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## Light therapy as a treatment for sexual dysfunctions – beyond a pilot study

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### Summary

**Aim.** Seasonal trends were demonstrated in reproduction and sexual activity. Through the secretion of melatonin the pineal gland plays an important role, in the neuroendocrine control of sexual function and reproductive physiology. We hypothesized that inhibition of the pineal gland activity through a light treatment may favorably affect sexual function.

**Method.** We recruited 24 subjects with a diagnosis of hypoactive sexual desire disorder and / or primary sexual arousal disorder. The subjects were randomly assigned to either active light treatment (ALT) or placebo light treatment (L-PBO). Participants were assessed during the first evaluation and after 2 weeks of treatment, using the Structured Clinical Interview for Sexual Disorders DSM-IV (SCID-S) and a self-administered rating scale of the level of sexual satisfaction (1 to 10). Repeated measures ANOVA were performed to compare the two groups of patients. Post-hoc analysis was performed by Holm-Sidak test for repeated comparisons.

**Results.** At baseline the two groups were comparable. After 2 weeks the group treated with Light Therapy showed a significant improvement in sexual satisfaction, about 3 times higher than the group that received placebo, while no significant improvement was observed in the group L-PBO.

**Conclusions.** Our results confirm a potentially beneficial effect of Light Therapy on primary sexual dysfunction. In the future, we propose to correlate clinical findings with testosterone levels pre / post treatment.

**Key words:** bright light, placebo, primary sexual dysfunction.

### Introduction

The pineal gland is an unpaired neuroendocrine organ located behind the third cerebral ventricle between the two cerebral hemispheres of the brain. Its name is derived from its shape, which is like that of a pine cone. Its principal function is to transfer light and dark information to the entire body physiology through the release of the hormone

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melatonin [1, 2]. In humans, melatonin is produced mainly in the pineal gland and less in the retina. Its synthesis and release are stimulated by darkness and inhibited by light; consequently, circulating melatonin levels are higher at night than during the day in all species [3, 4]. In lower vertebrates, the pineal gland is photosensitive and it is the site of the circadian clock, while in mammals, including humans, it has lost direct photosensitivity, but responds to light using a multisynaptic pathway. Photosensitive cells in the retina detect a light signal that is transmitted via the retinohypothalamic tract to the suprachiasmatic nuclei (SCN), the site of the master circadian clock. Fibers project from the SCN to the dorsomedial hypothalamic nucleus, to the cell of the spinal cord, to the superior cervical ganglia, and finally the postganglionic adrenergic fibers innervating the pineal gland. Changes in levels of noradrenaline (NA) released from these fibers ensure appropriate translation of the light information into melatonin synthesis by the pineal gland [5, 6]. Over a century ago a connection between melatonin and human reproductive function was established through clinical observation of the effects of pineal tumors on human sexual development. Animal studies, conducted in rodents and in seasonal breeders have also shown that the duration of the darkness related melatonin signal conveys photoperiodic information that modulates reproductive activity. However, the relationship between pineal melatonin and reproductive physiology in humans remains controversial [6, 7]. The pineal seems to perform its hormonal effect at different levels of the reproductive axis, including the hypothalamic-pituitary level [8] and the gonadal level [9]. Melatonin acts in gonads indirectly, reducing the secretion of gonadotropines and mainly LH; exerting antigonadal or antiovarulatory effects in humans. Many studies have demonstrated that elevated melatonin levels during the prepubertal age maintain the hypothalamic-pituitary-gonadal axis in quiescence, thus playing an inhibitory effect on pubertal development. With advancing age the decrease in serum melatonin activates hypothalamic pulsatile secretion of gonadotropin-releasing hormone and consequently the reproductive axis, which results in the onset of puberty [10]. This is likely the reason why the increased levels of melatonin in geographic areas with environmental conditions of poor light, as in northern countries, are found to have a reduction in the secretion of LH and a delayed age at menarche. Moreover, evidence suggests that abnormally high naturally or pharmacologic concentrations of melatonin in women are associated with altered ovarian function and anovulation or functional hypothalamic hypogonadism, and with primary hypogonadism or infertility with oligospermia or azoospermia in men [6, 11]. Another important function of the hormone melatonin is the increase in prolactin secretion in animals and humans [12, 13]. Furthermore, because of the presence of gonadotropin and gonadal steroids receptors in the pineal gland, melatonin exerts a direct action upon Leydig cells, inhibiting testosterone secretion, indicating a direct connection between pineal gland and gonadal function [14]. The results obtained in these studies suggest that an inhibition of pineal gland activity via a treatment with bright light could favorably influence sexual function, reducing plasma levels of melatonin and restore the physiological secretion of the latter.

