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Bright versus dim ambient light affects subjective well-being but not serotonin-related biological factors

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ABSTRACT

Light falling on the retina is converted into an electrical signal which stimulates serotonin synthesis. Previous studies described an increase of plasma and CNS serotonin levels after bright light exposure. Ghrelin and leptin are peptide hormones which are involved in the regulation of hunger/satiety and are related to serotonin. Neopterin and kynurenine are immunological markers which are also linked to serotonin biosynthesis. In this study, 29 healthy male volunteers were exposed to bright (5000 lx) and dim (50 lx) light conditions for 120 min in a cross-over manner. Subjective well-being and hunger as well as various serotonin associated plasma factors were assessed before and after light exposure. Subjective well-being showed a small increase under bright light and a small decrease under dim light, resulting in a significant interaction between light condition and time. Ghrelin concentrations increased significantly under both light conditions, but there was no interaction between light and time. Correspondingly, leptin decreased significantly under both light conditions. Hunger increased significantly with no light–time interaction. We also found a significant decrease of neopterin, tryptophan and tyrosine levels, but no interaction between light and time. In conclusion, ambient light was affecting subjective well-being rather than serotonin associated biological factors.

1. Introduction

Light is a potent synchronizer of the endogenous pacemaker in the hypothalamus (Boivin et al., 1996). Light impulses affect the suprachiasmatic nucleus (SCN) via the retinothalamic tract and photosensitive, melanopsin-expressing ganglions in the retina, where the light input is converted into an electrical signal by membrane potential changes (Lockley et al., 2003). These electrical signals are transmitted to the pineal gland which contains high levels of serotonin.

Serotonin has an impact on numerous behavioral functions including mood, impulsivity, the sleep–wake rhythm, sexual behavior, nociception, body temperature, the immune system, hunger/satiety and energy balance (Jonnakuty and Gragnoli, 2008; Marston et al., 2011).

Previous studies have described an effect of bright light exposure on plasma and central nervous system (CNS) serotonin levels in depressed patients as well as in healthy subjects (Even et al., 2008; Neumeister et al., 1996; Golden et al., 2005). Besides the well-known mood effects of bright light therapy (Neumeister et al., 1998; Benedetti et al., 2003), a number of light-induced alterations in psychological and behavioral functions in humans including cognition, memory, agitation, sleep and others have been reported (Benedetti et al., 2003; Golden et al., 2005; Lieverse et al., 2010). Recently, a 3-week treatment with bright light was found to reduce appetite and body fat in overweight women (Danilenko et al., 2013).

All of these features are subject to complex mechanisms with serotonin as a major modulating factor. There are several other serotonin-related hormones and messenger molecules which may be photosensitive, thus being potential moderators between ambient light and human functioning.

1.1. Fat hormones and adipokines

Ghrelin is a 28 amino-acid peptide, mainly produced in the stomach, but also in the CNS (Van der Lely et al., 2004; Portelli et al., 2012). During food restriction plasma levels of ghrelin are high while they decrease after food intake. There is also evidence

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that ghrelin, as an orexigenic hormone, mediates food intake, increases appetite, decreases thermogenesis and causes a positive energy balance via the hypothalamus (Van der Lely et al., 2004).

A number of other, partly serotonin mediated, physiological and behavioral functions of ghrelin have been described. E.g., ghrelin promotes slow wave sleep, is able to inhibit the expression of proinflammatory cytokines, stimulates neuroprotection and inhibits serotonin release in depolarized neurons (Weikel et al., 2003; Dixit and Taub, 2005; Frago et al., 2011; Brunetti et al., 2002).

Leptin is mainly produced in and released from the white adipose tissue and is considered an antagonist of ghrelin. Leptin is able to inhibit food intake via leptin receptors in the hypothalamus and affects meal size, food preference and glucose balance (Guo et al., 2012; Schoeller et al., 1997; Gautron and Elmquist, 2011). Further, leptin increases thermogenesis and is able to bind immune cells such as leukocytes and natural killer cells (Bruno et al., 2005; Carlton et al., 2012). Leptin has also a role in the stimulation of the serotonin synthesis. In turn, serotonin inhibits the leptin expression and secretion in adipocytes (Calapai et al., 1999).

Several factors have an influence on ghrelin and leptin concentrations. These include circadian rhythmicity (Spiegel et al., 2004), sleep deprivation (Dzaja et al., 2004) and exercise (Shiiya et al., 2011). An interrelationship between ghrelin and serotonin involving melatonin and a potential alterability of ghrelin by photic signals have been suggested (Kirsz and Zieba, 2012).

Adipokine is mainly produced in and released from adipocytes (Gelsinger et al., 2010). Decreased adiponectin levels have been found in patients with major depressive disorder (Cizza et al., 2010; Lehto et al., 2010).

1.2. Immunological variables

Neopterin is produced in human monocyte-derived macrophages. High neopterin plasma levels represent a sensitive marker for the activation of the immune system and may concur with tryptophan degradation as well as increased nitrite and phenylalanine levels in the incidence of psychological symptoms (Widner et al., 2002; Capuron et al., 2011).

Kynurenine is a metabolite of tryptophan. The conversion of tryptophan into kynurenine via indoleamine 2,3-dioxygenase (IDO) is facilitated by a variety of stimuli including IFN-γ and tumor necrosis factor (TNF)-α (Widner et al., 2002).

