

AMPHETAMINE ALTERS GROUP I mGluR EXPRESSION IN THE RAT STRIATUM AND MEDIAL PREFRONTAL CORTEX

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INTRODUCTION

- Group I metabotropic glutamate receptors (mGluR1 and mGluR5 subtypes) and their key scaffolding protein Homer1b/c are densely expressed in the striatum.
- These receptors are believed to play important roles in the regulation of psychostimulant action.
- Amphetamine, a psychostimulant, increases extracellular glutamate levels, which in turn activates postsynaptic mGluR1/5 in striatal neurons.
- We **hypothesize** that alterations in mGluR1/5 and Homer 1b/c expression in the rat striatum and medial prefrontal cortex (mPFC) would occur in response to acute injection of amphetamine *in vivo*.

METHODS

- Following IACUC approval, adult male Wistar rats received an intraperitoneal injection of saline (n = 4) or amphetamine (5 mg/kg, n = 5).
- Motor responses to amphetamine were monitored following drug and saline administration using infrared photo beams.
- For detecting gene expression, rats were anesthetized and sacrificed 1 h after saline or amphetamine injection.
- Brains were removed, and the striatum, including the dorsal (caudate putamen) and ventral (nucleus accumbens) striatum, and medial prefrontal cortex (mPFC) were dissected.
- Synaptic proteins were extracted for Western blot analysis of changes in mGluR1, mGluR5, and Homer1b/c protein levels with specific antibodies.
- The density of immunoblots was measured using optical scanning and statistically analyzed using t-test (p<0.05).