In a recent paper we reported on a small pilot project that indicates the possible utility of bright light therapy in a sample of 9 male patients with nonorganic sexual

dysfunction. Our findings suggest a potentially positive effect of bright light therapy on primary sexual dysfunctions [15]. In the present study, we propose to confirm our preliminary results in a larger sample of patients suffering from nonorganic sexual dysfunction.

### Materials and Methods

The sample of 24 male subjects was recruited among outpatients referred to the Urology Department of the University of Siena Medical Center on the basis of a diagnosis of primary (not due to another illness, or to a medication, or to drugs of abuse) hypoactive sexual desire disorder (HSDD, n=3) and sexual arousal disorder (SAD, n=21). The University of Siena's competent research ethics committee approved of all recruitment, assessment, and treatment procedures. Subjects were enrolled on the study during the fall and winter months, beginning September 15, 2011 and ending February 28, 2012.. All subjects provided written informed consent after receiving a complete description of the study and having the opportunity to ask questions. Sexual functioning was assessed via the Structured Clinical Interview for DSM-IV-Sexual Disorders (SCID-S), a modified version of the Structured Clinical Interview for DSM-IV[16], including a section on sexual disorders. Subjects suffering from a mood disorder and under treatment with medications causing sexual side effects (i.e. SSRIs) were excluded from the study.

Subjects were randomly assigned to active light treatment (ALT, n=12) or placebo light treatment (L-PBO, n=12). They were assessed at baseline (prior to starting ALT or L-PBO) and after 2 weeks of ALT/L-PBO treatment via the SCID-S and a sexual satisfaction self-report, that asked them to rate their sexual satisfaction on a scale from 1 to 10. The ALT consisted of daily exposure to a white fluorescent light box (Super-Lite 3S), fitted with an ultraviolet filter and rated at 10,000 lx at a distance of 1 meter from screen to cornea for 30 min as soon as possible after awakening, between 7.00 a.m. and 8.00 a.m. The L-PBO was an identical light box fitted with a neutral density gel filter to reduce light exposure to 100 lx.

All the subjects adhered to the protocol and the two groups had the same compliance. Data was entered in a Microsoft Excel 2003 spreadsheet and the GraphPad Prism 5 software was used to perform repeated measures ANOVA for comparing the two groups of patients. Post-hoc analysis has been performed by Holm-Sidak test for repeated comparisons.

### Results

The level of sexual satisfaction at baseline was 1.9 +/- 1.5 in L-PBO and 2.2 +/- 2.4 in ALT group (Fig. 1 – *next page*).

After 2 weeks of treatment, the level of sexual satisfaction was 2.9 +/- 0.8 in L-PBO and 6.2 +/- 2.6 in ALT (Fig. 2 – *next page*).

After treatment RM ANOVA reported a significant difference between time ( $p = 0.0017$ ; (Fig. 3 *next page*) and no difference between groups ( $p > 0.05$ ).

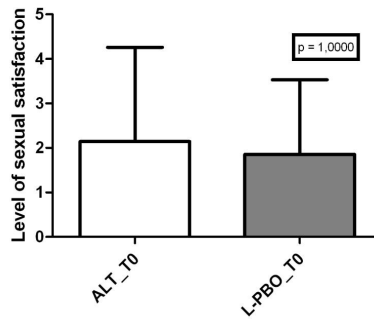


Figure 1. Level of sexual satisfaction in the two groups at baseline; values are means +/- standard deviation. Differences are not statistically significant

