Summary of published, peer-reviewed findings
Valkee Oy

Research efforts at Valkee follow a two-fold focus: Showing clinical effectiveness of the treatment while at the same time investigating the underlying mechanism of action of transcranial bright light.

The following results have been published in international, peer-reviewed journals:

1. Transcranial bright light treatment via ear canals in seasonal affective disorder: a randomized controlled double-blind dose-response study

Autoren: Jurvelin H, Takala T, Nissilä J, Timonen M, Rüger M, Jokelainen J, Räsänen P
Journal: BMC Psychiatry
Pub Med link: http://www.ncbi.nlm.nih.gov/pubmed/25330838

Summary:
In a 4 week trial, 89 patients suffering from SAD were randomly assigned to one of three treatment groups and received either a low (1 lumen), medium (4 lumen), or high dose (9 lumen) of daily bright light in the ear for 12 minutes in the morning. Depressive symptoms and cognitive performance were assessed using standard psychiatric instruments such as the Beck Depression Inventory (BDI) and the Trial Making Test (TMT) at the beginning, during, and at the end of the trial. The results showed a significant, at least 50% reduction of depressive symptoms in 74-79% of the patients according to the BDI in all three treatment groups as well as a significant improvement of cognitive performance compared to baseline

2. Transcranial bright light exposure via ear canals does not suppress nocturnal melatonin in healthy adults--a single-blind, sham-controlled, crossover trial.

Authors: Jurvelin H, Takala T, Heberg L, Nissilä J, Rüger M, Leppäluoto J, Saarela S, Vakkuri O.
Journal: Chronobiol Int. 2014 Aug;31(7):855-60. doi: 10.3109/07420528.2014.916297. Epub 2014 May 14.
PubMed link: http://www.ncbi.nlm.nih.gov/pubmed/24828616

Summary:
The present study investigated the effects of transcranial bright light (TBL) on melatonin and cortisol secretion in healthy volunteers. 8 subjects (3F, 5M; mean age ± SD: 27± 5 yrs) were exposed to TBL during the night-time in a randomized, placebo controlled study design. Subjects reported to the laboratory in the evening (21 h) and were subjected to the same light/dark rhythm in both conditions (16L:8D; lights off at 23 h, lights on at 07 h) prior to the TBL or placebo exposure form 01:10-01:34 h. Saliva and urine samples for melatonin and cortisol were collected at noon, 18, 21, 22, 23, midnight, 01, 02, 03, 06, 07, 08, and 09h. Results clearly showed that neither melatonin or cortisol secretion nor the circadian rhythm of both endocrine markers was affected by the nocturnal exposure to TBL compared to placebo. This is in line with recent findings showing no melatonin suppression due to TBL exposure in the late evening (Bromundt et al., 2013).

3. Effects of bright light treatment on psychomotor speed in athletes.

Authors: Tulppo MP, Jurvelin H, Roivainen E, Nissilä J, Hautala AJ, Kiviniemi AM, Kiviniemi VJ, Takala T.
Journal: Front Physiol. 2014 May 12;5:184. doi: 10.3389/fphys.2014.00184. eCollection 2014.
PubMed link: http://www.ncbi.nlm.nih.gov/pubmed/24860513

Summary:
Recent fMRI findings suggested that transcranial bright light (TBL) might have physiological effects on brain functions in humans. The present study investigated if TBL treatment was able to improve psychomotor speed in professional ice hockey players in a randomized, placebo controlled design. A total of 22 pro hockey players (N=11 TBL group; N=11 placebo group; overall mean age ± SD: 25 ±5 yrs) received either 12 min of TBL or placebo every morning between 8 and noon for a period of 24 days. Psychomotor speed using a visual warning signal paradigm was tested before and after trial completion and data were analyzed for mean reaction time and mean motor time. Results showed that psychomotor speed, particular motor time, improved after 24 days of TBL treatment compared to placebo in a group of professional ice hockey players.

4. Can transcranial brain-targeted bright light treatment via ear canals be effective in relieving symptoms in seasonal affective disorder? A pilot study.