RESULTS

FIGURE 1: AMPH increases rat motor activity

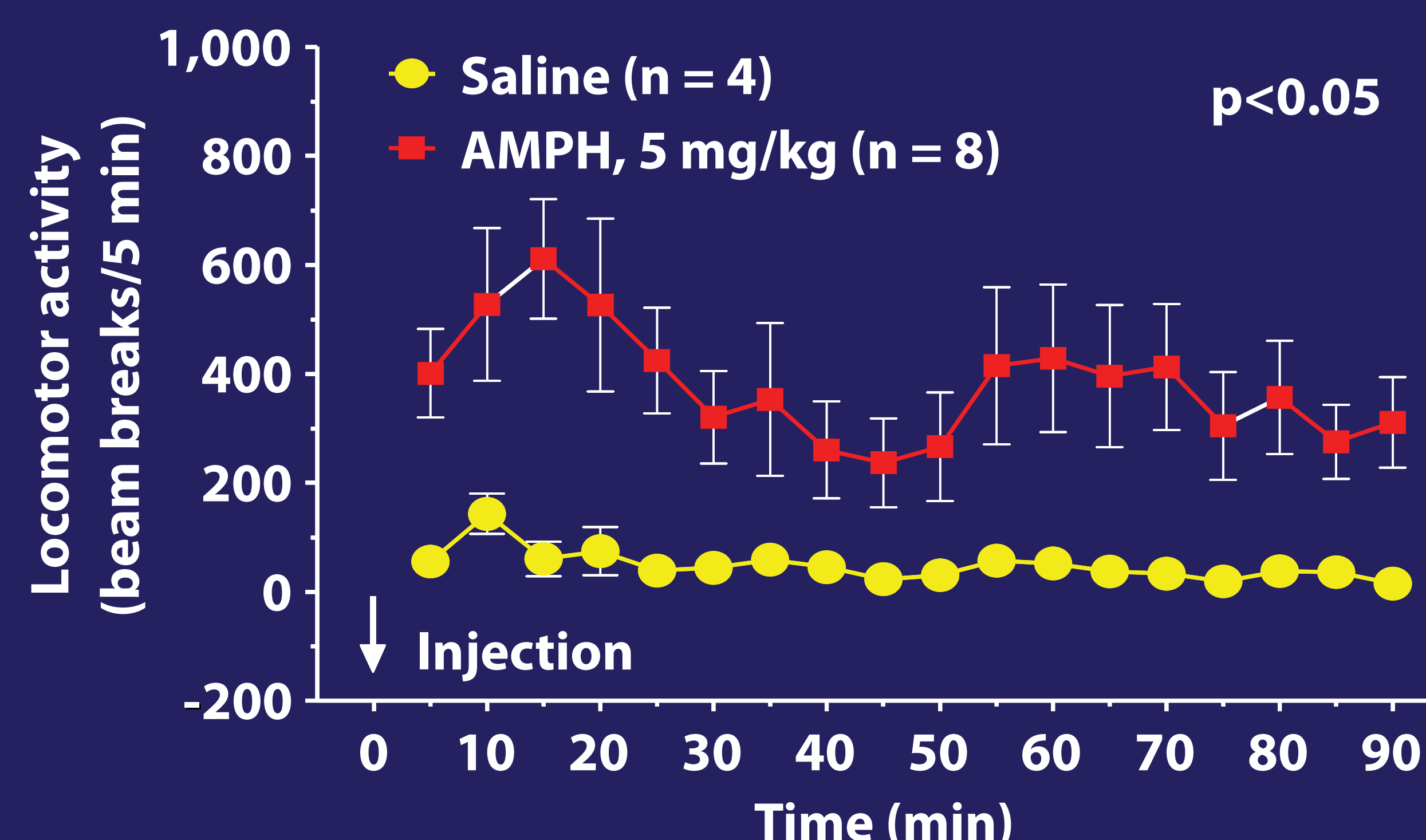
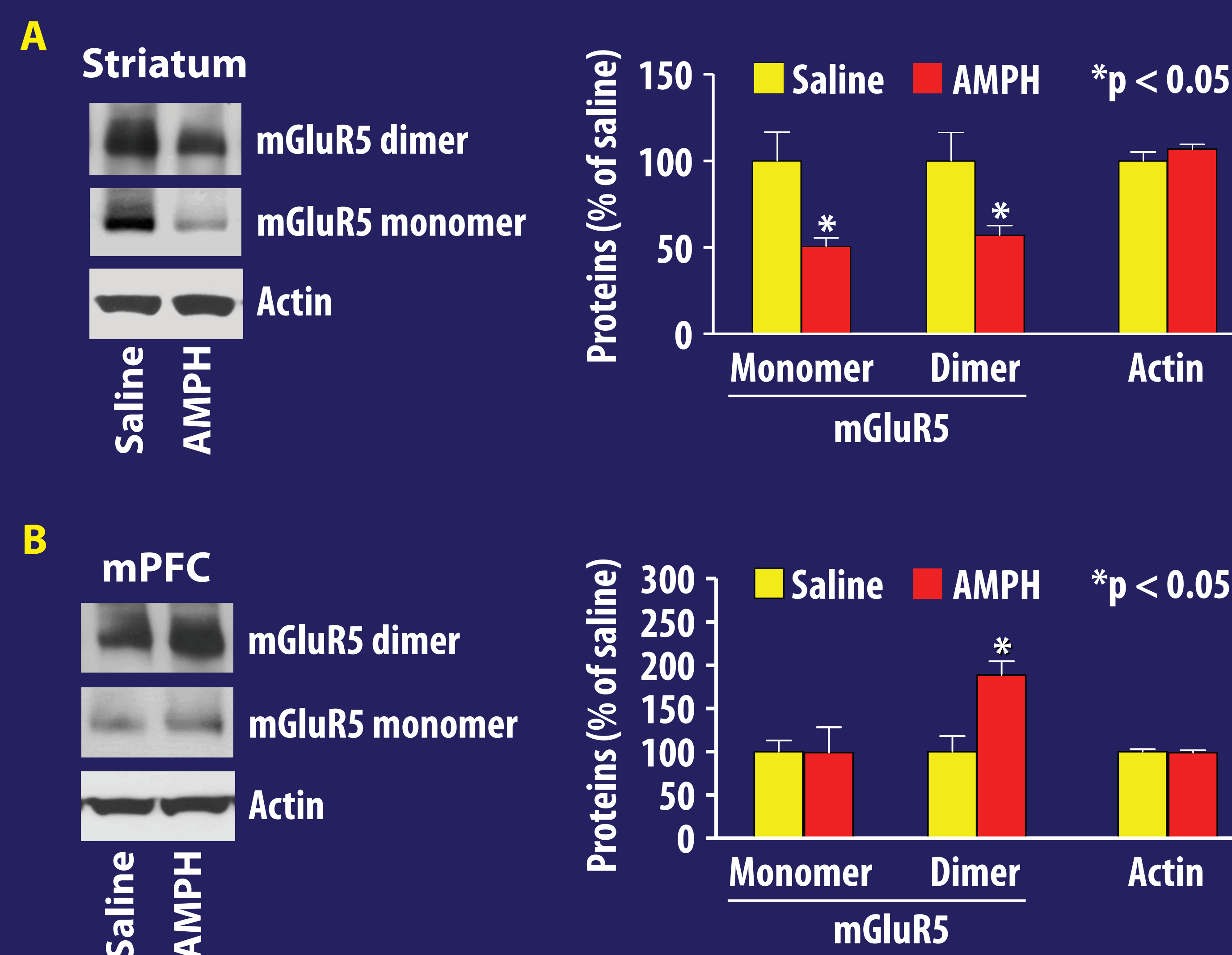


