could underestimate the true effect of melatonin because the hormone may provide greater benefits over time. This assertion is supported in the literature where studies found increasing benefits after several months of usage.
This study assessed change in the number of sleep hours. A stronger mediating effect of sleep might be found with more sophisticated measures of sleep quality (e.g., amount of REM sleep, number of waking episodes, etc.). Changes in end-of-shift fatigue could be directly assessed using physiological measures. Our criterion variable – change in job-related performance – mimicked performance rather than directly measured it. An improved measure would include the actual reduction in worker errors or the percentage of on-line defects.

Despite these measurement and sample limitations, the present research suggests that melatonin supplements, using relatively low dosages and simple oral administration, lead to improved sleep and improved work-related performance. Improvement in sleep accounts for some, but not all, of the melatonin-related improvement in performance. Additionally, melatonin-related improvements in sleep and performance may be stronger in older workers than younger workers.
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Table I - Descriptive Statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean Placebo/Melatonin</th>
<th>SD P/M</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>30.82 / 32.61</td>
<td>13.46 / 13.37</td>
</tr>
<tr>
<td>Pre-Intervention Performance</td>
<td>71.00 / 68.96</td>
<td>11.58 / 12.42</td>
</tr>
<tr>
<td>Post-Intervention Performance</td>
<td>71.30 / 76.90</td>
<td>10.96 / 10.72</td>
</tr>
<tr>
<td>Pre-Intervention Sleep Hours</td>
<td>6.73 / 6.13</td>
<td>1.02 / 1.15</td>
</tr>
<tr>
<td>Post-Intervention Sleep Hours</td>
<td>7.11 / 7.82</td>
<td>.99 / 1.08</td>
</tr>
</tbody>
</table>
Our responsibility is to provide strong academic programs that instill excellence, confidence and strong leadership skills in our graduates. Our aim is to (1) promote critical and independent thinking, (2) foster personal responsibility and (3) develop students whose performance and commitment mark them as leaders contributing to the business community and society. The College will serve as a center for business scholarship, creative research and outreach activities to the citizens and institutions of the State of Rhode Island as well as the regional, national and international communities.

Mission

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The creation of this working paper series has been funded by an endowment established by William A. Orme, URI College of Business Administration, Class of 1949 and former head of the General Electric Foundation. This working paper series is intended to permit faculty members to obtain feedback on research activities before the research is submitted to academic and professional journals and professional associations for presentations. An award is presented annually for the most outstanding paper submitted.