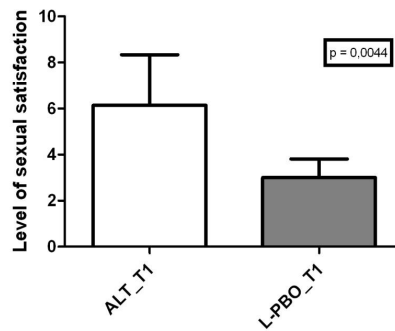


Figure 2. Level of sexual satisfaction in the two groups after two weeks of treatment; values are means +/- standard deviation. Differences between ALT and L-PBO are statistically significant

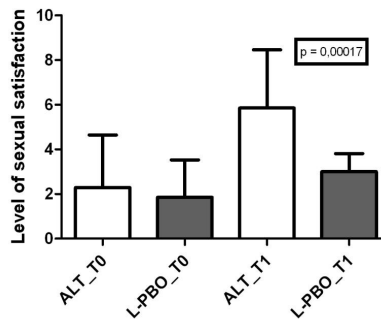


Figure 3. Comparison in level of sexual satisfaction between ALT and L-PBO groups, at baseline and after two weeks of treatment; values are means +/- standard deviation. Differences are strongly significant

Post-hoc Holm-Sidak confirmed significant improvement in sexual satisfaction ( $\alpha = 0.0149$   $p = 0.0102$ ) in the ALT group (Fig. 4), whereas no improvement was observed in the L-PBO group ( $p = 0.08$ ; Fig. 5).

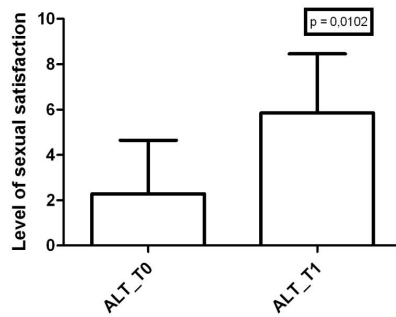


Figure 4. Level of sexual satisfaction in ALT group, at baseline and after two weeks of treatment; values are means +/- standard deviation. Differences are statistically significant

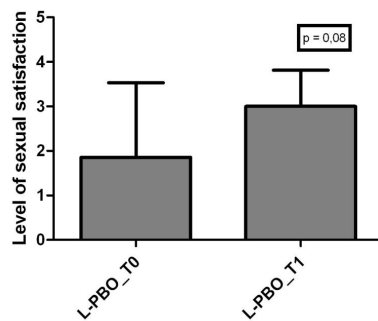


Figure 5. Level of sexual satisfaction in L-PBO group, at baseline and after two weeks of treatment; values are means +/- standard deviation. Differences are not statistically significant

### Discussion of results

Hypoactive Sexual Desire Disorder (HSDD) is one of two sexual desire disorders in the Diagnostic and Statistical Manual of Mental Disorders IV-R (DSM) [17] and is defined by the monosymptomatic criterion “persistently or recurrently deficient (or absent) sexual fantasies and desire for sexual activity, causing marked distress or interpersonal difficulty”. Sexual Arousal Disorder is defined as “the persistent or recurrent inability to attain, or to maintain until completion of the sexual activity, an adequate lubrication-swelling response of sexual excitement, causing marked distress or interpersonal difficulty. Seasonal trends have been demonstrated in reproduction and in sexual activities [18-21] and the pineal gland plays an important role in the neuroendocrine control of sexual function and reproductive physiology. Although we are still far from knowing exactly where and how the pineal suppressive role is exerted, the fact that the gland exerts an inhibitory function on the reproductive axis is widely accepted [19]. The pineal seems to exert its hormonal effect at different levels of the reproductive axis, both at the hypothalamic-pituitary level (for instance via the inhibition of the hypothalamic pulsatile secretion of gonadotrophin-releasing hormone) [8, 18] and at the gonadal level, where melatonin receptors have also been found [8, 9, 19]. Furthermore, melatonin appears to increase prolactin secretion which

may contribute to sexual dysfunction [13]. To date, studies suggest that an inhibition of pineal gland activity via a treatment with bright light could favorably influence sexual function [15]. Phototherapy shows a very low percentage of side effects, primarily linked to excessive exposure or proximity to light. The only noted contraindication for phototherapy is retinal disorders such as detachment or partial detachment, retinal degeneration etc. The most common side effects, are discomfort in the eyes (19%), headache (13%), irritability (6%), nausea (7%), the sweating (6%). These are usually mild, well tolerated and may be eliminated by decreasing the exposure period or finding a precise custom time in the course of the day in which to perform the therapy.

