

All expts. carried out in adult MPS I (IDUA deficient) mice

Route of Adm.	Mice	CP	Age at inj.	Sacrificed
1. ICV	Immunodeficient	No		10 wks post inj.
2. ICV	Immunocompetent	Yes	4.5 mths	8 wks post inj.
3. Intrathecal	Immunocompetent	Yes	4.5 mths	11 wks post inj.
4. ICV	Immunotolerized	No	3 mths	9 wks post inj.

All animals injected with 10 ul AAV9 vector (3 x 10¹¹ particles)

ICV injections: Right lateral ventricle
IT injections: Lumbar area

Fig 1

IDUA Activity in: Immunodeficient (ID) mice: Intracranial ventricular (ICV) injection

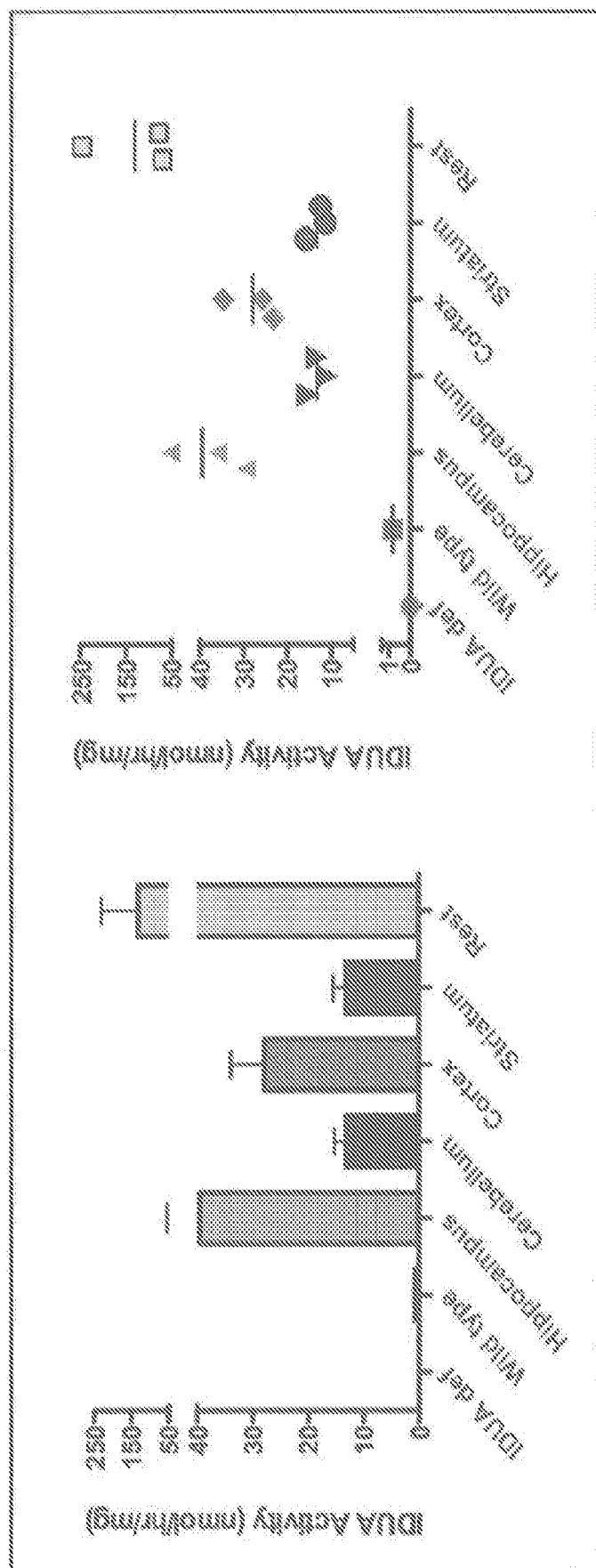


Fig 2

**IDUA Activity in:
Immunocompetent mice (IC): ICV injection +
Cyclophosphamide (CP)**

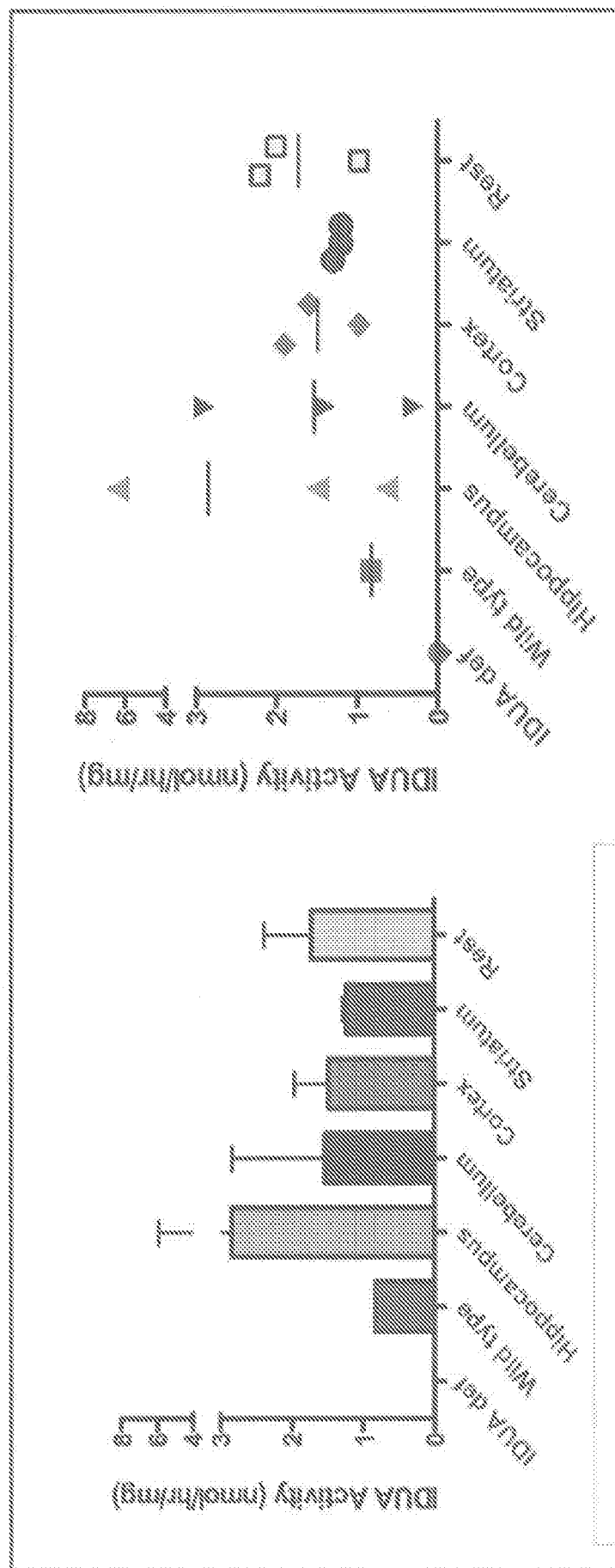


Fig 3

**IDUA Activity in:
Immunocompetent (IC) mice: Intrathecal (IT) injection
+ Cyclophosphamide (CP)**

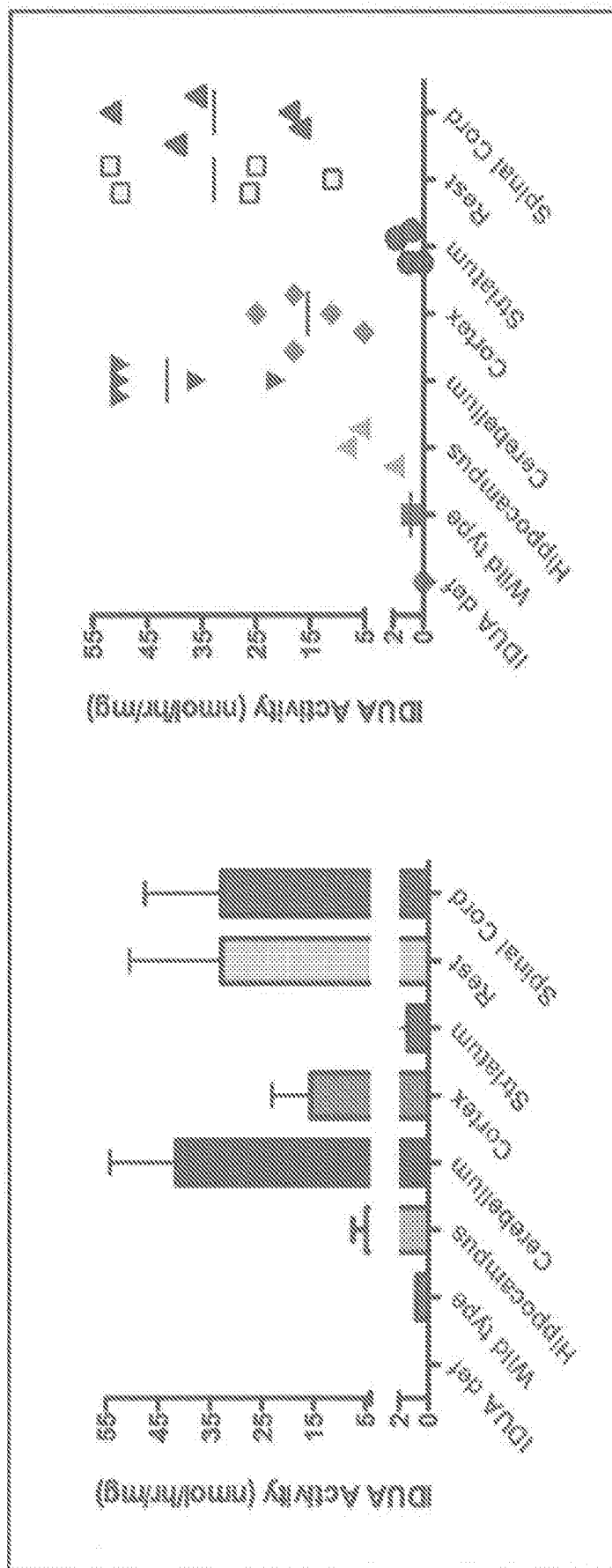


Fig 4

IDUA Activity in:
Immunocompetent (IC) mice: Immunotolerized (Itol)

