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The Role of the STAT3 Signaling for Melatonergic Synthetic Pathway in the Rat Pineal Gland

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Abstract : The pineal gland of the vertebrate brain is a circumventricular organ which serves as a major neuroendocrine gland with the primary function of rhythmic secretion of neurohormone melatonin under the control of the hypothalamic suprachiasmatic nucleus (SCN). Soon after the onset of the darkness, the activity of the key rate-limiting enzyme for melatonin synthesis, arylalkylamine N-acetyltransferase (AANAT), raises due to the increased release of norepinephrine from sympathetic neurons terminating on the parenchymal cells where it binds to β-adrenergic receptors. Melatonin codes the length of the night, and it is well recognized for its anti-inflammatory effects. However, to our knowledge, less is known about the effect of the immune system on the melatonin biosynthesis and the precise role of the STAT3 in the signaling pathway leading to the expression of AANAT. Lipopolysaccharide (LPS) is the essential component in the outer surface membrane of gram-negative bacteria and acts as a strong stimulator of natural and innate immunity. STAT3 acts as an important factor in immune response. Here we investigated the effect of LPS on the components of the melatonergic synthetic pathway in the pineal gland. The experiments were performed both in vivo and in vitro. The changes in AANAT activity were determined by radioenzymatic assay. PCR analyses were carried out to detect aa-nat, icer, spi-3 and stat3 gene expression. From our results, it is apparent that the high basal level of phosphorylated forms of STAT3 can be elevated after systemic as well as in vitro administration of LPS. Our experiments have shown that LPS reduces melatonin synthesis, nevertheless, the activity of AANAT was increased. Moreover, the basal level of phosphorylated STAT3 counteracts β-adrenergic receptor-mediated aa-nat gene expression and sustains its own and spi-3 gene expression. In conclusion, LPS can affect immunomodulators such as melatonin in the pineal gland.

Keywords : AANAT, lipopolysaccharide, pineal gland, rat, STAT3
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