Activation of the mesostriatal reward pathway with exposure to ultraviolet radiation (UVR) vs. sham UVR in frequent tanners: a pilot study

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ABSTRACT

Frequent and excessive tanning persists despite a growing understanding of its associated morbidity and mortality, suggesting that ultraviolet radiation may impart rewarding effects beyond the assumed cosmetic benefits. To empirically measure putative centrally rewarding properties of ultraviolet radiation (UVR), we assessed the effects of a commercially available tanning bed upon regional cerebral blood flow (rCBF), a measure of brain activity, using single-photon emission computed tomography (SPECT). Seven frequent salon bed tanners were placed under a UVA/UVB tanning light during two sessions; one session with UVR and the other with filtered UVR (sham UVR). Session order was randomized and subjects were blinded to study order. During the UVR session, relative to sham UVR session, subjects demonstrated a relative increase in rCBF of the dorsal striatum, anterior insula and medial orbitofrontal cortex, brain regions associated with the experience of reward. These changes were accompanied by a decrease in the subjective desire to tan. These findings suggest that UVR may have centrally rewarding properties that encourage excessive tanning.

Keywords Neuroimaging, reward, single-photon emission computerized tomography, striatum, tanning, ultraviolet radiation.

INTRODUCTION

Almost 30 million Americans, including 20% of 18- to 39-year olds, visit indoor tanning salons each year (Levine et al. 2005). The voluntary exposure to sunlight continues unabated despite progressively increasing rates of ultraviolet radiation (UVR)-induced illness and death (Levine et al. 2005). Between 50 and 90% of skin cancers are caused by UV radiation. In 2000, the WHO estimates that there were 200 000 cases of melanoma and 65 000 melanoma-associated deaths worldwide, coupled with 2.8 million squamous cell and 10 million basal cell carcinoma cases (WHO 2009).

The use of tanning beds to administer UVR is a particularly prevalent form of exposure. Ten annual tanning bed visits increases the risk of developing malignant melanoma almost eightfold for those under 30 years of age (Westerdahl et al. 1994). Although persons using tanning beds exhibit a high level of knowledge about the risks of UVR exposure, often more than non-users, the awareness of these adverse effects does not decrease or alter tanning activity, especially for those in their teens and 20s (Mawn & Fleischer 1993; Arthey & Clarke 1995; Robinson et al. 1997a). In fact, while public knowledge regarding the hazards of sun exposure grew from 1986 to 1996, sun-burning and the regular use of tanning beds also increased (Robinson, Rigel & Amonette 1997b).

Persistent tanning, despite both perceived and experienced adverse consequences, has led some investigators to suggest that tanning has ‘addictive’ properties (Nolan & Feldman 2009). Over half of the persons who endorse frequent sunbathing (Warthan, Uchida & Wagner 2005)
and the use of tanning beds (Harrington et al. 2011) report behaviors consistent with addictive disorders, including an inability to decrease their tanning frequencies, compulsive tanning and continued tanning despite adverse consequences. In fact, the term ‘tanorexia’ has been coined to refer to persons who compulsively tan (Warthan et al. 2005). Underlying these behaviors is the implication that UVR has physiologic reinforcing properties distinct from any known psychosocial benefits of having a tan (Feldman et al. 2004). For instance, two of the top most frequent reasons selected by the indoor tanners were to ‘feel good’ and for ‘relaxation’ (the top reason being cosmetic) (Harrington et al. 2011). Importantly, the perceived rewarding effects of UVR was reportedly blocked by an opioid receptor antagonist (Kaur et al. 2006).

To our knowledge, the central nervous system (CNS) effects of UVR have not been explored. As UVR is passively experienced, UVR administration may assist not only in understanding compulsive tanning but provide a novel method to assess reward-related CNS processes. We therefore assessed the neural response to UVR in frequent tanners using a methodology developed by Feldman et al. (2004). In this paradigm, subjects were exposed to UVR in a tanning bed in the presence of a filter that did or did not remove UVR (UVR or sham UVR), such that the only experiential difference between sessions was the subject’s reception of UVR (or not). Using this procedure, we hypothesized that UVR, relative to sham UVR, would elicit activation in the brain regions associated with reward. Specifically, we predicted that striatal regions, including the nucleus accumbens, caudate and putamen, would be activated during UVR exposure relative to sham-UVR exposure. We utilized single-photon emission computed tomography (SPECT) to measure the effect of UVR (relative to sham UVR) on brain perfusion.

