Amphetamine analogs are known to induce not only neurotoxicity at serotonergic axon terminals but also neocortical neuronal degeneration. However, a much less studied aspect involves the impact of amphetamine exposure on neuronal development. The present study investigated whether pretreatment of PC12 cells with dioxyamphetamine (DA) alters differentiation of PC12 cells by NGF and, if so, which components of the Ras/Raf/MEK/ERK pathway known to be involved in the differentiation response to NGF are particularly affected. Though exposure of PC12 cells to DA 1h prior to NGF treatment resulted in apoptosis, several PC12 cells survived. However, neurite outgrowth of these NGF-responsive cells was repressed. Immunoblots of whole cell extracts revealed a strong induction rather than inhibition of ERK phosphorylation up to 48h after DA/NGF treatment. Our results indicate that NGF-mediated neurite outgrowth was inhibited by pretreatment with DA, and this blockage of NGF-induced neuritogenesis was not due to an inhibition of ERK phosphorylation.