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ANGIOTENSIN II (Ang II) TYPE 1 (AT_1) RECEPTOR-MEDIATED NEURONAL MIGRATION IN MOUSE OLFACTORY EPITHELIUM EXPLANT CULTURES.

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It is known that both AT_1 and Ang II type 2 (AT_2) receptors participate in the processes of growth, proliferation and differentiation of several non-neuronal cell types. However, it is not clear whether Ang II receptor subtypes have similar roles in the nervous system. We have studied the effects of Ang II on neuronal migration, proliferation and differentiation in a model culture system, the olfactory epithelium (OE) of the mouse. The presence of both AT_1 and AT_2 receptors in embryonic mouse OE and OE explant cultures was demonstrated by RT-PCR and receptor binding assays. Addition of Ang II (10-100 nM; 15-48 hr.) to the culture medium immediately following plating caused time- and concentration-dependent increases in the total number of neurons migrating from OE explants. This effect of Ang II was abolished by the AT_1 receptor antagonist losartan (1 μM), but not by the AT_2 receptor blocker PD123,319 (1 μM). The effect of Ang II did not appear to be due to changes in progenitor cell proliferation or neuronal differentiation, since neither the percentage of cells incorporating [^{3}H]-thymidine, nor the number of progenitor cells that differentiated into post mitotic neurons (assessed by aquisition of immunoreactivity for the neural cell adhesion molecule NCAM, a marker of neuronal differentiation) was increased in Ang II-treated cultures. Together; the data suggest that the AT_1 receptor- mediated effect of Ang II on the total number of migratory neurons is due to an enhancement of neuronal migration, rather than an effect on proliferation or differentiation. This effect of Ang II does not involve AT_2 receptors. (Supported by NS-19441).