**MATERIALS AND METHODS**

**Study subjects**

After protocol approval by the University of Texas Southwestern Medical Center (UTSW) Institutional Review Board, subjects were recruited from frequent tanners responding to a notice in two local tanning salons (see Harrington et al. 2010 for further details). The notice asked for volunteers for a study on tanning if they like to tan in a tanning bed at least three times a week and if maintaining a tan was important to them. Subjects contacting the clinic were requested to fill out self-administered surveys assessing: (1) demographic information, prescription medications and supplements, and past medical and psychiatric history; (2) information on tanning behaviors, including age at first tanning bed use, frequency of tanning bed use and individual reasons for tanning; and (3) a modified Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) Criteria for Substance Dependence Disorder. Eight items from the DSM-IV criteria for Substance Dependence Disorders (Warthan et al. 2005; Kourosh, Harrington & Adinoff 2010) were modified to reflect tanning behaviors rather than substance dependence. Following completion of the survey, subjects were offered the opportunity to be contacted to participate in additional research. Subjects were contacted if they regularly tanned in a tanning bed at least twice per week over the past 90 days and if they endorsed at least three of the seven modified criteria (Harrington et al. 2010). Twenty subjects were contacted and eight agreed to participate in the study. Consent was obtained and subjects were financially compensated for their participation. One of these was subsequently excluded because of concurrent illicit drug use.

Additional medical and psychiatric history was obtained by self-administered health report form. Subjects were excluded from the study if they self-reported major psychiatric disorders or active substance use disorders, the use of any medication with central nervous system effects, or were females who were pregnant, breast-feeding or sexually active without birth control. All female participants were required to have a negative urine pregnancy test during initial assessment and just prior to each scanning session.

**Scanning procedure**

On the two subsequent visits, the subjects were imaged via SPECT while exposed to either UVR or sham UVR. Sessions for each subject were conducted in the afternoon or early evening and between 2 and 8 days apart (6.3 ± 2.1 days). Tanning was conducted in a Sunquest 3000S tanning canopy, which includes both UVA and UVB wavelengths. Irradiance at the exposure site was measured using probes for UVA and UVB radiation positioned at 12 in. from the bulbs. Fluence rate of UVA was 0.1 W/cm² and UVB was 0.061 W/cm². Two matching, visually identical (Kucenic et al. 2002) plastic/acrylic filters, obtained from Dr. Steven Feldman, were placed over the tanning bed panel and tested as previously published (Feldman et al. 2004). These filters were transparent to visible/infrared light; one blocked UVR (Polycast UF3, Sterling Industries, Shawnee, KS, USA) and the other was transparent to UVR (Polycast SUVT, Sterling Industries, Shawnee). As the filters were transparent to infrared light, the same heat load was provided during both sessions. Fluence rate for UVA with the transparent filter (active session) was 0.1 w/cm²; with UVR blocked
filter (sham session) 0.001 w/cm². Fluence rate for UVB with transparent filter was 0.047 w/cm²; with UVR blocked filter 0.0 w/cm². The estimated dose delivered to each subject for the UVR transparent filter was 6 J/cm² UVA and 0.282 J/cm² UVB; for the UVR blocked filter 0.06 J/cm² UVA and 0 J/cm² UVB. The order of sham-UVR and UVR tanning sessions were pseudo-randomly determined and subjects were blinded to session order. The same tanning canopy (with either the UVR or non-UVR filter) was used for both sessions. Four subjects received the sham-UVR filtered radiation on their first sessions.

Upon arrival to each session, subjects changed into bathing suits of their choice. An intravenous line was then placed into each subject’s left arm. Subjects were then brought into the study room and immediately lay down on the tanning bed. Prior to turning on the tanning bed, subjects were asked to rate ‘how much you feel like tanning right now’ on a 10 cm visual analogue Likert scale, from ‘Not at all’ to ‘More than I ever have’. Opaque eye shields were then placed over the eyes and the tanning bed was turned on. Lamps were placed 12 in. above the subjects. One minute after turning on the tanning light, 20 mCi of ⁹⁹mTc HMPAO (GE Healthcare, Princeton, New Jersey) was administered intravenously over 30 seconds and followed by a 10 ml saline flush over 30 seconds. [⁹⁹mTc HMPAO assesses regional cerebral blood flow (rCBF) from 1 to 3 minutes following administration]. Tanning sessions lasted ten minutes, which was consistent with the subjects’ usual practice. After the tanning light was turned off, the eye covering and intravenous lines were removed. While still on the tanning bed and prior to being able to view their skin color, subjects filled out two questionnaires about the tanning session, the first again asking how much they wanted to tan and the second asking ‘How much did you like this tanning bed?’ [from ‘not at all’ (1) to ‘excellent’ (5)] and ‘How much tan do you expect to get from this tanning bed?’ [from ‘no tan’ (1) to ‘the perfect tan’ (4)]. Following the second session, subjects were also asked whether they preferred the first tanning session, the second tanning session or had no preference. As subjects exposed to sham UVR might notice that they did not tan, subjects were asked to cover exposed body areas with Oil of Olay A Touch of Sun immediately following termination of the tanning session.

