

# AMPHETAMINE ALTERS ACID-SENSING ION CHANNEL EXPRESSION IN THE RAT STRIATUM

## INTRODUCTION

- The acid-sensing ion channels (ASICs) are widely expressed in mammalian brains and modulate synaptic transmission, in addition to a variety of other neuronal activities.
- In the striatum, two ASIC subtypes (ASIC1 and ASIC2) are densely expressed.
- Given the fact that the striatum is a central site for processing biological actions of drugs of abuse, expression of abundant ASICs in this CNS structure implies a potential involvement of the channels in expressing drug effects.
- In this study, we examined the expression of ASIC1 and ASIC2 in the rat striatum in response to chronic exposure of the psychostimulant, amphetamine, *in vivo*.
- We **hypothesized** that ASIC would be a sensitive target to repeated psychostimulant exposure.

## METHODS

- Following IACUC approval, adult male Wistar rats (2 groups, n = 6 per group) received intraperitoneal injections of saline or amphetamine (once daily for 7 days, 1.25 mg/kg for day 1 and day 7, 4 mg/kg for days 2-6).
- 14 days after drug exposure, the rats were sacrificed using a standard methodology.
- Brains were immediately removed, cooled, and sliced into coronal sections (400  $\mu$ m).
- The dorsal caudate putamen (CPu) and ventral nucleus accumbens (NAc) were dissected in artificial cerebrospinal fluid (ACSF).
- A membrane-impermeable cross-linking reagent bis (sulfosuccinimidyl) suberate (BS<sup>3</sup>) was added.
- BS<sup>3</sup> only cross-links ASICs on the surface of live cells to form high-molecular weight aggregates which can then be readily separated from the normal intracellular monomer ASIC proteins for use in Western blots.
- Densities of immunoblots were measured using optical scanning and the data were analyzed using Student's t-test (p < 0.05).

## RESULTS

Figure 1: Surface and intracellular expression of ASICs in normal striatal neurons