In our sample, level of sexual satisfaction at baseline was roughly comparable in the two groups, with no statistically significant differences. After 2 weeks of treatment the group that received active light treatment showed a significant improvement in sexual function with respect to baseline level, about 3 times higher than the group that received placebo. A slight improvement in sexual satisfaction was even observed in L-PBO group, but it was not statistically significant and was mostly influenced by a single case of hypersensitivity to placebo light treatment.

### Conclusions

The pineal gland is a neuroendocrine organ and its principal function is to transfer light and dark information to the entire body physiology through the release of the hormone melatonin. The pineal gland is photosensitive: in humans, the synthesis and the release of melatonin are stimulated by darkness and inhibited by light. A connection between melatonin and human reproductive function was established and the pineal seems to exert its hormonal effect at different levels of the reproductive axis. In a recent pilot study we suggested that an inhibition of pineal gland activity via a treatment with bright light could favorably influence sexual function [15] and in the present work we proposed to confirm these results on a larger sample of patients suffering from nonorganic sexual dysfunction.

Our results confirm a potentially beneficial effect of Light Therapy on the course of primary sexual dysfunction. In the future, we propose to correlate clinical findings with testosterone levels pre / post treatment.

#### **Роль фототерапии при лечении лиц с нарушениями сексуальных функций. Верификация результатов пилотажного исследования**

##### **Содержание**

**Задание.** Отмечено, что так репродукция, как и сексуальная активность подвергаются влиянию годовых ритмов. Гипифиз (орган, продуцирующий мелатонин) исполняет существенную роль в процессах гормонального контролирования сексуальных функций, а также физиологии репродукции. Принято решение использования фототерапии (для уменьшения функции гипофиза), которая может положительным образом повлиять на сексуальные функции.

**Метод.** В исследование включено 24 лица с диагнозом нарушения полового влечения и/или нарушения первичного сексуального возбуждения. Больные безвыборочно включили в группу с использованием активной фототерапии. АФ, или же в группу, в которой использована

фототерапия плацебо (ФТП). Клиническое состояние пациентов было оценено во время первого визита, а потом после двух недель лечения, структурного анализа сексуальных нарушений DSM-IV, а также шкалы самооценки сексуальной сатисфакции (0–10). Данные, полученные от пациентов, входящих до выделенных групп подвергнуты сравнению с проведением анализа вариантности АНОВА с повторяемыми измерениями. В рамках анализа пост хок использован тест сравнений Холма-Сидака.

**Результаты.** Вначале исследования не отмечено статистически достоверных различий между двумя группами. А после двух недель терапии в группе пациентов, использующей АФ отмечен существенный рост сексуальной сатисфакции, почти в три раза больший, нежели в группе, принимающей плацебо, в то время как в 1 группе ФП не отмечено существенных различий.

**Выводы.** Результаты проведенного исследования подтверждают факт, что применение фототерапии может принести пользу лицам с первичными нарушениями сексуальной потребности. Можно указать на факт необходимости определить корреляцию между эффектами лечения и концентрации тестостерона (как перед началом лечения ,так и его окончания).

**Ключевые слова:** яркий свет, плацебо, первичные сексуальные нарушения.

### **Rolle der Lichttherapie bei der Behandlung der sexuellen Dysfunktionen. Verifikation der Ergebnisse einer Pilotstudie**

#### **Zusammenfassung**

**Ziel der Studie.** Es wurde bemerkt, dass sowohl die Fortpflanzung als auch sexuelle Aktivität den Jahresrhythmen unterliegen. Die Zirbeldrüse (Organ, das für Melatonin verantwortlich ist) spielt eine signifikante Rolle in den Prozessen der hormonellen Kontrolle der sexuellen Aktivitäten und Physiologie der Fortpflanzung. Es wurde angenommen, dass die Anwendung der Lichttherapie (zwecks Senkung der Aktivität der Zirbeldrüse) günstig die sexuellen Aktivitäten beeinflussen kann.

