UV-irradiation down-regulates immune functions and causes fatigue by photo-optico-neuronal network: Lesson from iNOS-knockout mice

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Ultraviolet B and A have been known to stimulate melanin synthesis by melanocytes and to inhibit immune functions of the skin locally at a site of irradiation. To our surprise, topical irradiation of UVB to the eye increased plasma levels of α-MSH and stimulated dermal melanocytes to proliferate and synthesize melanin pigment systemically by a mechanism that was inhibited by either hypophysectomy or cilliary ganglionectomy but not by optic nerve resection while UVA systemically down-regulated immune functions by a mechanism which was selectively inhibited by optic nerve resection. These observations suggested that UV-B selectively stimulated α-MSH secretion by the hypothalamo-pituitary pro-opiomelanocortin system via the first branch of the trigeminal nerve, thereby stimulating dermal melanocytes. Systemic irradiation of UVB and/or UVA has been known to suppress immune functions. We recently found that topical irradiation of UVA also suppresses immune functions of dermal Langerhans cells and induced apoptosis of B-cells in lymph nodes. UVA-induced suppression of immune functions was inhibited by either optic nerve denervation or hypophysectomy, but not cilliary ganglionectomy. These results suggest that UVA reached to the retina stimulates the hypothalamo-pituitary network through the optic nerves. The dermal reactions and immunosuppression induced by topical irradiation of UVA and UVB to the eye were not observed with animals that lack the activity of inducible-type of NO synthase (iNOS). These observations suggest that biological reactions induced by topical UV-irradiation of the eye are mediated by NO. The prsent work shows for the presence of a novel signaling pathway that modulates immune functions and induces the sense of fatigue via the NO-dependent photo-optico-neuronal network.