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INTRAVENTRICULAR APPLICATION OF C-FOS and JUN B ANTISENSE-OLIGONUCLEOTIDES BLOCKS LIGHT-INDUCED PHASE SHIFTS OF THE MAMMALIAN CIRCADIAN SYSTEM

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Light-induced phase shifts of the mammalian circadian system result in the expression of c-Jun, JunB, JunD, c-Fos, FosB and Krox-24 transcription factor gene proteins in the ventrolateral subdivision of the suprachiasmatic nucleus (SCN) lasting up to 8 hrs. In order to assess the role of these transcription factors in the control of the circadian system we blocked the expression of c-Fos and JunB proteins by intraventricular application of antisense phosphorothioate oligodeoxynucleotides (ASO; 4mM in 2 μ l).

While a light pulse (300 lux, 1 hr) at circadian time (CT) 15 induced a phase shift (-125 \pm 15 min) of the circadian rhythm, application of ASO 6 hours before the light pulse blocked the phase shift (-10 \pm 16 min). Application of nonsense-(control)-ASO (NSO; 4mM in 2 μ l) did not prevent the effect of the light pulse, resulting in a phase shift (-127 \pm 20 min) not significantly different from the one induced by light alone. These results demonstrate that transcription factors of the *jun* and *fos* gene families are an essential part of the cellular signal transduction pathway mediating light-induced phase shifts of the circadian pacemaker.