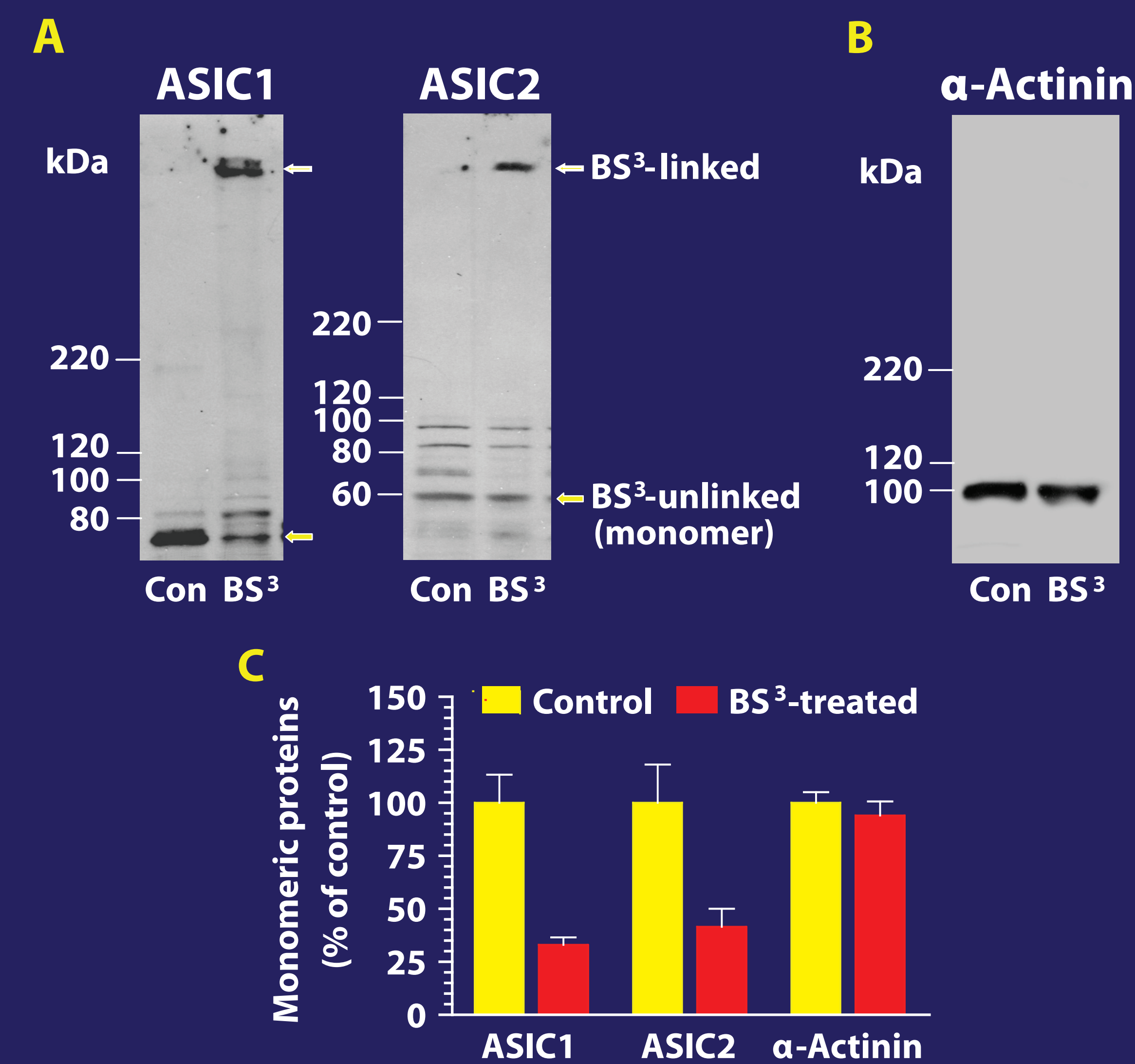


Figure 2: Effects of chronic AMPH administration on ASIC and  $\alpha$ -actinin expression in the CPu