Increased levels of phenylalanine have been reported in inflammation and immune activated conditions. Phenylalanine is the precursor amino acid of tyrosine which plays an important role in the biosynthesis of catecholamines (Neurauter et al., 2008). A correlation between phenylalanine and immune parameters such as interleukin-6 (IL-6) has been found (Haroon et al., 2012).

In this pilot study, the effect of short-term bright versus dim light exposure on subjective well-being and feelings of hunger/satiety as well as on potentially photosensitive plasma markers was investigated in healthy male volunteers. The hypothesis of the study was that ghrelin levels decrease as an effect of bright light exposure and increase during dim light intervention. In contrast, leptin levels were expected to increase under bright light and decrease under dim light exposure. Further a decrease of neopterin as an effect of bright light exposure was hypothesized. A potential finding of an influence of light on the parameters studied may have clinical implications in terms of regulation of weight and inflammation.

2. Methods

2.1. Subjects

A total of 29 healthy male volunteers were recruited for the study. The inclusion criteria were age 18–40 years, body mass index (BMI) between 20 and 25, a Morningness-Eveningness Questionnaire (MEQ) score between 30 and 70 (signifying a moderate eveningness, intermediate or moderate morningness type) and sleep duration of at least 6 h per night. Exclusion criteria included active smoker, current drug treatment, a psychiatric disorder assessed with the Mini-International Neuropsychiatric Interview (M.I.N.I.), somatic illness including acute flu/cold, intolerance for lactose, fructose or histamine, gastrointestinal surgery, dieting and extensive sport activities. All participants were screened by a psychiatrist.

In addition, probands were instructed to avoid training exercise in the evenings preceding the study interventions. Furthermore, in the evenings before the intervention days subjects had to refrain from eating and drinking caloric liquids from 8:00 pm until the next day.

2.2. Procedure

All participants were seen three times. During the first visit they underwent clinical screening with the M.I.N.I. and the MEQ and signed the informed consent form.

On the other two days, the actual study procedures took place. Participants arrived at the hospital at 7:30 am and were placed in a separate room with dim light conditions for 90 min. To reduce natural morning light bias to a minimum, the study was performed in January and February. At 9.00 am *t*0 baseline assessment procedures consisting of blood sampling in sitting patients and completing of the Hunger Fullness Scale (HFS) as well as Visual Analog Scales (VAS) for hunger and well-being took place. Between *t*0 and *t*1 (9.00–11.00 am) participants were permanently exposed to one of the two light conditions: bright light with 5000 lx and 4061 K (SD = 50.9 K) or dim light with 50 lx and 4249 K, SD = 41.1 K) generated by a specifically produced LED light cabin. During light exposure, participants had to sit in front of the light cabin and did not eat or drink, except of water. The participants were allowed to read during the intervention time. At *t*1 the above described assessments were repeated.

The time interval between the two interventions was seven days. Light conditions were applied in a cross-over design, thus all participants underwent the testing procedure in both light conditions. Half of the participants received the light conditions in the sequence dim light–bright light, the other half in the reverse order.

Electrical Body impedance Analysis (BIA, including lean mass, total body adipose tissue mass) were determined by impedance analysis using InBody 720 Body Composition Analyzer from Biospace Europe with an integrated scale using software Lookin Body Version 3.2, Body Composition Analysis Management System.

The study procedure was approved by the Ethics Committee of Innsbruck Medical University.

2.3. Light sources

Light sources were three semicircular light cabins equipped with LEDs (light-emitting diodes) specifically developed and produced by a light design manufacturer, Bartenbach GmbH, Aldrans, Austria.

2.4. Blood samples

In order to take the pulsatile secretion of ghrelin into account, blood samples were taken three times per assessment (at time 0, after 5 min and after 10 min). The mean value of the respective 3 measurements was used for the statistical analysis. We used 4.5 ml EDTA tubes and stored the blood samples on ice before centrifugation. The blood samples were centrifuged for 15 min with 2000 rpm, at +4 °C. After centrifugation plasma was frozen at −20 °C for 24 h and then stored at −80 °C until analysis.

Total plasma concentration of ghrelin, leptin and adiponectin were measured at the Department of Internal Medicine I, Medical University Innsbruck using commercially available Enzyme-Linked Immuno-Sorbent Assays (ELISA's) (manufacturers: Millipore, Darmstadt, Germany, for ghrelin and human adiponectin and R&D Systems, Abington, UK, for human leptin).

Concentrations of neopterin were measured by ELISA according to the protocol of the manufacturer (BRAHMS, Hennigsdorf, Germany). Kynurenine and tryptophan concentrations were analyzed by HPLC on reversed phase C18 columns and monitoring their UV absorption at 360 nm (kynurenine) and fluorescence (tryptophan) at 286 nm excitation and 366 nm emission wavelengths (Widner et al., 1997). Phenylalanine and tyrosine concentrations were measured with an alternative HPLC method using reversed phase C18 columns and utilizing the fluorescence of both compounds at excitation of 210 nm and emission of 302 nm wavelengths (Neurauter et al., 2013). Nitrite concentrations were analyzed by the Griess