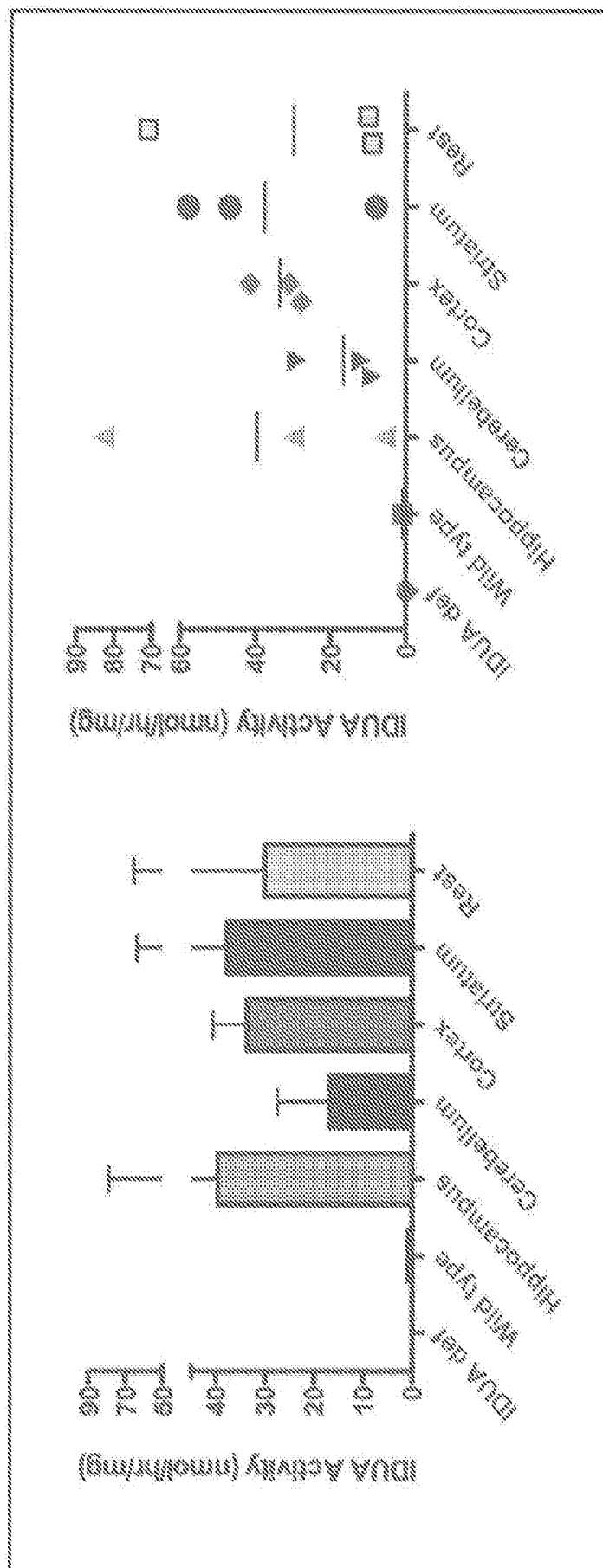


Fig 5

Comparison of Different Routes of Delivery

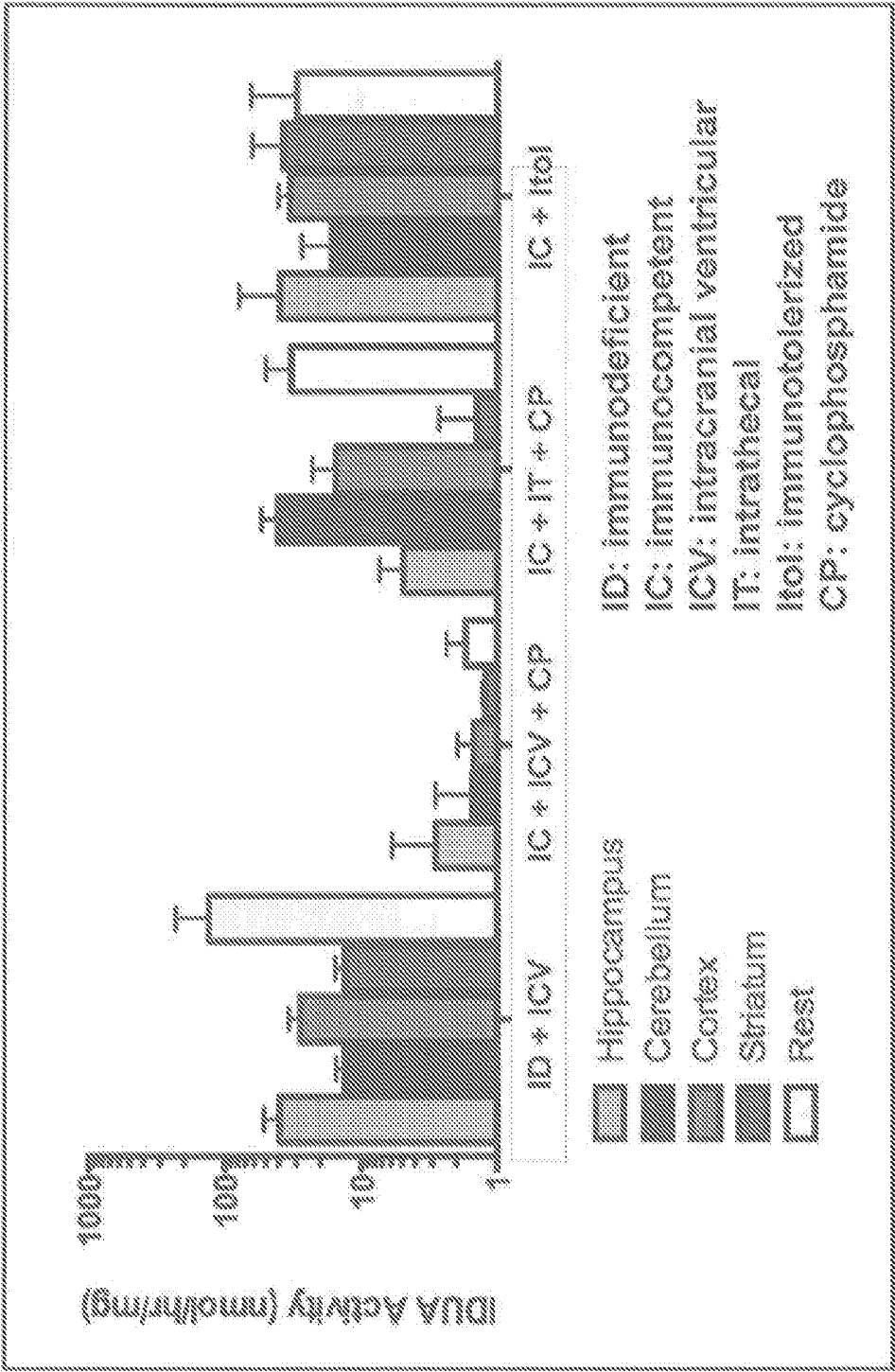


Fig 6

Comparison of Routes of Administration and IDUA Activity in Brain

ID: immunodeficient
 IC: immunocompetent
 ICV: Intracranial ventricular
 IT: Intrathecal