SPECT scans were obtained in the Nuclear Medicine Center at UT Southwestern Medical Center 90 minutes following ⁹⁹mTc HMPAO administration to allow time for tracer activity to clear from blood and non-brain tissues. Because ⁹⁹mTc HMPAO is extracted during the first arterial pass and remains distributed in the brain in proportion to rCBF for many hours, this perfusion image represents rCBF at the time of radiotracer administration and not at the time of the scan. SPECT images were acquired on a PRISM 3000S 3-headed SPECT camera (Picker International, Cleveland, OH, USA) using ultra-high-resolution fan-beam collimators (reconstructed resolution of 6.5 mm) in a 128 x 128 matrix in three-degree increments. For our system, voxels in reconstructed images were 1.9 mm³. Reconstructed images were smoothed with a sixth-order Butterworth threedimensional filter, and attenuation was corrected using a Chang first-order method with ellipse size adjusted for each slice.

**Statistical analysis**

**Demographic and clinical data**

Basal and post-light exposure changes in Desire to Tan were assessed using repeated measures analysis of variance with post hoc paired t-tests for both within sessions (pre- and post-light exposure) and between sessions (UVR versus sham UVR) using delta responses (post-light versus pre-light scores).

**Image analysis**

SPECT images were resliced to 2 mm³ voxels, co-registered to Montreal Neurologic Institute (MNI) space using the MNI T1 SPECT template, smoothed to a final resolution of 10 mm and normalized to whole brain counts (to correct for individual variability in global cerebral blood flow). The accuracy of spatial normalization of functional brain images (fSPECT, positron emission tomography and functional magnetic resonance imaging (fMRI)) is limited by the spatial resolution of the original data (6 mm for these data), by partial volume effects and by the limits of the normalization algorithm used. Thus, the accuracy of normalization in our data is about 2–4 mm, and the anatomic designations assigned to observed rCBF effects are constrained by these limitations, as well as by our spatial resolution and partial volume effects. Voxel-wise analyses (voxel z score at $P < 0.01$, cluster size >50 voxels) comparing UVR versus sham-UVR effects were conducted using Statistical Parametric Mapping (SPM5; University College, London, England). Regions reaching our statistical threshold were overlaid on the MNI MRI template. Regions are identified by $x, y, z$ MNI coordinates and cluster size. Regions of interests (ROIs) defined by cluster boundaries for four regions we considered relevant to reward processes were also identified (see Table 1) and the average rCBF within each cluster was determined for each subject in each condition. Differences between sessions were obtained by paired t-test and Pearson product moment correlation was used to assess the association between clusters and Desire to Tan. RCBF responses are relative; that is, a region showing increased rCBF reflects...
either an increase in rCBF during UVR compared with sham UVR, a decrease in sham UVR relative to UVR or a combination of both.

RESULTS

Subjects

The seven subjects (four females) consisted of five Caucasians and two Asians. Subjects were 30.7 ± 9.0 (mean ± SD) years old, started regular tanning at 21.4 ± 8.9 years old and had tanned 26.9 ± 6.0 days in the previous ninety days. All subjects reported tanning on a regular basis two to three times per week.

Change in rCBF following UVR versus No-UV exposure

The rCBF response to UVR was compared with the rCBF response to sham UVR (MNI coordinates and cluster size in Table 1 except as noted). Increases in rCBF were observed during UVR exposure, relative to sham UVR, in the left caudate, right putamen and left anterior insula, extending up to the boundary between the inferior frontal gyrus (BA 44) and middle frontal gyrus (BA 9) (Fig. 1). Three regions show a relative increase in the orbitofrontal cortex (OFC): medial OFC; lateral left OFC extending superiorly to the left dorsolateral prefrontal cortex; and a smaller, more medial left cluster. Other regions of increased rCBF included a large region of the left superior temporal gyrus (Brodman Area 42) and left dorsolateral prefrontal cortex. The only relevant area of decreased rCBF following UVR relative to the sham UVR was a small area in the left OFC (−30, 54, −18; 75).

