Effect of Bright Light Intervention on Cerebral Serotonin Transporter Binding

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Background:
Although bright-light intervention has proven successful for treatment of depression, in particular seasonal affective disorder, the neurobiological mechanisms mediating its effects are not known. We have previously shown that the striatal serotonin transporter (SERT) binding fluctuates with seasons, with high striatal binding around winter solstice and low binding around summer solstice. In the same study, we also identified a genotype-dependent interaction with the effects on SERT binding depending on the environmental stressor and the carrier status of the 5-HTTLPR promoter polymorphism (Kalbitzer et al 2010). This gene*environment paradigm predicts the SERT fluctuations with a negative correlation between SERT binding and daylight minutes in carriers of the short 5-HTTLPR allele (S-allele), but less so in homozygote carriers of the long allele (L-allele).

Further, recent MRI data from our group show that threat-related amygdala and prefrontal reactivity decreases inversely to extent of bright-light exposure. At the same time, amygdala-prefrontal and intra-prefrontal functional coupling increased significantly, also in a dose-dependent manner. 5-HTTLPR genotype status modulated the effect of bright-light intervention on intra-prefrontal functional coupling significantly (Fisher et al, in prep). Since serotonin signaling modulated this circuit and is thought to be involved in the pathophysiology of seasonal and other affective disorders, we here investigated brain SERT binding before and after bright light intervention.

Methods:
In a randomized double-blind study design conducted in the winter, 24 healthy males were every morning over a period of three weeks exposed to variable doses of bright light intervention (range: 0.1 – 11.0 kilolux) for 30 minutes. SERT binding was assessed with DASBE-PET prior to the exposure and after the 3 weeks, we evaluated the effects of the intervention on striatal SERT.

For each lightlamp, the spectrum of the emitted light was characterized and the decline in intensity as a function of distance and angle was measured with a photometer (Elma 1355). We made home-visits to measure the exact position of the brightlight in relation to the participant, when it was used.

All PET scans were conducted with a HRRT PET scanner (mean dose of 11C-DASBE 599±29 MBq, range: 421-609 MBq). PET data were motion-corrected and quantification was done with MRTM2 that generates the outcome parameter BPND.

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Results:
This is the first study to evaluate the effects of bright light intervention on brain serotonin transporter function.

We found that:
• SERT binding did not differ between people who spend less time indoors than those who spend more time.
• The relationship between striatal SERT BPND and lux dose can not be explained by a linear dose response correlation. This finding was present irrespective of 5-HTTLPR genotype.
• In the subset of individuals who reported to have an energizing effect of the bright light intervention a tendency toward larger changes in SERT BPND in putamen vs. lux dose exposure.

Table 1: Demographics of all subjects and of the 5-HTTLPR genotype subgroups.

<table>
<thead>
<tr>
<th>Group</th>
<th>n=24</th>
<th>n=7</th>
<th>n=17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Striatum BPND (BPND)</td>
<td>0.34</td>
<td>0.18</td>
<td>0.36</td>
</tr>
<tr>
<td>BMI (Kg/M²)</td>
<td>25±3</td>
<td>25±3</td>
<td>25±3</td>
</tr>
<tr>
<td>Age (year)</td>
<td>24±4</td>
<td>24±4</td>
<td>24±4</td>
</tr>
</tbody>
</table>

Tabel 2: Best fit values for R² and the 95% CI from a linear regression analysis of light dose in lux and change in SERT BPND (L-allele homozygous, n=7, S-allele carriers, n=17).

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Slope</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>L-allele</td>
<td>0.0001</td>
<td>-0.0003 to 0.0001</td>
</tr>
<tr>
<td>S-allele</td>
<td>0.0001</td>
<td>-0.0003 to 0.0001</td>
</tr>
</tbody>
</table>

Conclusion:
In healthy individuals, three weeks exposure to bright light was not associated with any significant change in striatal SERT binding. Either the effect of bright light biomaps is insufficient to mimic exposure to daylight in the summer, or season-related factors other than light determine striatal SERT fluctuations.

References:

Acknowledgements:
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Conflict of interest:
Nothing to declare.