 Itol: immunotolerized
 CP: cyclophosphamide

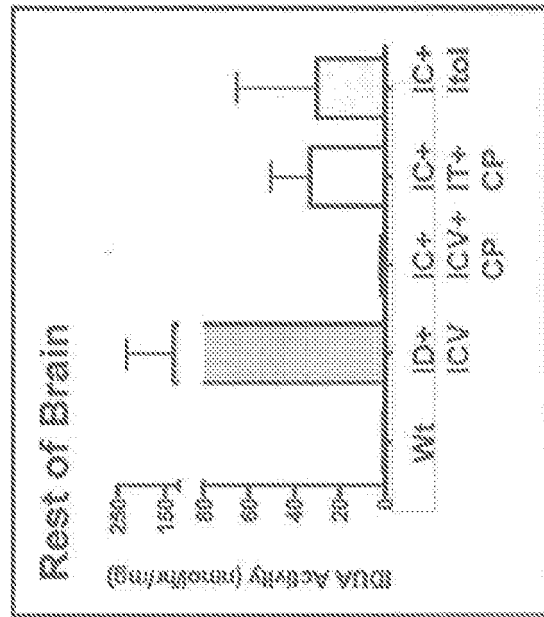
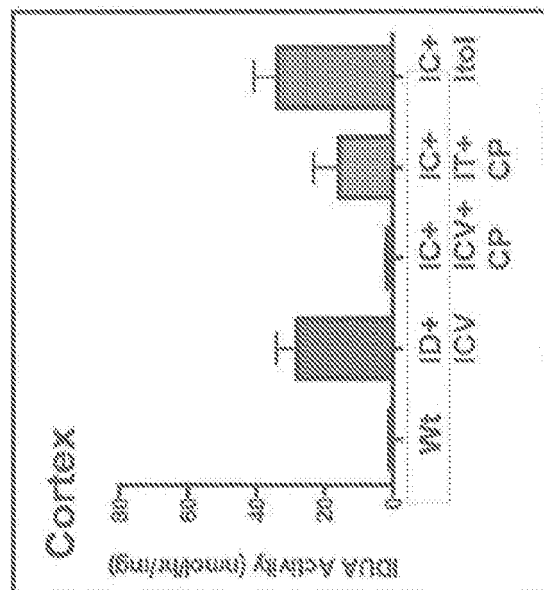
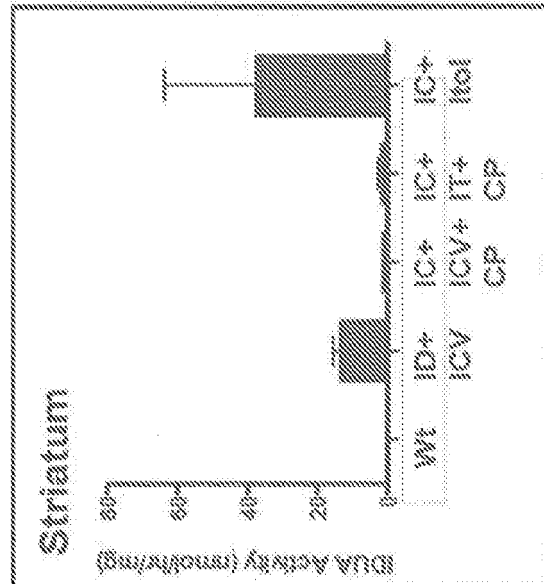
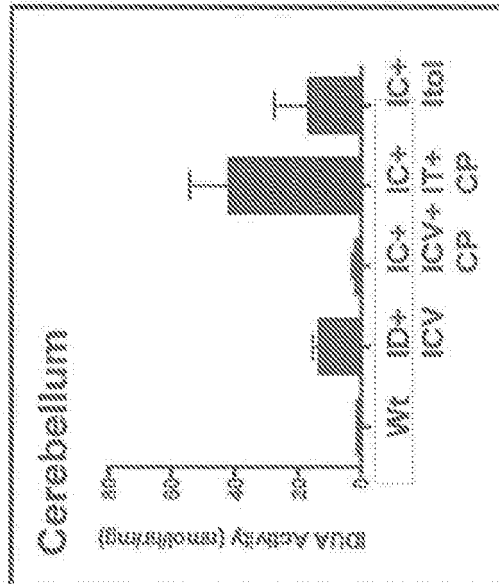
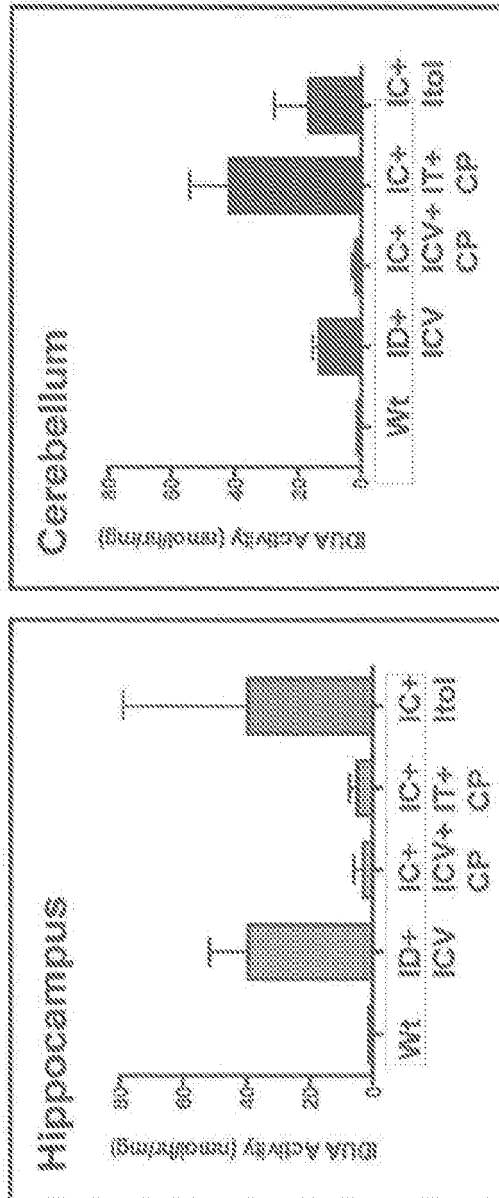
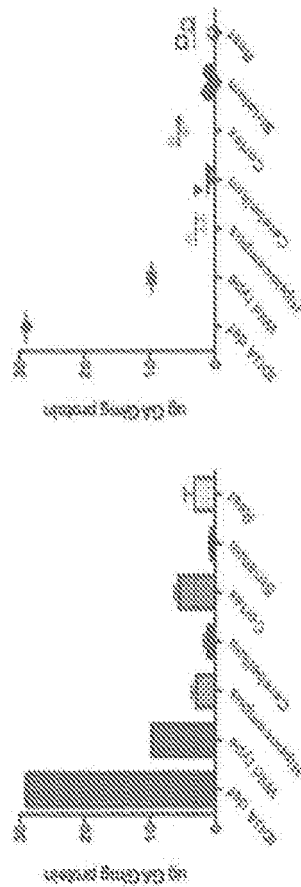