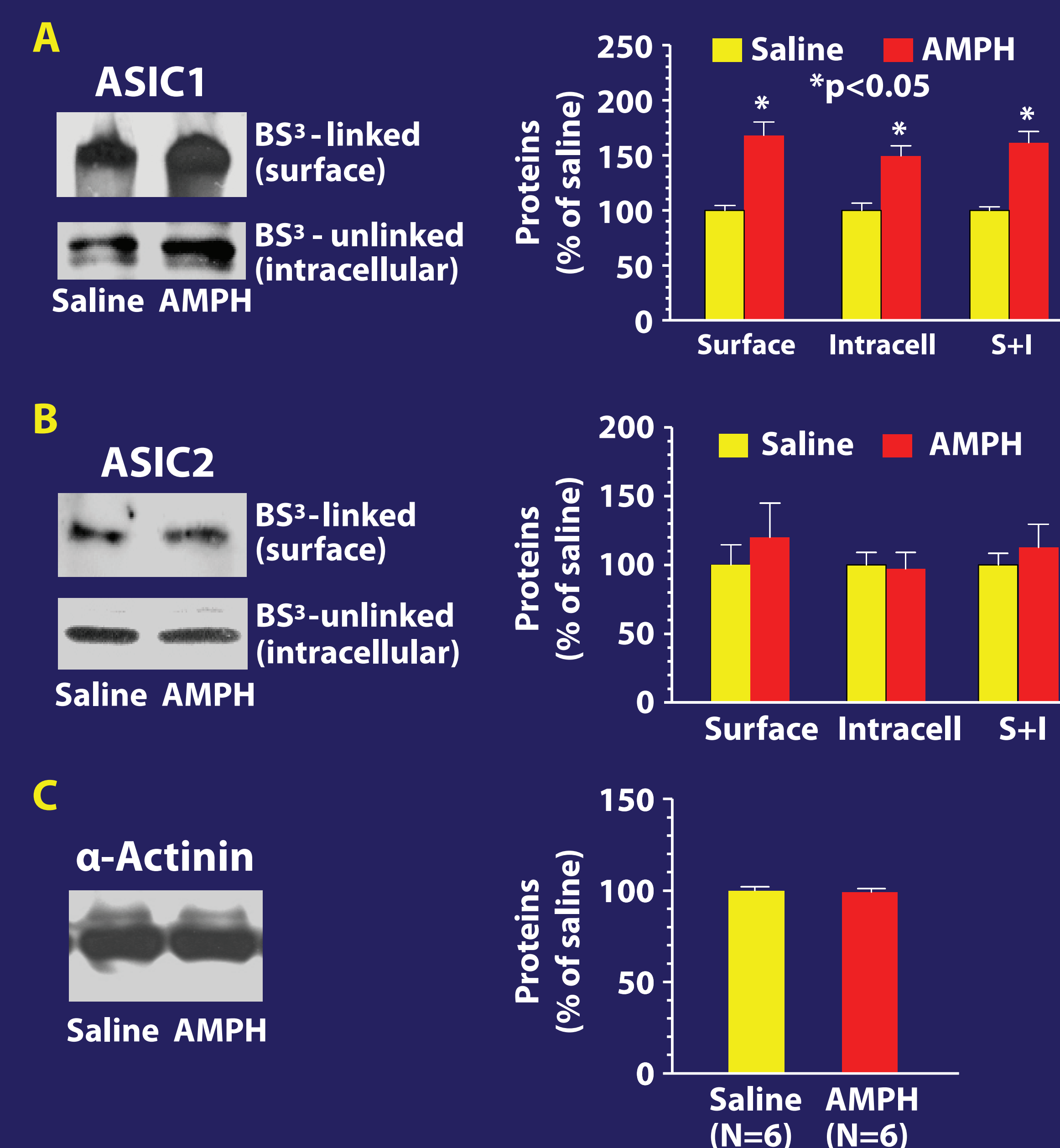
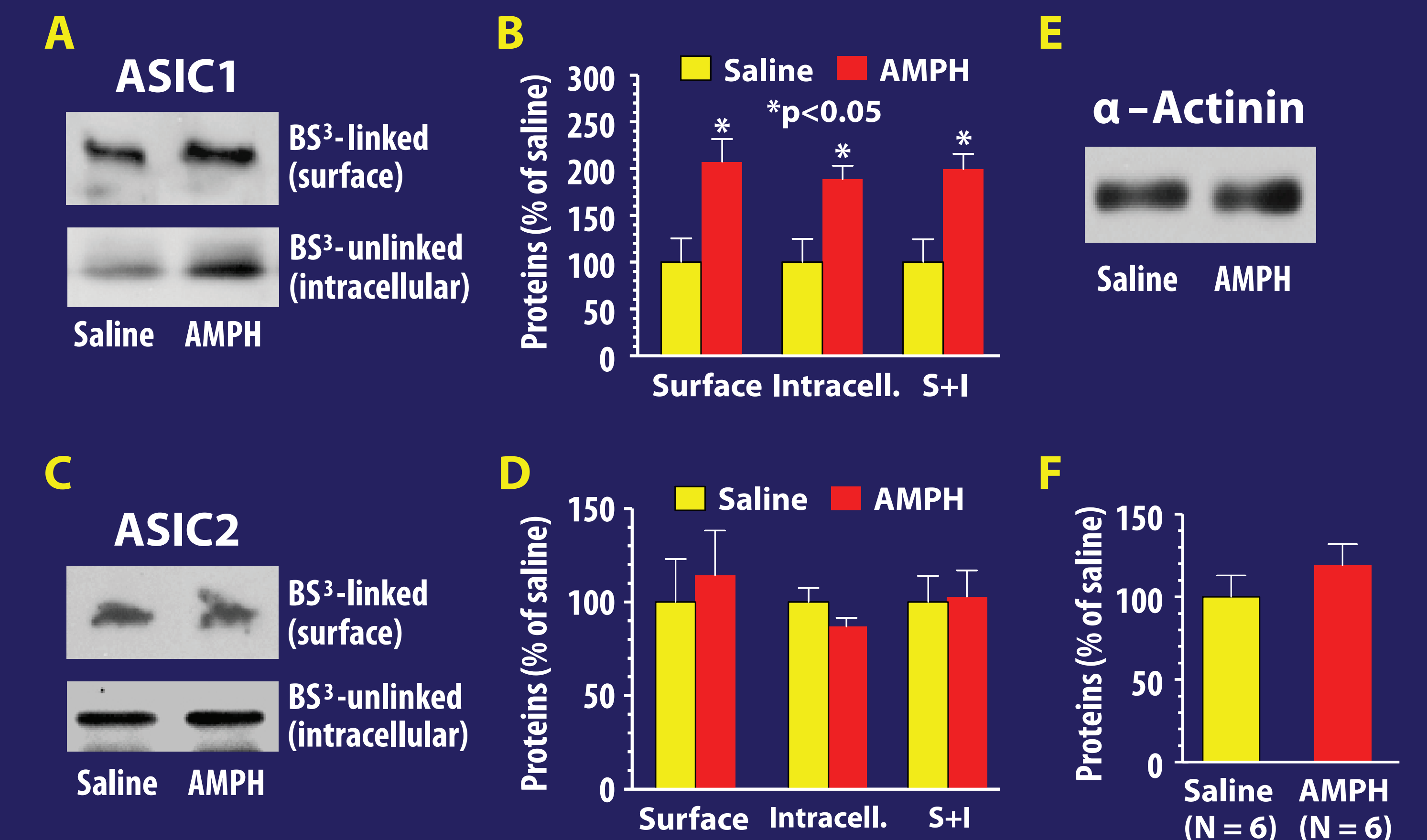


Figure 3: Effects of chronic AMPH administration on ASIC and  $\alpha$ -actinin expression in the NAc



## CONCLUSION

- These data identified that the central ASIC1 is a sensitive target to repeated stimulant exposure.

## DISCUSSION

- Plastic changes in the expression and function of all responsive proteins are thought to operate in concert to control drug effects. In this study, a new responsive protein is identified.
- Following repeated amphetamine administration, ASIC expression was upregulated in the CPu and NAc.
- These data identify the channel as an important element of molecular adaptations to drug exposure and thus, ASIC1 may participate in the neural adaptations critical for the addictive properties of amphetamines.
- From a clinical perspective, ASICs have been implicated in various mental disorders.
- This study represents an initial effort toward elucidating the precise role of ASICs in processing the addictive action of amphetamines.