Authors: Timonen M, Nissilä J, Liettu A, Jokelainen J, Jurvelin H, Aunio A, Räsänen P, Takala T.
Journal: Med Hypotheses. 2012 Apr;78(4):511-5.
PubMed link: http://www.ncbi.nlm.nih.gov/pubmed/22296809

Summary:
In this initial pilot study, 13 SAD patients were subjected to a daily dose of 8-12 min. of transcranial bright light therapy for 3 weeks. Depressive and anxiety symptoms were measured using standard questionnaires such as the 17-item Hamilton Depression Rating Scale (HAMD-17), the Beck Depression Inventory-21 (BDI), and the 14-item Hamilton Anxiety Rating Scale (HAMA) prior to the 4 week trial and afterwards. When comparing the depression and anxiety score between week zero (baseline) and week 4 (study endpoint), results showed a significant reduction in reported symptoms on all three measures. The findings suggest that transcranial bright light therapy might be an alternative to the traditional light therapy and should be explored in more depth.

5. Stimulating brain tissue with bright light alters functional connectivity in brain at the resting state.

Authors: Starck T, Nissilä J, Aunio A, Abou-Elseoud A, Remes J, Nikkinen J, Timonen M, Takala T, Tervonen O, Kiviniemi V.

Journal: World Journal of Neuroscience 2012; 2:81-90.
Journal link:
http://www.scirp.org/journal/paperinformation.aspx?paperid=19417#.UtwENhA1iM8

Summary:
50 healthy subjects were randomized into two groups (N=24 experimental group, N=26 control group) and either received 12 min of transcranial bright light therapy or sham, i.e. no light, while being subjected to Functional Magnetic Resonance Imaging (fMRI).
The results of the fMRI showed a clear increase in neural connectivity of the visual cortex and senso-motoric areas of the cortex under the transcranial light compared to the sham group. This suggests the brain to be light perceptive. In addition, these were the same brain areas that showed increased connectivity in the studies by Abou-Elseoud et al. (2011; 2014), summarized below.

6. Altered resting-state activity in seasonal affective disorder.

Authors: Abou Elseoud A, Nissilä J, Liettu A, Remes J, Jokelainen J, Takala T, Aunio A, Starck T, Nikkinen J, Koponen H, Zang YF, Tervonen O, Timonen M, Kiviniemi V.

Journal: Hum Brain Mapp. 2014 Jan;35(1):161-72.
PubMed link: http://www.ncbi.nlm.nih.gov/pubmed/22987670

Summary:
Resting state functional brain activity provides a method to detect an existing neurobiological substrate for various disorders, including Seasonal Affective Disorder (SAD). For this purpose, a total of 90 subjects (45 SAD patients; 45 healthy controls) underwent an fMRI to determine functional connectivity of various brain areas in the resting state. A total of 47 resting state networks (RSNs) were investigated. The results showed a clear difference in functional connectivity between SAD patients and healthy, age, gender and ethnicity-matched controls in 11 out of the 47 tested RSNs. The SAD patients showed increased functional connectivity in attentional, visual, and sensomotoric RSNs. These findings support previous findings of psychomotor, attentional, and cognitive impairments seen in SAD patients. Interestingly enough, the same brain areas showed increased activity in healthy controls when exposed to TBL in the previous study.

7. Group-ICA model order highlights patterns of functional brain connectivity.

Authors: Abou-Elseoud A, Littow H, Remes J, Starck T, Nikkinen J, Nissilä J, Timonen M, Tervonen O, Kiviniemi V.
Journal: Front Syst Neurosci 2011;5(37):1-17.
PubMed link: http://www.ncbi.nlm.nih.gov/pubmed/21687724

Summary:
90 subjects (45 SAD patients; 45 healthy controls) underwent a fMRI to determine functional connectivity of brain areas. Results from the fMRI scans were analyzed with different mathematical models. In addition to increased neuronal connectivity within the visual and senso-motoric cortex of the SAD patients, results showed that depending on the model order and analysis, the sensitivity towards disease detection can be significantly improved and resting state brain activity might prove to be a very useful tool to detect the underlying neurobiological substrates of diseases.

8. Encephalopsin (OPN3) protein abundance in the adult mouse brain.

Authors: Nissilä J, Mänttäri S, Särkioja T, Tuominen H, Takala T, Timonen M, Saarela S.
Journal: J Comp Physiol A Neuroethol Sens Neural Behav Physiol. 2012 Nov;198(11):833-9
PubMed link: http://www.ncbi.nlm.nih.gov/pubmed/22991144

Summary:
The presence of light-sensitive opsins in the retina has been shown successfully in various studies. The present study investigates the expression encephalopsin (OPN3) proteins in brain and peripheral tissue of mice. Tissue samples of 10 mice were analysed using Western blotting and immunohistochemistry. Results showed the OPN3 protein expression could be shown in almost all brain areas as well as in the peripheral tissue analyzed. This suggests that OPN3 might be involved in the mechanism of transcranial bright light.