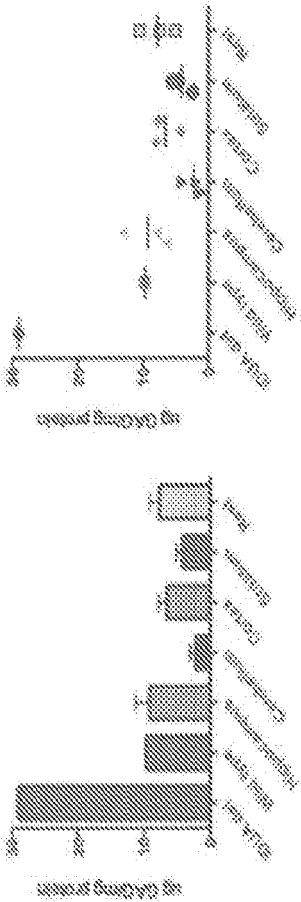
Fig 7

GAG Activity in Mouse Brain. Microdissected brains were analyzed for GAG accumulation

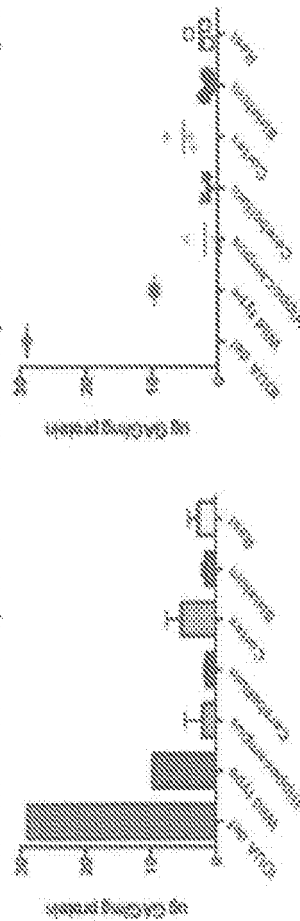
A. Immunodeficient mice, ICV injections



B. Immunocompetent mice, ICV injections + CP



C. Immunocompetent mice, ICV injections + Aldurazyme



D. Immunocompetent mice, IT injections + CP

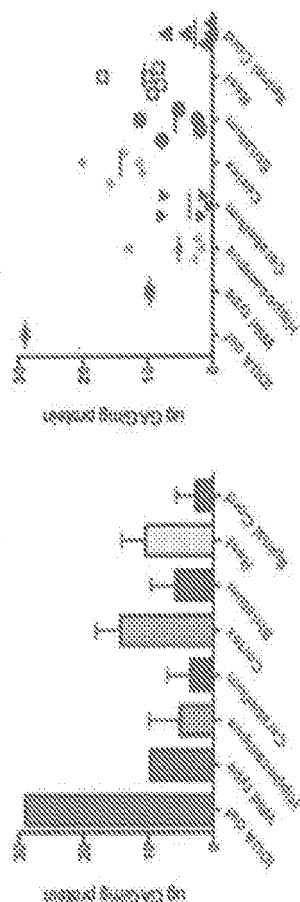


Fig 8

Figure 9. Experimental design

Route of Vector administration	Immune competency	Immune modulation	Age of animals at injection	Expt. end point (post-injection)
ICV	Immunodeficient	None		10 weeks
ICV	Immunocompetent	Immunosuppression w/CP (partial regimen)	4.5 months	8 weeks
ICV	Immunocompetent	Immunotolerization	4.5 months	11 weeks
ICV	Immunocompetent	None	3 months	
ICV	Immunocompetent	Immunosuppression w/CP (full regimen)	3 months	
IT	Immunocompetent	Immunosuppression w/CP (full regimen)	3 months	9 weeks
IT	Immunocompetent	Enzyme tolerization	4.5 months	10 weeks
IT	Immunocompetent	None	4.5 months	11 weeks

Abbreviations:
ICV: Intracerebroventricular
IT: Intrathecal
CP: Cyclophosphamide

Expts. were carried out in adult MPS I (IDUA deficient) mice
All animals were injected with 10 μ L AAV9_vector (3 x 10¹¹ particles)

