Paroxetina, fluoxetina, clomipramina, mas não a imipramina e a mianserina provocam apoptose em duas linhagem de neuroblastoma humano - glioma

Differential induction of apoptosis by antidepressants in glioma and neuroblastoma cell lines: evidence for p-c-Jun, cytochrome c, and caspase-3 involvement.

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Abstract

Several antidepressants, mainly selective serotonin-reuptake inhibitors (SSRIs) and some tricyclic antidepressants (TCAs), have been shown to possess potent apoptotic activity in different cell lines. Our aim was to screen and select those agents with significant activity and elucidate the molecular pathway underlying this process in rat glioma and human neuroblastoma cell lines. We studied the effect of different antidepressants on apoptotic markers, including: cell viability, DNA fragmentation, cytochrome c (Cyt c) release from mitochondria, and caspase-3- like activity. In addition, the involvement of MAPK genes, c-Jun, and ERK was determined. **Paroxetine and fluoxetine, SSRIs, clomipramine, a TCA, but not imipramine or mianserin (an atypical antidepressant), caused apoptosis in both cell lines,** as assessed by flow cytometry of propidium iodide-stained C6 cells and typical fluorescence microscopy in glioma cells. These apoptotic changes were preceded by rapid increase in p-c-Jun levels, Cyt c release from mitochondria, and increased caspase-3-like activity. Assessment of paroxetine cytotoxicity in primary mouse brain and neuronal cultures showed significantly lower sensitivity to the drug's proapoptotic activity. These results strongly suggest that selected antidepressants induce apoptosis in neuronal and glial cell lines. Activation of p-c-Jun and subsequent increased Cyt c mitochondrial release participate in the apoptotic mechanism of the antidepressant. **The high sensitivity to these drugs of the cancer cell, compared with primary brain tissue, suggests the potential use of these agents in the treatment of brain-derived tumors.**

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