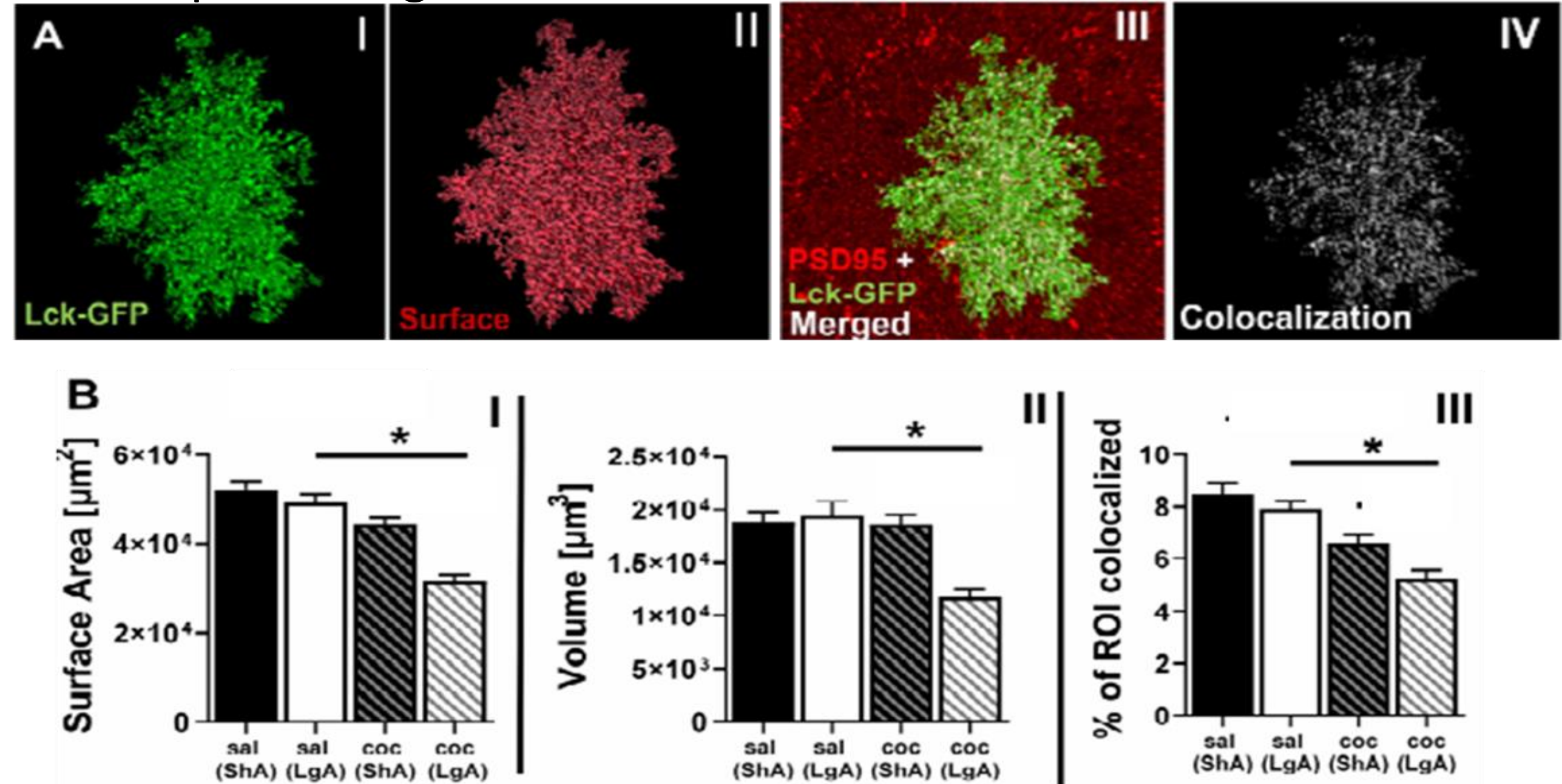


Examining the Contingency of Volition on the Abstinence-Dependent Effects of Long-Access Cocaine Self-Administration on Nucleus Accumbens Core Astrocytes

