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 fMRI 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 moderated 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 three weeks exposed to variable doses of bright-light intervention (range: 0.1 – 11.0 kilolux) for 30 minutes. SERT binding was assessed with DASB-PET prior to the exposure and after the 3 weeks; we evaluated the effects of the intervention on striatal SERT.

For each biolamp, the spectrum of the emitted light was characterized and the decline in intensity as function of distance and angle was measured with a luxmeter (Elma 1335). We made home-visits to measure the exact position of the biolamp in relation to the participant, when it was used.

•All PET scans were conducted with a HRRT PET scanner (mean inj.dose of 11C-DASB:589±29, range 421-609 MBq).
•PET-data were motion-corrected and quantification was done with MRTM2 that generates the outcome parameter BPND.

Results:

(Two datasets were removed from analysis, one due to movement and another one where the time activity curves indicated irreversible binding in high binding regions)

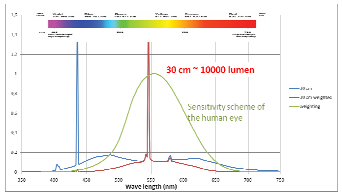

Figure 1: Biolamp characteristics showed a peak in both the blue and the green spectrum where the human eye is most light sensitive

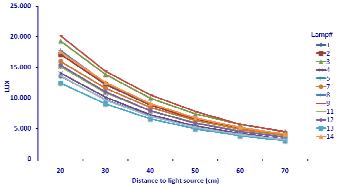

Figure 2: The light intensity as a function of distance to the light source for the15 biolamps used.

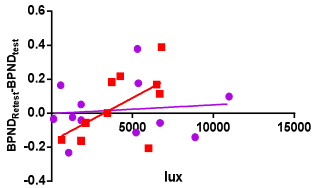

Figure 3: The responders to bright light intervention (n=12, purple graph) showed a trend for a positive linear correlation between BPnd change in putamen (1/slope=19564, R squared= 0.34, P=0.08). There was no association in the non-responders (n=10, red graph) (1/slope=195428, R squared=0.01, P=0.74)

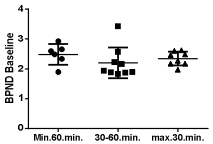

Figure 4: The amount of time spend outdoor in daylight time per day did not predict baseline BPND in putamen and there was no significant difference between the three groups (one way ANOVA P=0.74)

	Age (year)	BMI (Kg/M2)	Bright Light Intensity (lux)
All subjects	24±4,5 (18-36)	23±2,7 (18-30)	4112±2851 (126-10.971)
S-allele carriers	25±4.9 (20-36)	23±1.81 (20-27)	3957±3194 (572-10.971)
L-allele homozygotes	23±4.3 (18-32)	23±3.92 (18-30)	4276±2296 (126-6880)

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

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 indoor 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.

Tabel 2: Best fit values for R^2 and the 95% CI from a linear regression analysis of light dose in lux and change in SERT BP_{ND} from baseline (L-allele homozygotes, n=7, S-allele carriers, n=15).

R Square 95% CI	Striatum	Neocortex
L-allele homozygotes	95% -8.855e-005 ± 2,942e-005	92% -2.537e-005 ± 1.023e-005
S-allele carriers	76% -1.799e-005 ± 4.441e-005	47% -1.2224e-005 ± 9.871e-006

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 biolamps is insufficient to mimic exposure to daylight in the summer, or season-related factors other than light determine striatal SERT fluctuations.

References

[1] Seasonal changes in brain serotonin transporter binding in short serotonin transporter linked polymorphic region-allele carriers but not in long-allele homozygotes.Kalbitzer J, Erritzoe D, Holst KK, Nielsen FA, Marner L, Lehel S, Arentzen T, Jernigan TL, Knudsen GM.Biol Psychiatry. 2010 Jun 1;67(11):1033-9. Epub 2010 Jan 27.

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Conflict of interrest:

Nothing to declare.

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