Figure 10. Intracranial Delivery into
Immunodeficient Animals

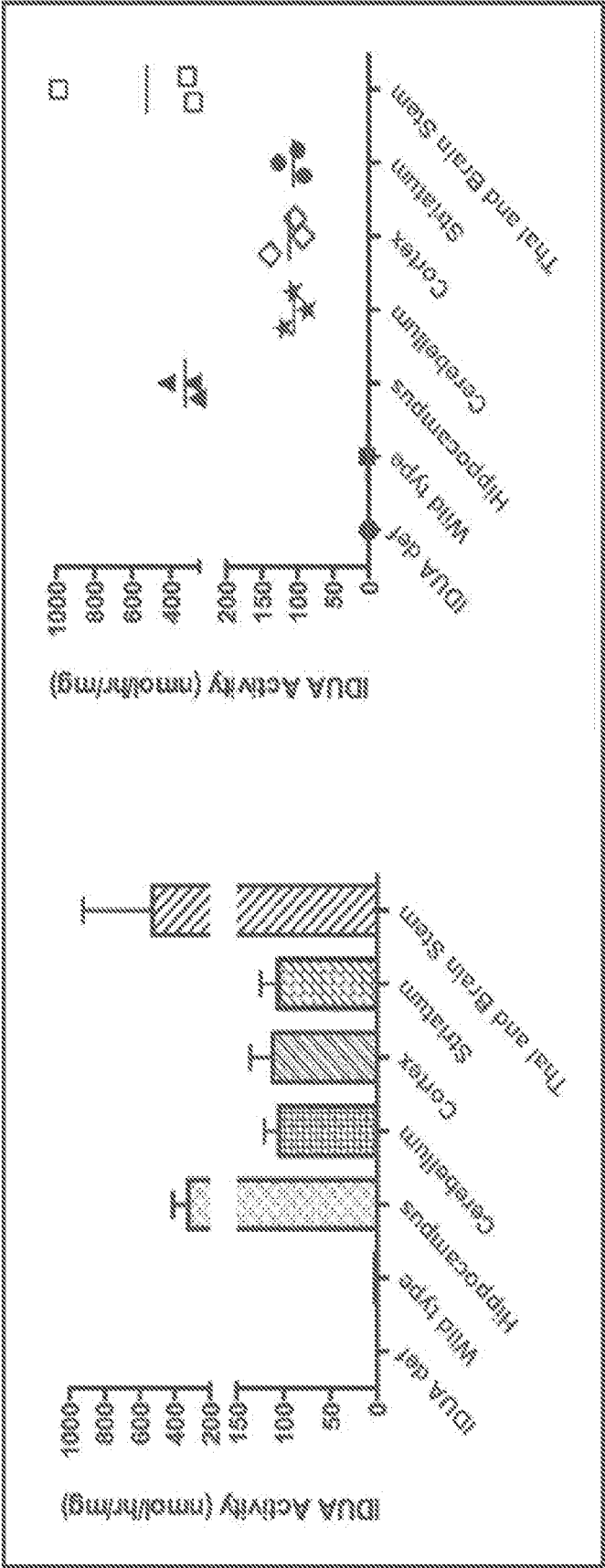


Figure 11. Intracranial Delivery into Immunocompetent mice + Immunosuppression with Cyclophosphamide

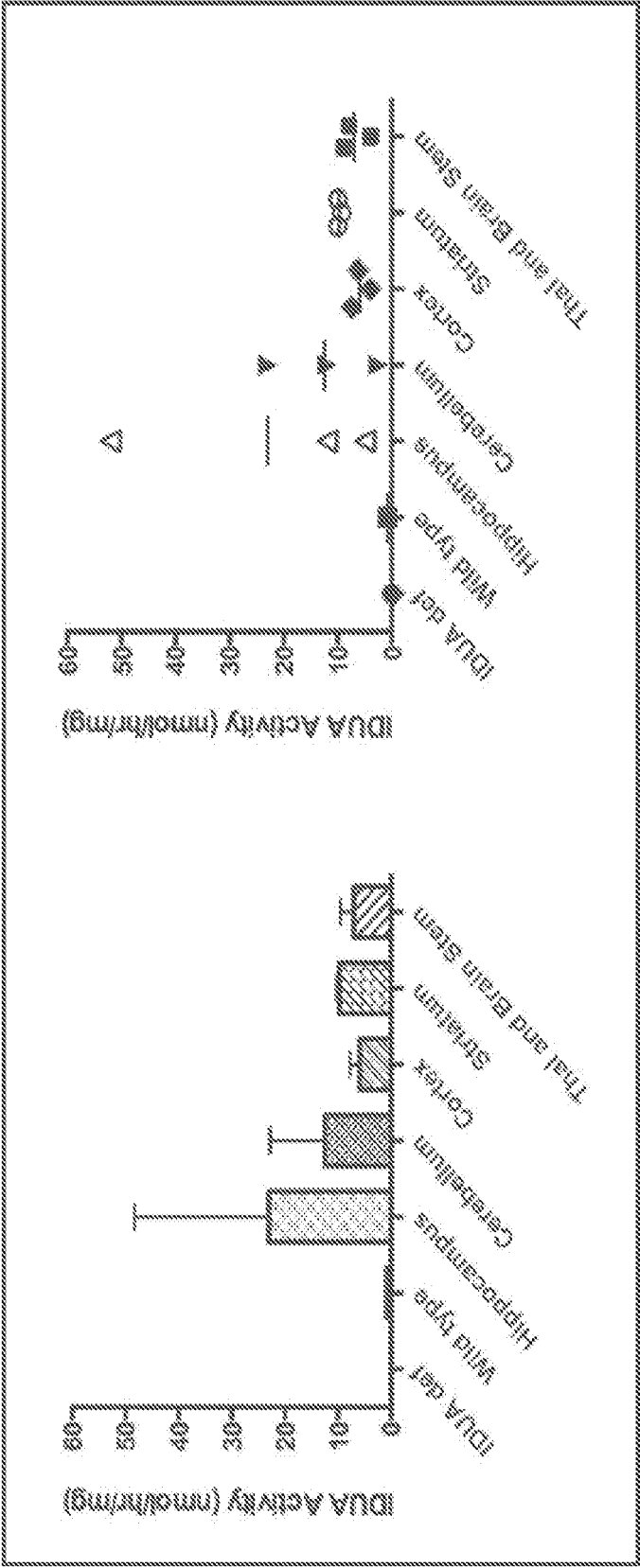


Figure 12. Intracranial Delivery to Immunocompetent mice
+ Immunotolerization with Aldurazyme

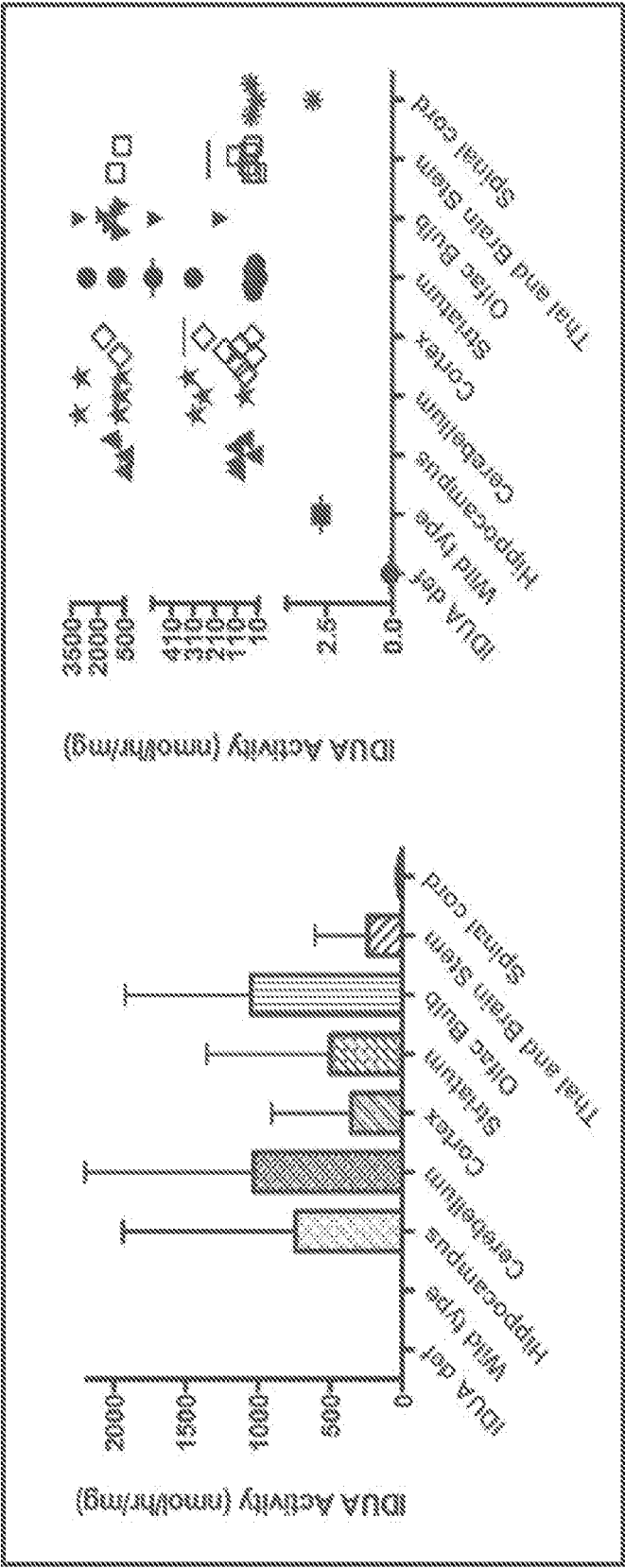


Figure 13. Intrathecal Delivery to Immunocompetent Mice + Immunosuppression with Cyclophosphamide