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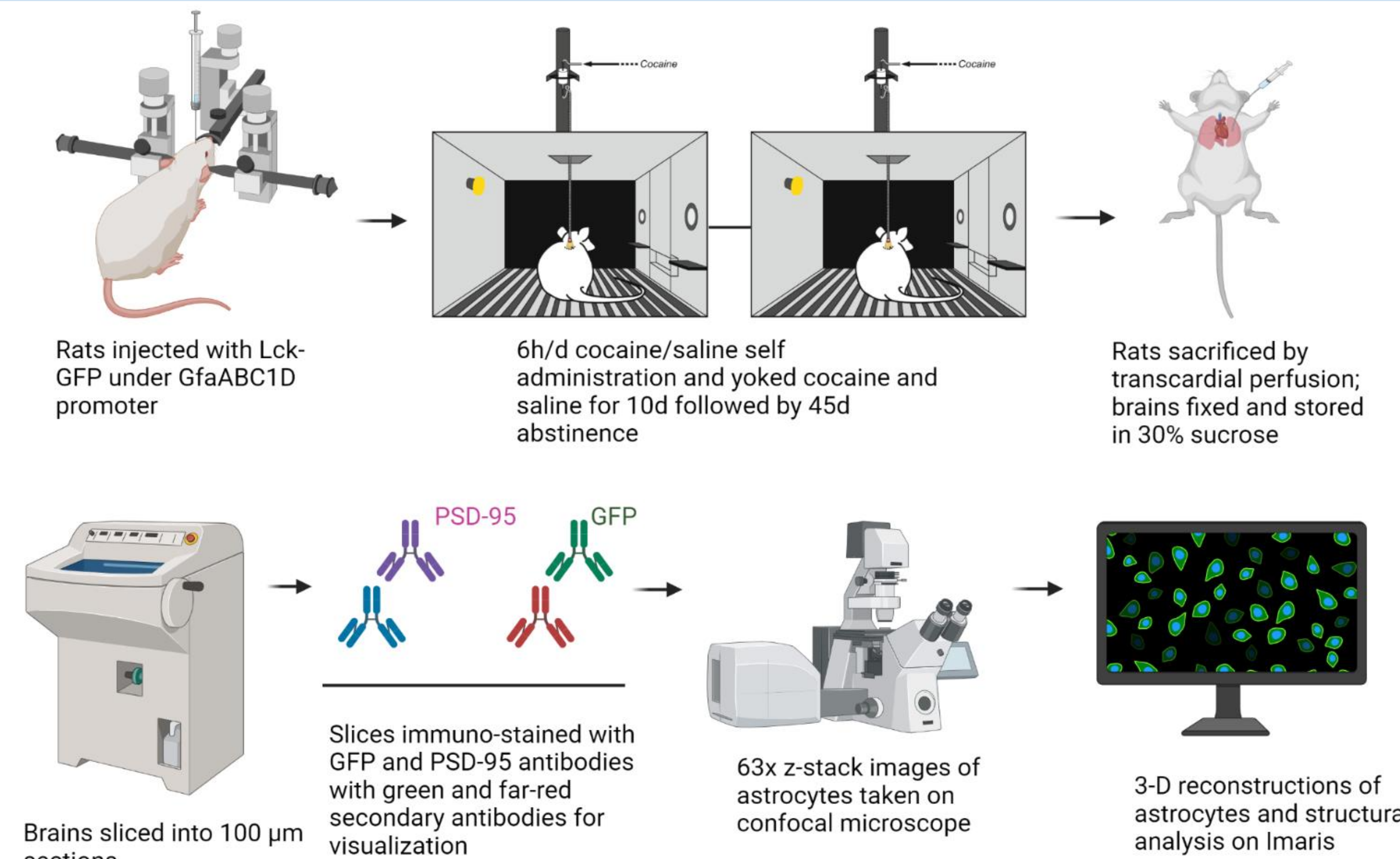
Introduction

- Cocaine is a stimulant that targets the **reward circuitry** of the brain **via dopamine modulation**
 - Astrocytes** are the brain's most abundant type of glial cell and are involved in numerous key regulatory processes within the brain
 - Previous research has shown that **NAc astrocytes** in rats undergo **structural deficits** following cocaine self-administration and subsequent drug abstinence
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- The underlying mechanisms behind these changes remain **unknown**
 - By examining the **contingency of volition** on the structural deficits in NAc astrocytes, the mechanisms underlying the changes can be further elucidated

Hypothesis

NAc CORE ASTROCYTES WILL ONLY EXHIBIT STRUCTURAL DEFICITS AND REDUCTIONS IN SYNAPTIC COLOCALIZATION FOLLOWING VOLITIONAL COCAINE SELF-ADMINISTRATION, BUT NOT AFTER NON-CONTINGENT COCAINE