SPM-derived clusters showed a significant increase in the left dorsal caudate \([t = 4.5, \text{ degrees of freedom (d.f.)} = 6, P = 0.004]\), medial OFC \([t = 5.0, \text{ d.f.} = 6, P = 0.002]\) and left anterior insula \([t = 6.7, \text{ d.f.} = 6, P = 0.0005]\), but not right putamen \([t = 1.4, \text{ d.f.} = 6, P = 0.21]\), during the UVR relative to sham UVR session.

Subjective responses

Desire to Tan significantly changed from basal to post-UVR measures \((F = 16.1, \text{ d.f.} = 12, P = 0.002)\) and there was a significant time × session (UVR versus sham UVR) interaction \((F = 12.70, \text{ d.f.} = 12, P = 0.004)\) (Fig. 2). Post-hoc analyses demonstrated similar Desire to Tan.

Table 1 Brain regions demonstrating increased \((P < 0.01)\) regional cerebral blood flow (rCBF) following ultraviolet radiation (UVR) compared with sham UVR in frequent tanners.

<table>
<thead>
<tr>
<th>Identified region</th>
<th>MNI coordinates</th>
<th>k</th>
<th>Z score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caudate, leftb</td>
<td>−12  0  18  56  2.96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Putamen, rightb</td>
<td>26  −16  14  78  3.68</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior insula, left, extending dorsally to inferior/middle frontal gyrusb</td>
<td>−36  20  36  231  3.54</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orbitofrontal cortex, lateral, left, extending to dorsolateral prefrontal cortex</td>
<td>−40  34  −18  333  3.47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orbitofrontal cortex, left</td>
<td>−12  46  −16  85  3.41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Orbitofrontal cortex, medialb</td>
<td>12  24  −14  68  3.09</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superior temporal gyrus (BA42), left</td>
<td>−62  −34  20  575  4.36</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dorsolateral prefrontal cortex, right</td>
<td>52  36  10  72  3.41</td>
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aCluster size. bRegions considered in cluster-derived region of interest analyses.

Figure 1 Areas of relative increases and decreases in regional cerebral blood flow (rCBF) following ultraviolet radiation (UVR), relative to sham UVR, in frequent tanners \((n = 7)\). Transverse images are on top row, sagittal image in bottom left, and coronal image in bottom right. Red areas reveal voxels increased following UVR relative to sham UVR and blue areas reveal voxels decreased following UVR relative to sham UVR. MNI coordinates noted at the bottom left of each image. L = left; R = right. OFC = orbitofrontal cortex, STG = superior temporal gyrus. All transverse, sagittal and coronal images are available in Supporting Information Appendix S1.
properties given the importance of UV-mediated synthesis of vitamin D for human survival. Biological mechanisms underlying the connection between UVR and neural activity may include UV-induced changes in the gene p53, which upregulates the transcription of POMC in keratinocytes. POMC is cleaved into α-melanocyte-stimulating hormone that induces melanogenesis, increasing the free-radical absorbing molecule melanin and thereby the photoprotective mechanism represented by a suntan (Pathak & Fanselow 1983; Riley 1997; Bykov, Marcusson & Hemminki 2000; Cui et al. 2007) and β-endorphin, an opioid-receptor agonist. β-endorphin may act peripherally on the skin to induce the relief from pain and irritation or centrally to induce relaxation or euphoria. UVR can also alter serotonin levels, a neurotransmitter strongly implicated in anxiety disorders and depressive disorders, through light-induced changes in pineal N-acetyltransferase (Klein et al. 1997). Interestingly, over 80% of female undergraduate students who frequently tan (≥40 times per year) report symptoms consistent with seasonal affective disorder (SAD) or sub-syndromal SAD compared with 46% of non-tanners (Hillhouse, Stapleton & Turrisi 2005).

