Volatile organic compounds such as toleune, trichloroethylene and perchloroethylene are potent and reversible blockers of voltage-gated calcium current in nerve growth factor (NGF)-differentiated pheochromocytoma (PC12) cells. It is hypothesized that effects of VOCs on ICa contribute to the acute neurotoxicity of VOCs. The present experiments examined the ability of xylene, a VOC that is structurally similar to toluene, to block ICa in PC12 cells. Whole-cell patch clamp techniques were utilized to examine xylene effects on currents elicited by a 200 ms voltage-step from a holding potential of -70 to +10 mV. Following exposure to 3000 M xylene (as mixed xylene isomers), peak ICa was reduced to 21 ? 9 % of control amplitude while current amplitude immediately prior to the end of the voltage step was reduced to 12 ? 6 % of control (n = 3). Xylene, at nominal concentrations between 150 and 3000 M, reduced ICa in a concentration-dependent manner. In addition to decreasing amplitude, xylene also altered the inactivation kinetics of ICa. In the absence of xylene, currents decayed with a single exponential and had a tau value of 133 ? 39 msec (n = 3). In the presence of 1500 M xylene, inactivation kinetics were best fit by two exponential components with tau values of 17 ? 9 and 57 ? 10 msec (n=3). These data indicate that voltage-gated calcium channels are sensitive to the effects of xylene, and that xylene produces the same characteristic alterations in calcium channel function that are observed following exposure to toluene, perchloroethylene and trichloroethylene. Thus, VOCs have a common ability to disrupt calcium channel function, and this action may contribute to the neurotoxic effects of VOCs. (This abstract does not reflect EPA policy).