Experimental Design



Results

DRUG SELF-ADMINISTRATION DATA

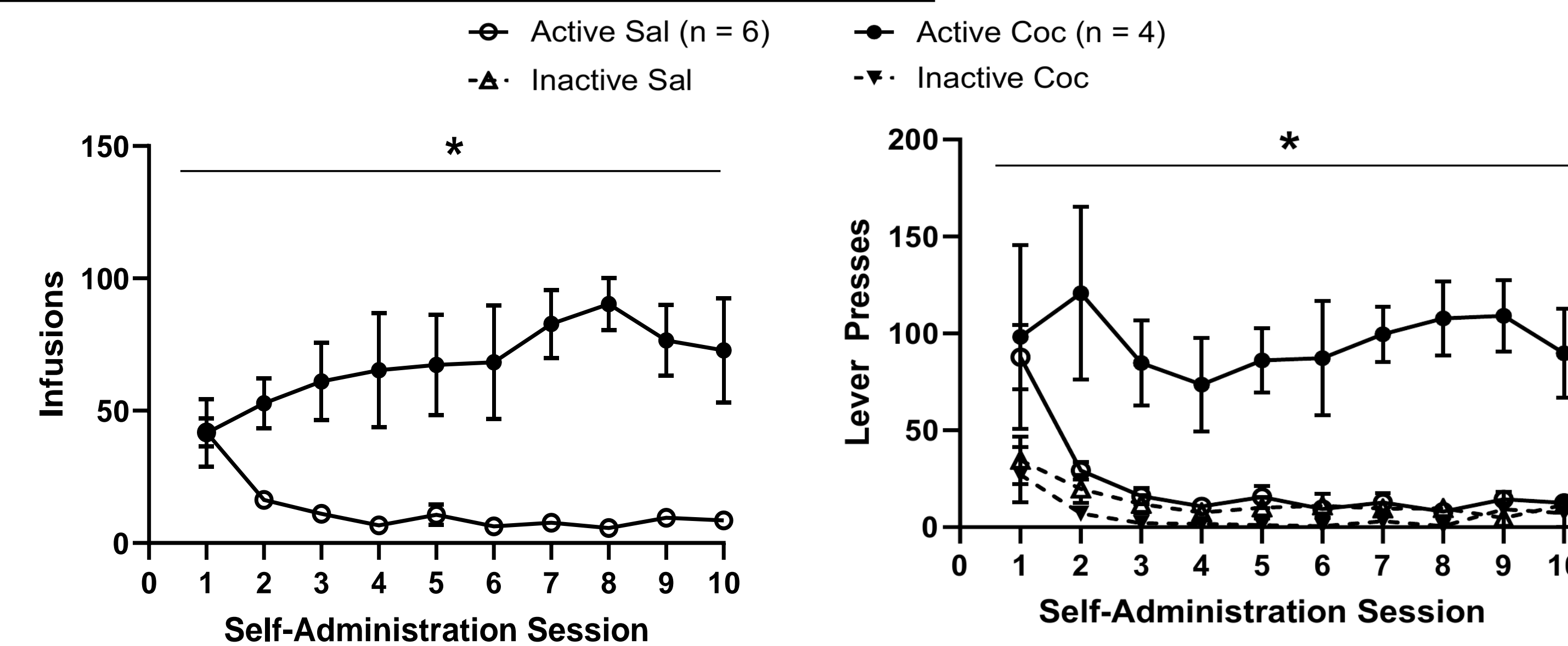


Figure 1. Active presses, inactive presses, and infusions received during self-administration in male rats. Operant chamber setup had two self-administering groups of saline and cocaine. The cocaine self-administering rats were linked to the yoked saline and yoked cocaine rats, such that infusions were simultaneous for all 3 groups. * $p < 0.05$ between groups, error bars represent standard error of the mean (SEM).