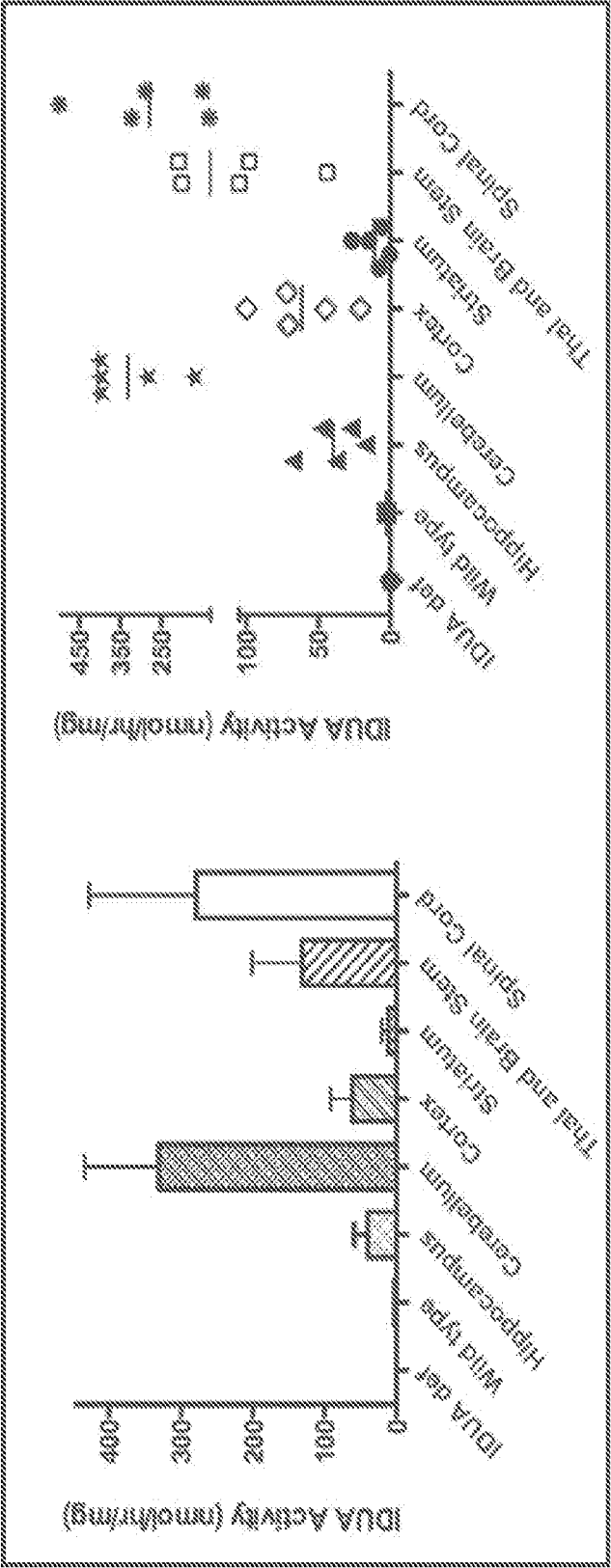


Figure 14. Intrathecal Delivery to Immunocompetent Mice
+ Immunotolerization with Aldurazyme

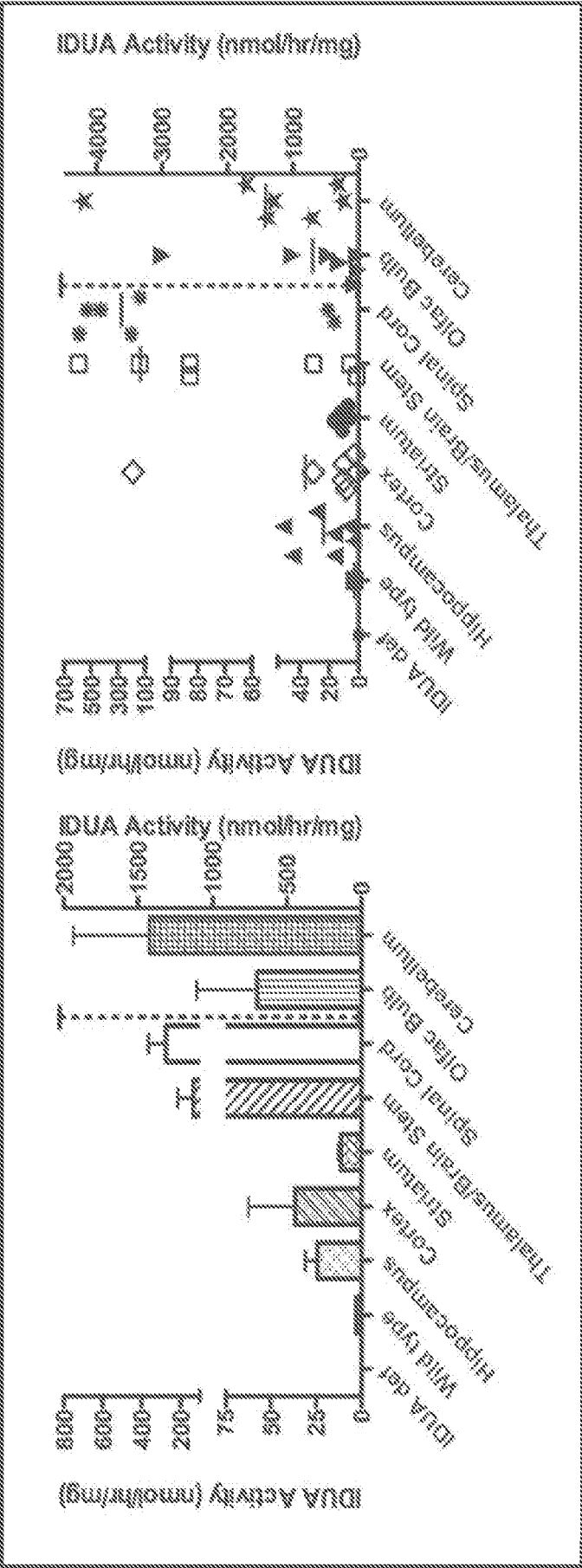


Figure 15. Intrathecal Delivery to Immunocompetent Animals
(Controls-No Immunosuppression, No Immunotolerization)

