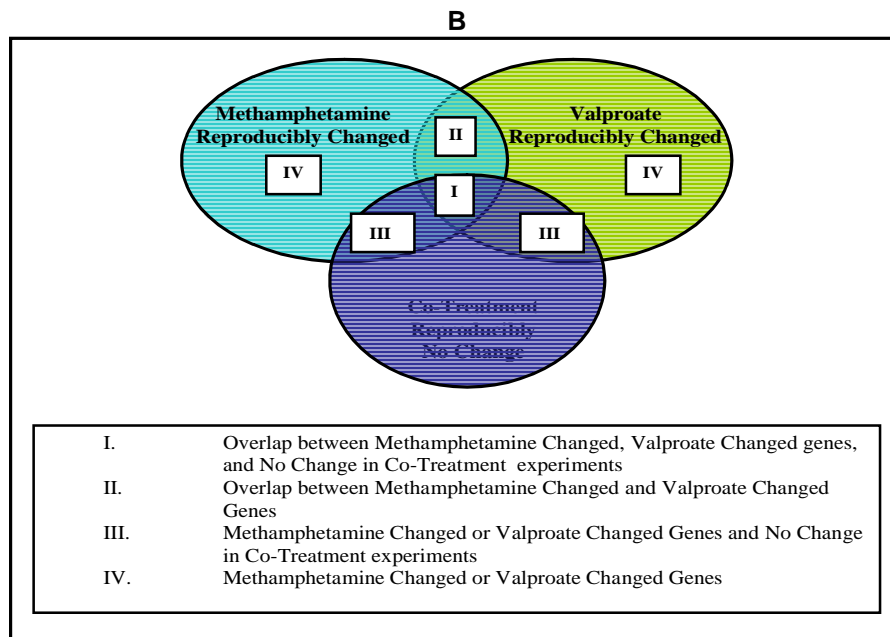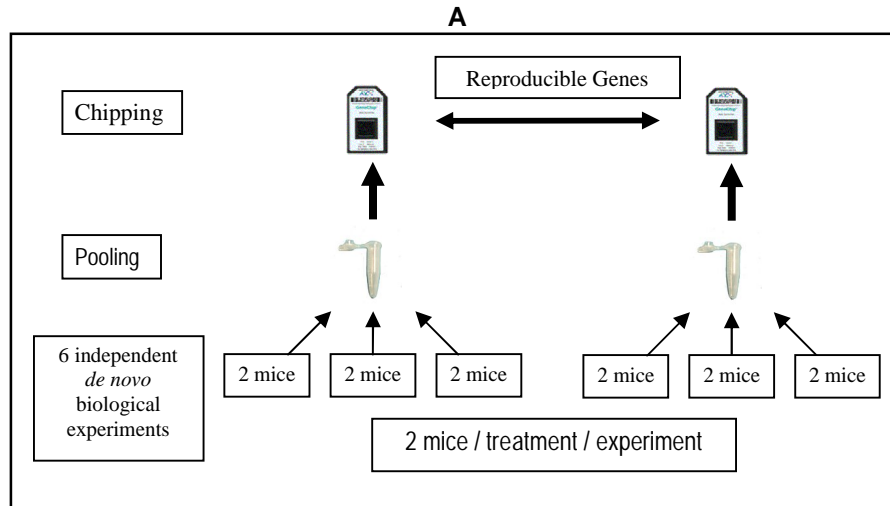Figure 1. Design of experiments and data analysis. (A) experimental design (B) Venn diagram categorizing genes changed
by various drug treatments - Categories I, II, III, and IV (C) Multiple converging independent internal and external
lines of evidence for cross –validation of findings.

A

Reproducible Genes

Chipping

Pooling

6 independent *de novo* biological experiments

2 mice 2 mice 2 mice   2 mice 2 mice 2 mice

2 mice / treatment / experiment

B

Methamphetamine Reproducibly Changed

Valproate Reproducibly Changed

II

IV   IV

I

III   III

Co-Treatment Reproducibly No Change

I.	Overlap between Methamphetamine Changed, Valproate Changed genes, and No Change in Co-Treatment experiments
II.	Overlap between Methamphetamine Changed and Valproate Changed Genes
III.	Methamphetamine Changed or Valproate Changed Genes and No Change in Co-Treatment experiments
IV.	Methamphetamine Changed or Valproate Changed Genes

C

**Internal Lines
of Evidence**

**External Lines
of Evidence**

Meth AND
Valproate
Responsive (1)

Convergent
Functional
Genomics (4)

Stopped By
Co-
Treatment (2)

Gene
expression
changes from
target brain
regions

Biologically
relevant (5)

Changed in more
than one target
brain region (3)

Human Post-
Mortem evidence
(6)