ASTROCYTE RECONSTRUCTION AND PSD-95 COLOCALIZATION

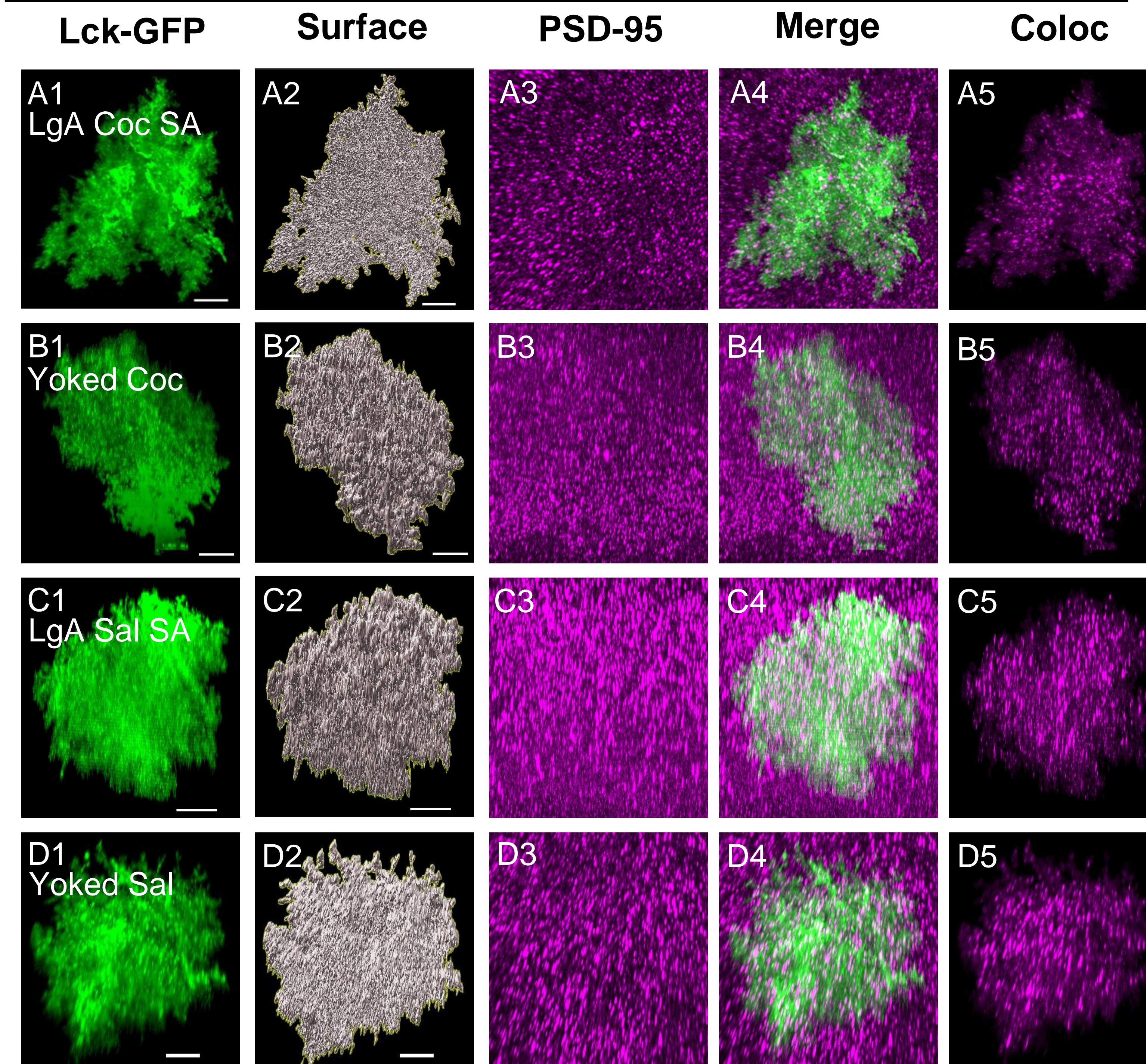


Figure 2. 3-D Astrocytic reconstructions with PSD-95 colocalization. Rows **A, B, C, and D** correspond to LgA Cocaine SA, Yoked Cocaine, LgA Saline SA, and Yoked Saline with 45d abstinence respectively. **Column 1** represents 63x images of isolated Lck-GFP-expressing astrocytes in the NAc. **Column 2** represents the 3-D surface reconstructions of isolated astrocytes. **Column 3** represents immunohistochemistry of the postsynaptic marker PSD-95. **Column 4** represents merge of the Lck-GFP and PSD-95 channels. **Column 5** represents the colocalization of Lck-GFP-expressing astrocytes with the PSD-95. Scale bar: 10 micrometers.

