INTERNATIONAL SYMPOSIUM ON PINEAL HORMONES

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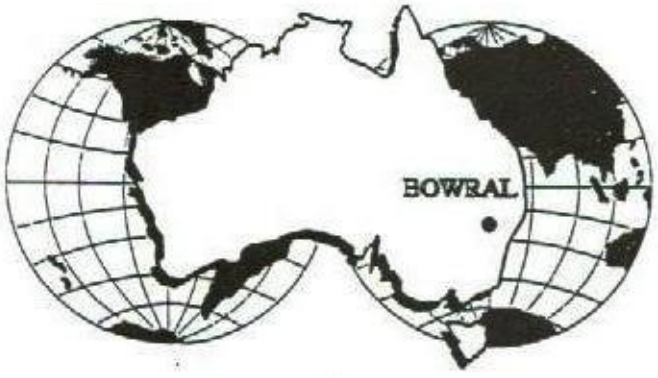
PROGRAMME AND ABSTRACTS OF PAPERS



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Serotonin/melatonin biological interrelations.

Serotonin (5-HT) and Melatonin (MLT) originate from dietary L-tryptophan, through tryptophan hydroxylase: the enzyme is highly active in pineal, enterochromaffin and carcinoid cells, whereas it is lacking in platelets (P), that do not synthetize, but accumulate 5-HT via a Na-dependent transport process, and release it through a Ca-dependet exocytotic mechanism. MLT easily crosses the megacariocyte (M) membrane and accumulates within the nucleus. The M cytosol MLT fluorescence disappears when the Behnke committed membrane system welds and forms P. In the nucleus MLT interferes with some phases of translation and transduction.

The cytosol MLT is desacetylated to 5-HT, while alkyl-acyl-glycerophosphorylcholine gives rise to the P-activating factor (PAF), that is partly retained intracellularly, partly released so as stimulate a variety of cells through specific receptors. AChE reaction product is absent from the demarcation membrane system, as if ACh were incompatible with 5-HT. The bone marrow serotonergic nerve endings and varicosities release 5-HT, that diffuses between cells and acts on the surrounding cellular targets. The serotonergic axons descend along the intermediary column of the spinal cord from the serotonergic Raphe obscurus and Raphe pallidus nuclei, where NMDA receptors receive excitatory inputs from the lateral habenulae. The bone marrow P have a 5-HT uptake carrier, associated with a saturable, high affinity binding site (5-HT_2). The residual MLT of P contributes to the stability of P membrane, thus preventing P aggregation and prolonging the P life span. P behave as an ubiquitous, fully available reservoir of 5-HT and MLT. MLT is the only compound that can be safely administered when the dietary essential amino acid tryptophan is insufficient, or the endogenous MLT synthesis is inadequate. The therapeutis use of MLT in many impairments of the CNS is efficacious, provided that the local uptake and binding to receptors are normal: however, a suitably long treatment is generally necessary.

The efficacy of MLT (but not of 5-HT) in cancer therapy is mainly dependent on the regulation of the transcription and translation of growth factors. However, two essential points must be kept in mind: 1) MLT is necessary, but not sufficient by itself to cure cancer; 2) MLT must be supported by simultaneous administration of retinoids and tocopherols, SRIF and PIF. In such conditions the results are good or even excellent.

The best results are obtained in almost every blood disease.