Up-regulation of acetylcholine receptors during subchronic infusion of pancuronium is caused by a posttranscriptional mechanism related to disuse.

**Objective:** Contrasting with the classic theory that competitive block of the acetylcholine receptor induces up-regulation of the receptor, recent studies show that irreversible block of acetylcholine receptors with alpha-bungarotoxin decreases acetylcholine receptor number within hours. This study investigated the early effects of competitive acetylcholine receptor block with the reversible, competitive muscle relaxant, pancuronium. **Design:** Prospective, randomized, placebo-controlled experimental study. **Subjects:** Healthy adult Sprague-Dawley rats. **Setting:** Animal laboratory in a university hospital. **Interventions:** After internal review board approval, Sprague-Dawley rats were anesthetized and received pancuronium at a rate to completely suppress neuromuscular twitch. The control group received saline. Infusion times were 0, 3, 6, or 12 hrs (n = 8 per group). One sciatic nerve was stimulated to induce muscle twitch, and the other nerve remained unstimulated. Total acetylcholine receptor expression, as well as expression of messenger RNA of the five subunits, was assayed. **Measurements and main results:** There were no differences in acetylcholine receptor number between groups at time points 0, 3, and 6 hrs. At 12 hrs, acetylcholine receptor numbers in both the
stimulated (35.2 +/- 4.8 fmol acetylcholine receptor/mg protein) and nonstimulated (38.3 +/- 4.8)
pancuronium group, as well as the nonstimulated control saline group (37.5 +/- 4.6), were significantly
increased compared with stimulated controls (27.6 +/- 4.0). Pancuronium did not potentiate the
acetylcholine receptor up-regulation of the nonstimulated control group at 12 hrs. There were no
changes in messenger RNA expression between groups. CONCLUSIONS: Infusion of the reversible
competitive inhibitor pancuronium up to 12 hrs does not reduce acetylcholine receptor number and
therefore contrasts with the irreversible acetylcholine receptor blocker alpha-bungarotoxin. This study
documents that 12 hrs of disuse per se leads to an increased expression of the acetylcholine receptor
number by a posttranscriptional mechanism that can be prevented by nerve-evoked muscle
contraction.