MORPHOLOGICAL DATA AND PSD-95 COLOCALIZATION

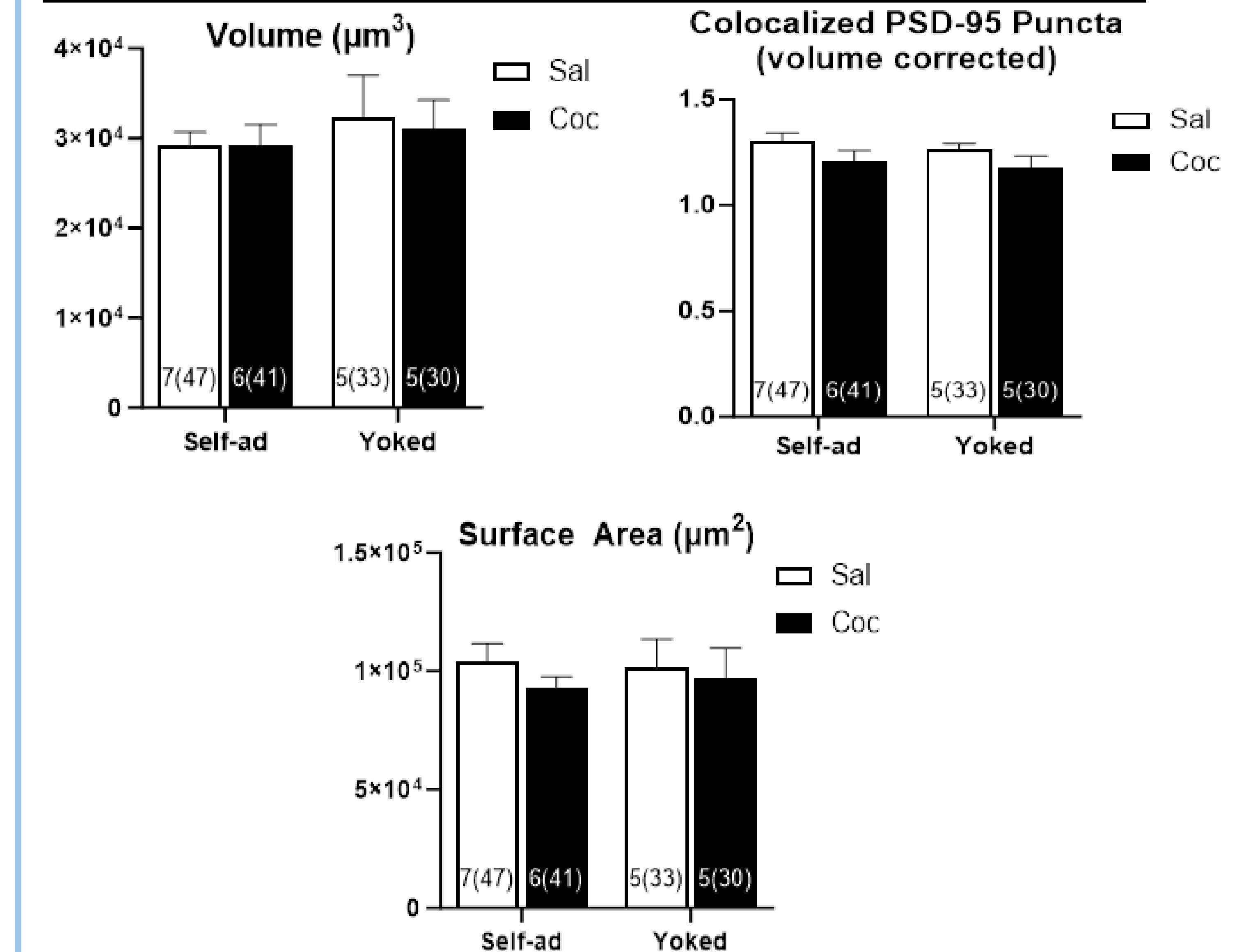


Figure 3. No significant changes in structural measurements between saline and cocaine administering male rats. Volume (**A**) and surface area (**C**) of NAc astrocytes from each group. **B**, volume corrected colocalization of PSD-95 puncta with Nac astrocytes. Error bars represent SEM. For all graphs, n represents the number of rats with total number of cells in parentheses. All p-values > 0.05.

Discussion

- The results of the morphological analysis and PSD-95 colocalization for the cocaine SA group did not replicate the structural deficits seen in Kim et al., 2022
 - Throughout the experiments, due to various reasons, a number of animals were excluded from the study, leading to underpowered statistical analyses (when using number of animals as N instead of total cells as N)
- Future directions for research:**
- Adding more animals to study to compensate for low values of N in statistical analyses
 - Evaluation of astrocyte structural effects due to chronic dopamine D1 receptor agonism
 - Utilizing the same yoked paradigm with the presence/absence of a D1 inhibitor to measure abstinence-dependent effects on astrocyte morphology

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