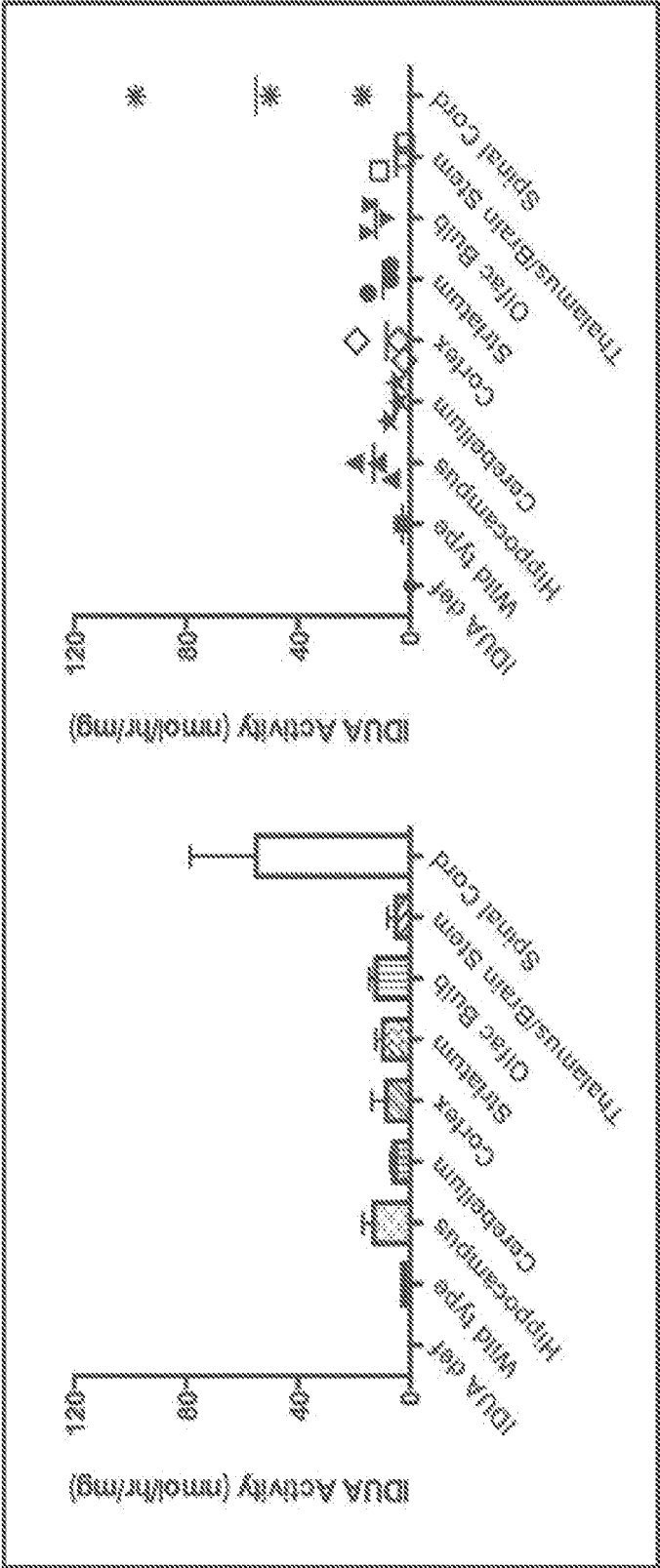


Figure 16. Normalization of Glycosaminoglycans after Intracranial or Intrathecal Administration of AAV9-IDUA

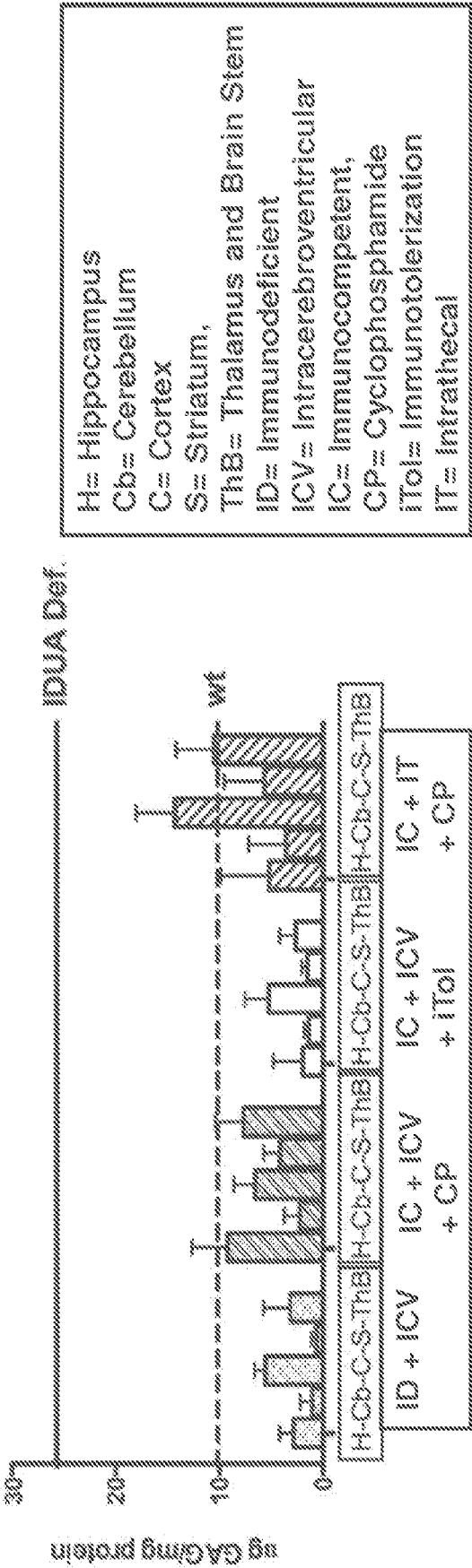
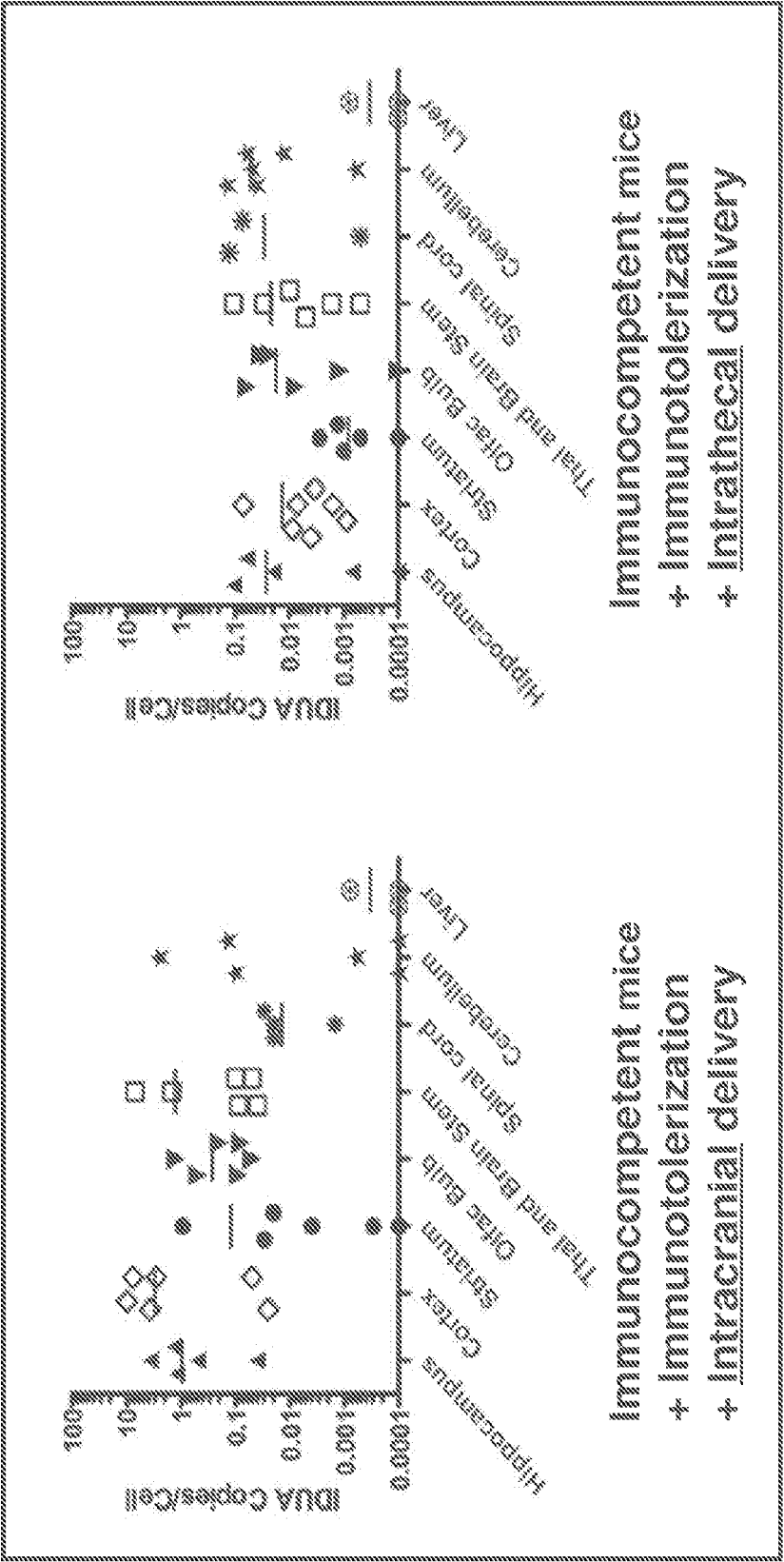