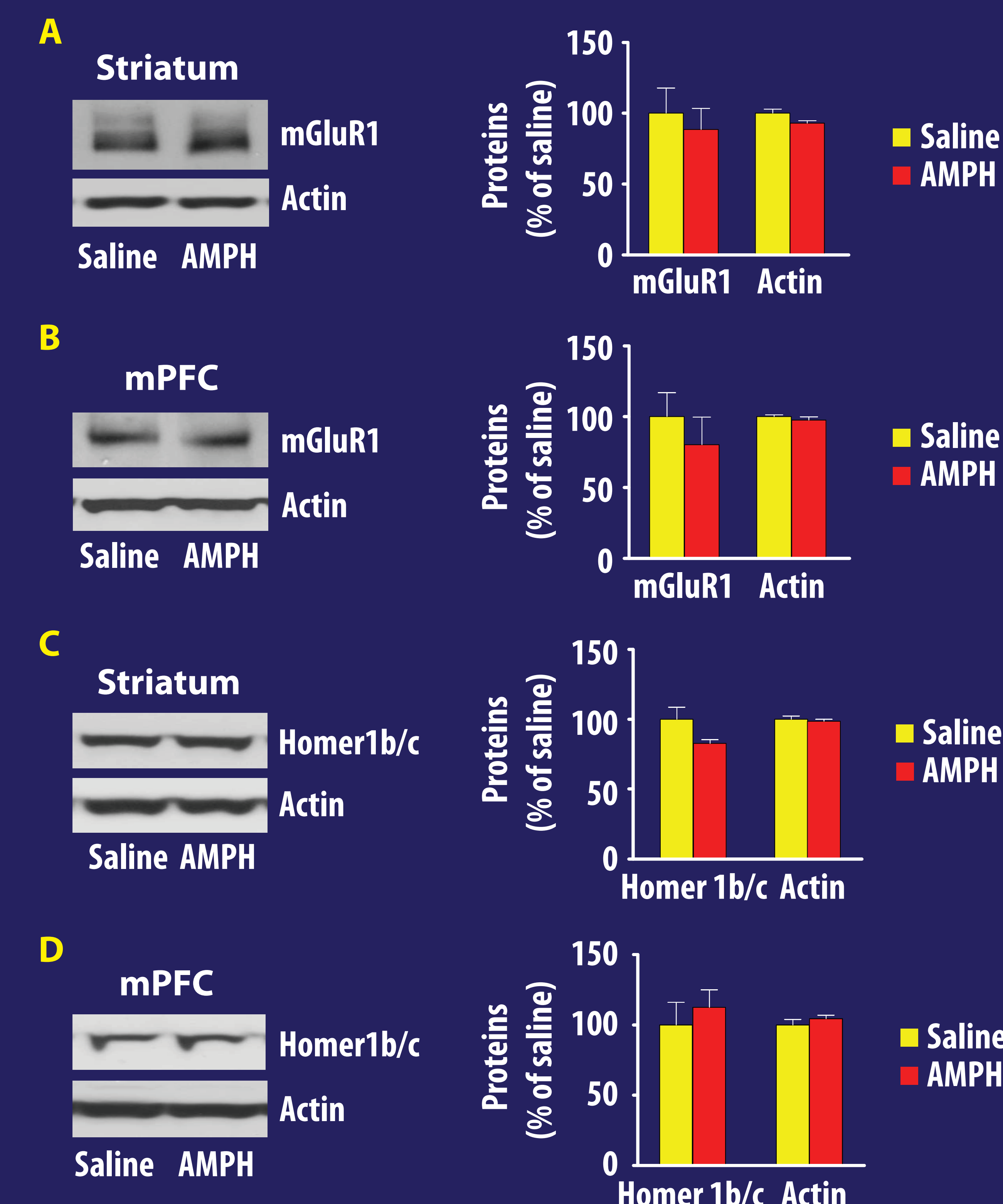
FIGURE 2: AMPH alters mGluR5 expression



CONCLUSION

- The data identify mGluR5 as a sensitive target of amphetamine.
- Acute amphetamine exposure is able to alter striatal mGluR5 expression in a subtype- and region-specific manner.

FIGURE 3: AMPH did not alter mGluR1 or Homer 1b/c expression



DISCUSSION

- Amphetamine increases glutamate release in the striatum.
- Released glutamate can activate mGluRs in striatal neurons to produce drug effects.
- Group I mGluRs have been demonstrated to undergo rapid desensitization following ligand stimulation of the receptor.
- Our finding of a loss of synaptic mGluR5 after amphetamine within the striatum suggests a previously unrecognized mechanism for such desensitization.
- Amphetamine has no effect on glutamate release in the mPFC
- Future studies are needed to define the role of amphetamine-stimulated mGluR5 expression in this region.