**Methode.** Zur Studie wurden 24 Personen mit vermindertem sexuellen Interesse und/oder der diagnostizierten Störung der sexuellen Erregung eingeschlossen. Die Kranken wurden stichweise in die Gruppen eingeordnet: mit aktiver Fototherapie (active light treatment – ALT) oder mit Placebo-Licht (placebo light treatment – L-PBO). Der klinische Zustand der Patienten wurde beim ersten Besuch und nach zwei Wochen Behandlung ermittelt, und zwar mit Structured Clinical Interview for Sexual Disorders DSM-IV (SCID) und mit dem zehnstufigen Fragebogen zur sexuellen Zufriedenheit (0-10). Die von den einzelnen Patienten aus ausgesonderten Gruppen erzielten Angaben wurden verglichen, und die Varianzanalyse ANOVA wurde durchgeführt. Im Rahmen der post-hoc Analyse wurde der Mittelwertvergleichstest von Holm-Sidak eingesetzt.

**Ergebnisse.** Am Anfang wurden keinen statistisch signifikanten Unterschiede zwischen den beiden untersuchten Gruppen nachgewiesen. Nach zwei Wochen Therapie, in der ALT – Gruppe, wurde eine wesentliche Steigerung der sexuellen Zufriedenheit festgestellt, dreimal größer als in der Placebo-Gruppe, während in der L-PBO-Gruppe keine signifikanten Unterschiede nachgewiesen wurden.

**Schlussfolgerungen.** Die Ergebnisse unserer Studie bestätigen, dass die Anwendung der Lichttherapie die Personen mit vermindertem sexuellen Interesse positiv beeinflussen kann. Es wird suggeriert, dass man in der Zukunft die Korrelation zwischen den Behandlungseffekten und Testosteronkonzentration bestimmen soll (sowohl vor der Behandlung als auch nach dem Abschluss der Behandlung).

**Schlüsselwörter:** helles Licht, Placebo, vermindertes sexuelles Interesse

### **Le rôle de la luminothérapie dans le traitement des patients souffrant des troubles sexuels. La vérification de l'étude-pilote**

#### **Résumé**

**Objectif.** On observe que la reproduction et l'activité sexuelle sont sous l'influence des rythmes annuelles. La glande pinéale (qui produit la mélatonine) joue le rôle important dans le contrôle

hormonal des activités sexuelles et de la physiologie de la reproduction humaine. Les auteurs supposent que la photothérapie (en but de réduire l'activité de la glande pinéale) peut influencer favorablement sur l'activité sexuelle.

**Méthodes.** On examine 24 patients souffrant des troubles du désir et/ou de l'excitation sexuelle. Ces patients sont divisés au sort en deux groupes : 1/ avec la luminothérapie active (active light treatment – ALT) ; 2/ avec la luminothérapie placebo (placebo light treatment – L-PBO). On analyse l'état psychiques des patients deux fois : au début de la thérapie et après deux semaines avec les instruments suivants : Structured Clinical Interview for Sexual Disorder DSM-IV (SCID-S) et avec l'échelle de la satisfaction sexuelle (autoévaluation ,0-10). Les résultats de ces deux groupes sont comparés dans l'analyse ANOVA et dans l'analyse post-hoc de teste d'Holme-Sidak.

Résultats. Au début on n'observe pas de différences valables statistiquement dans les deux groupes examinés. Après deux semaines de la luminothérapie ALT on note dans ce groupe l'augmentation importante de la satisfaction sexuelle, environ trois fois plus forte que dans l'autre groupe de placebo, dans le groupe avec L-PBO on ne note pas de différences significantes.

Résultats. Ces résultats attestent que la luminothérapie peut aider les personnes avec les troubles sexuels primaires. Les auteurs suggèrent d'analyser au futur la corrélation des effets thérapeutiques et de la concentration de la testostérone (au début de la thérapie et après).

**Mots clés :** lumière forte, placebo, troubles sexuels primaires

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