Figure 17. Vector Copy Number in Brain



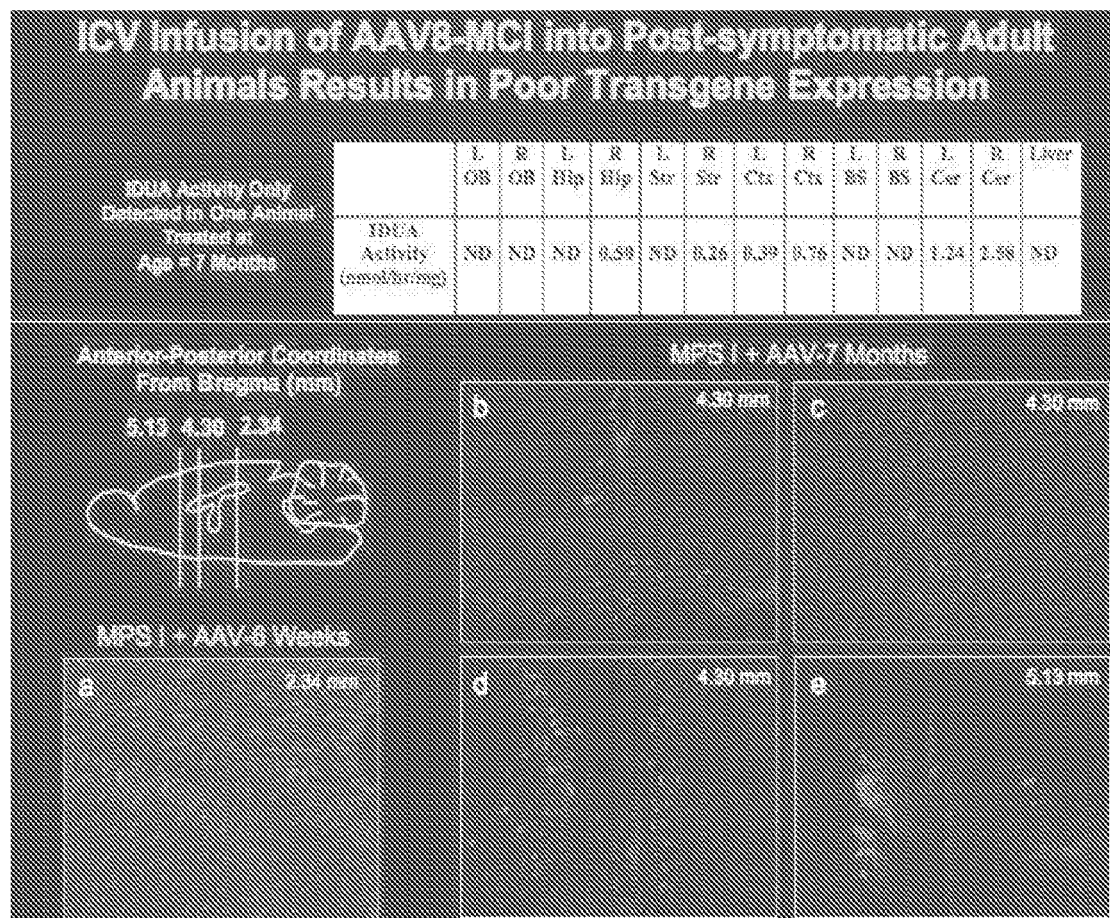


Figure 18

Figure 19. Intranasal Delivery to Immunocompetent Animals
+ Immunosuppression with Cyclophosphamide

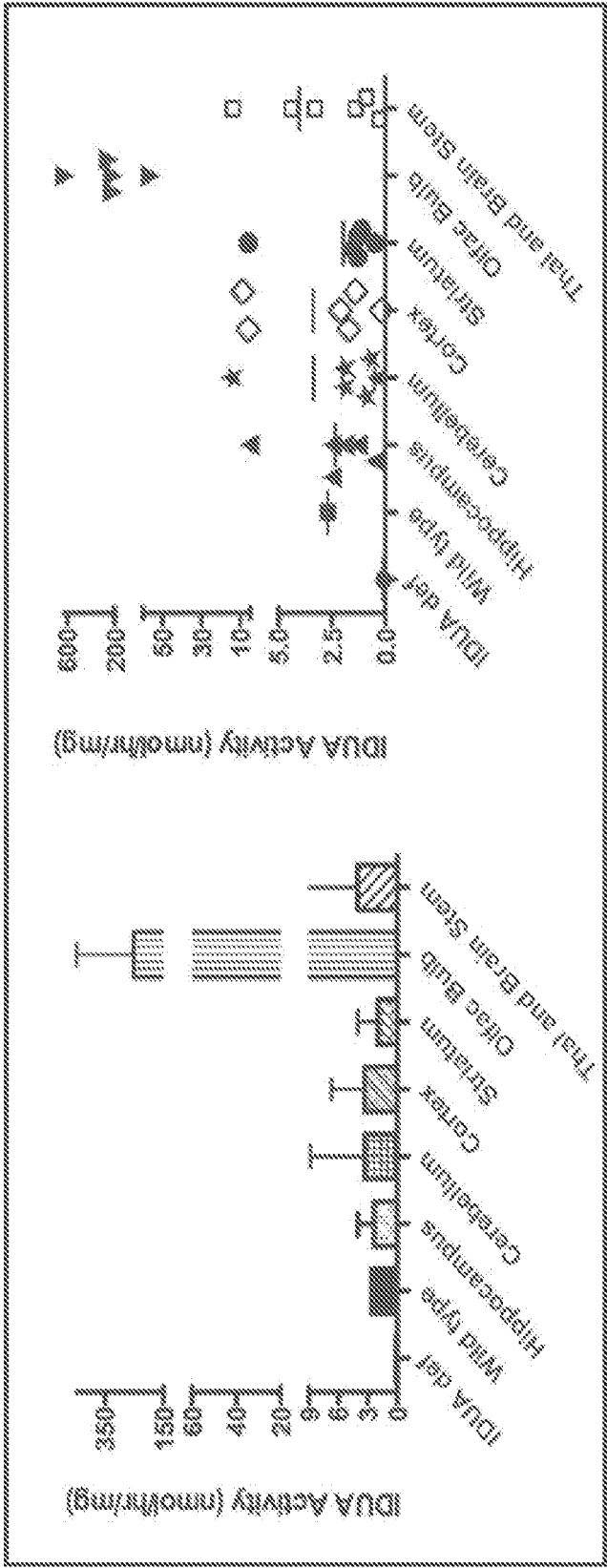


Figure 20. Vector Copy Number in Brain