Clinically relevant brain regions showing changes following UVR included the dorsal striatum (i.e. caudate, putamen), medial OFC and left anterior insula. The ventral striatum, or nucleus accumbens, is typically associated with drug-induced reward (Drevets et al. 2001; Martinez et al. 2003). However, several studies have implicated the dorsal striatum in the affective experience of both reward and punishment (Balleine, Delgado & Hikosaka 2007; Delgado 2007). A strong correlation is observed between dopamine release in the dorsal caudate ($P < 0.0001$) and putamen ($P < 0.05$) with the elation/euphoria experienced after nicotine inhalation (Barrett et al. 2004). Dopamine transmission in both the left medial caudate (the same region of change observed in the present study) and putamen also show increased dopamine release following monetary rewards (Zald et al. 2004). The medial OFC is thought to monitor the reward value of several different reinforcers (Kringlebach & Rolls 2004). Neuroimaging studies using fMRI have shown increased medial OFC responses to monetary rewards (Elliott & Deakin 2005; Elliott, Agnew & Deakin 2010), to methamphetamine administered to healthy controls (Vollm et al. 2004) and to cocaine administered to cocaine-addicted subjects (Kufahl et al. 2005). The insula, particularly the anterior insula, is preferentially involved in the evaluative, experiential or expressive aspects of internally generated emotions (Reiman et al. 1997; Craig 2003) and anterior/middle insular activation has been observed during the ingestion of chocolate in ‘chocolate lovers’ (Small et al. 2001) and cocaine administration (Kufahl et al. 2005).

DISCUSSION

These findings reveal that UVR exposure via a commercially available tanning bed, relative to sham UVR, increases mesostriatal activity in frequent tanners. Furthermore, we have confirmed the findings of Feldman et al. (2004) revealing that most frequent tanners can successfully identify UVR from sham UVR based solely upon their subjective response. These findings strongly suggest that frequent tanning may involve CNS reward and/or reinforcement over and above the oft-stated goal of ‘getting tan’.

The epidermis and nervous system both emerge from the ectoderm germ layer and there are well recognized associations between dermatologic and psychiatric disorders (Locala 2009). In fact, the term ‘psychodermatology’ has been used to describe the mind–skin connection. From an evolutionary perspective, it is reasonable to suggest that sunlight may have centrally rewarding properties given the importance of UV-mediated synthesis of

![Figure 2](image)

**Figure 2** Change in Desire to Tan in individual subjects pre- and post-sham ultraviolet radiation (UVR) and UVR exposure sessions.
The strengths to our design included the blinded administration of UVR and sham UVR, including the use of self-tanning cream to prevent the subject’s ability to objectively determine UVR exposure. The use of SPECT allowed us to assess brain reactivity early in the tanning sessions during the circumscribed (1–3 minutes) period of time most expected to coincide with subjective rewarding effects. Nevertheless, the small n, coupled with apparently distinct groups of subjects (Asian and Caucasian) and responses (high versus low Desire to Tan, high versus low dorsal striatal rCBF), limit the significance and interpretation of our findings. The absence of skin phototype assessments did not allow us to consider skin tone as a covariate. Salon tanning obtained by participants between their two study sessions, which ranged from 2 to 8 days, may also have affected the findings. Limits of spatial resolution and the ability to only determine relative measures of limbic activation are inherent in our SPECT methodology and camera. It should also be noted that the SPECT technique assessed relative (to whole brain), not absolute, rCBF differences between groups. Larger studies assessing neural processing of UVR in both frequent and infrequent tanners of various racial backgrounds are clearly indicated to determine the role of UVR exposure (both frequency and years of tanner) and skin type (Fitzgerald 1975) upon brain reactivity. Future studies would also benefit from a more thorough assessment of skin phototype and other co-morbid psychiatric pathology, such as other substance use, SAD and body dysmorphic disorder (Phillips et al. 2006), that may effect the central rewarding response to UVR. Although fMRI would offer the advantage of assessing neural activity during the whole tanning session, the metal in a tanning bed would not allow its use in an fMRI environment.

Our findings of dorsal striatal activation by UVR, relative to sham UVR, provide a unique approach to our understanding of persistent tanning. Despite the near universal awareness of skin cancer risk and the acceleration of the skin’s aging process, the use of tanning salons continues to increase. If CNS reward mechanisms, similar to those observed in other addictive disorders, are involved in frequent tanning, novel and more dramatic behavioral and pharmacologic treatment approaches to tanning may be useful in preventing morbidity and mortality.

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Authors Contributions

CRH, HTJ, MDD and BA were responsible for study concept and design. CRH and BA were responsible for paper preparation. TSH was responsible for obtaining SPECT imaging and SPECT analysis. TCB, MG and SK were responsible for subject recruitment, data collection and monitoring of all imaging sessions. HTJ and MDD provided critical revision of the paper. All authors critically reviewed content and approved final version for publication.

References


SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Appendix S1 Complete transverse, sagittal and coronal images showing areas of relative increases and decreases in regional cerebral blood flow (rCBF) following UVR, relative to sham UVR, in seven frequent tanners. Please note: Wiley-Blackwell are not responsible for the content or functionality of any supporting materials supplied by the authors. Any queries (other than missing material) should be directed to the corresponding author for the article.