UV-induced beta-endorphin production causes addiction-like symptoms in mice

June 19 2014

Why has it been so hard to discourage people from spending time in the sun when the dangers of ultraviolet light exposure are so well recognized? A new study from Massachusetts General Hospital (MGH) investigators adds important support to the theory that ultraviolet (UV) light can actually be addictive, finding that chronic UV exposure raises circulating levels of beta-endorphin in mice and that UV-habituated mice exhibit withdrawal symptoms if beta-endorphin activity is blocked. Their report appears in the June 19 issue of *Cell*.

"Our study identified an organic pathway encoded in skin whereby UV radiation causes the synthesis and release of beta-endorphin and produces opiate-like effects, including addictive behavior," says David E. Fisher, MD, PhD, chair of Dermatology and director of the Cutaneous Biology Research Center (CBRC) at MGH, who led the study. "This provides a potential explanation for the 'sun seeking' behavior that may underlie the relentless rise in most forms of skin cancer."

Several studies – particularly those enrolling individuals who use indoor tanning facilities – have found evidence of addiction-like behavior in frequent tanners. For example, frequent tanners were somehow able to tell the difference between tanning beds using UV radiation and those delivering non-UV light. Other studies found that administration of an opioid blocker produced withdrawal-like symptoms in frequent tanners, implying but not proving that something had been regularly activating opioid pathways.

Part of skin's natural response to UV light is production of a protein called POMC, which is then clipped into several smaller fragments, one of which induces production of the pigment melanin. Processing of another segment of POMC leads to generation of beta-endorphin in the skin. The current study was designed to investigate whether this UV-induced beta-endorphin produces opioid-like effects such as pain relief and dependency. The study also examined whether the pathway mediating these effects is initiated by the production of endorphin in the skin.

The investigators delivered a daily dose of UV light – equivalent to the exposure of fair-skinned humans to 20 to 30 minutes of midday Florida sun – on the shaved backs of a group of mice for 6 weeks. The dose was calculated to induce tanning but not burning of the animals' skin. Within a week of the first UV exposure, the animals' blood beta-endorphin levels rose significantly, remaining elevated during the study period and gradually returning to normal after UV exposure was discontinued. Tests conducted at regular intervals during the study period showed that the UV-treated animals were less responsive to light touch or temperature changes than a control group with no UV exposure. The higher the animals' beta-endorphin levels, the less sensitive they became. But administration of naloxone, which would broadly block opioid-pathway activity, returned skin sensation back to normal in the UV-treated animals.

In UV-habituated animals, naloxone treatment also produced classic symptoms of opioid withdrawal, such as trembling, shaking and teeth chattering. And mice trained to associate the effects of naloxone with an environment they would naturally prefer – a dark box instead of a light box – invariably choose to enter the area where they had not experienced naloxone-produced symptoms. In contrast, a strain of mice in which production of POMC was selectively blocked in skin or which lacked the beta-endorphin gene altogether exhibited none of the responses or

symptoms seen in normal mice after UV treatment, confirming the presence of a UV-activated opioid pathway in the skin.

"It is possible that a natural mechanism reinforcing UV-seeking behavior may have developed at certain stages of mammalian evolution through its contribution to the synthesis of vitamin D," Fisher says. "But such behavioral effects would also carry the carcinogenic risks of UV light that we now recognize. Today's alternative sources of vitamin D, such as inexpensive oral supplements, are both safer and more accurate in maintaining healthy vitamin D levels.

"Our finding that persistent UV seeking really does appear to be an addiction-related behavior suggests that reducing an individual's skin cancer risk may require actively confronting factors that influence this hazardous behavior – like the promotion of indoor tanning – instead of the more passive risk messages that have been relied on," he adds. "We also wonder whether this interaction of sun, skin and endorphins might be involved in other behaviors or disorders and whether this may represent one of the earliest behavioral responses that can be considered addictive." Fisher is the Wigglesworth Professor of Dermatology at Harvard Medical School.

More information: *Cell*, Fell et al.: "Skin -endorphin mediates addiction to ultraviolet light." www.cell.com/cell/abstract/S0092-8674(14)00611-4

Provided by Massachusetts General Hospital