Does the presence of morphine counteract adaptive changes in expression of G-protein α subunits mRNA induced by chronic morphine treatment?

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Abstract:
Opiate dependence develops due to changes in intracellular signaling caused by long-term exposure to morphine. Here we investigated changes in the mRNA expression of the main classes of G-protein alpha (Gα) subunits in various brain regions in morphine-dependent rats. Rats received increasing doses of morphine, 10–50 mg/kg, b.i.d., for 14 days. G-protein alpha-subunit mRNA expression was determined shortly following the conclusion of chronic morphine administration (2 h after the final dose) and during withdrawal (48 h after the final dose). Significant changes in mRNA expression for Gα subunits were observed in several brain areas during withdrawal, while the changes were much less evident or absent 2 h after the final drug injection. Changes in mRNA expression were particularly evident in the nucleus accumbens (increases in Gα(12), Gα(q), Gα(11), and Gα(0) during withdrawal, increase in Gα(i) and decrease in Gα(s) just following treatment). The direction of the changes, which were not all significant, for Gα(12), Gα(q), and Gα(11) was generally consistent in the amygdala and prefrontal cortex; changes in G proteins coupled to the adenylyl cyclase cascade were less consistent. These results suggest that morphine dependence leads to alterations in intracellular signaling, which are reflected in changes in the expression of genes encoding various G proteins. The results may explain why signs of opiate dependence are not expressed during chronic administration of morphine, but only after cessation of the treatment.

Key words: chronic morphine, withdrawal, rat brain areas, G-protein alpha subunits, mRNA