



# Is damage to the cytoskeletal architecture a common pathological hallmark of neurotoxicants?

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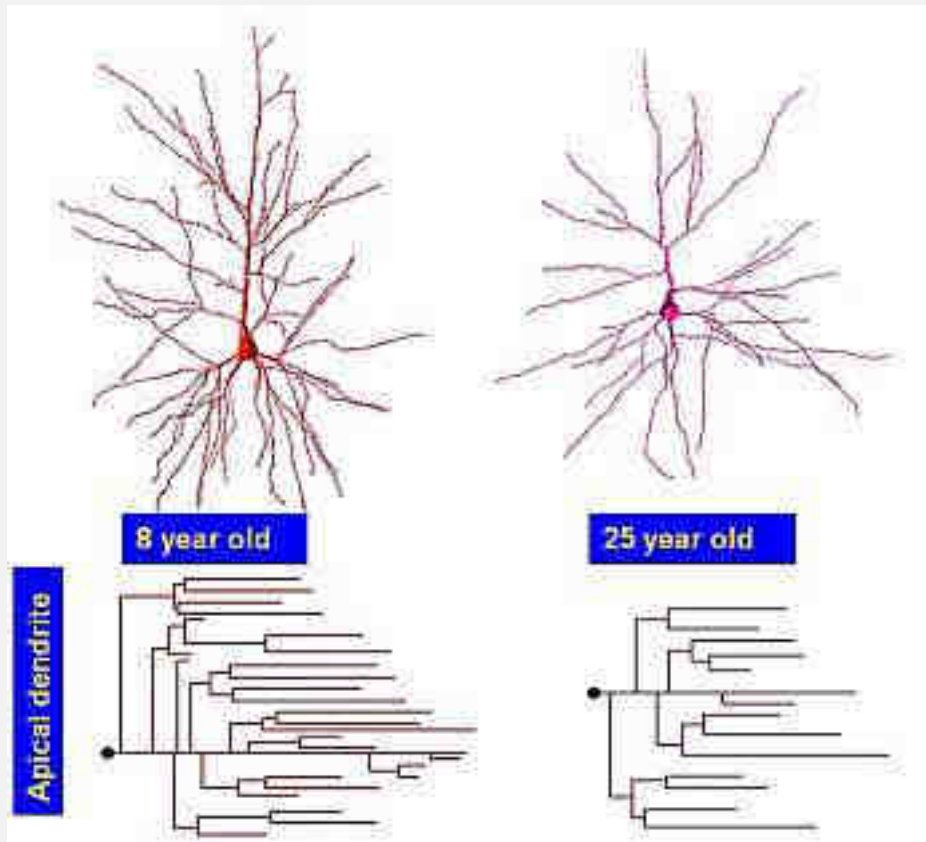
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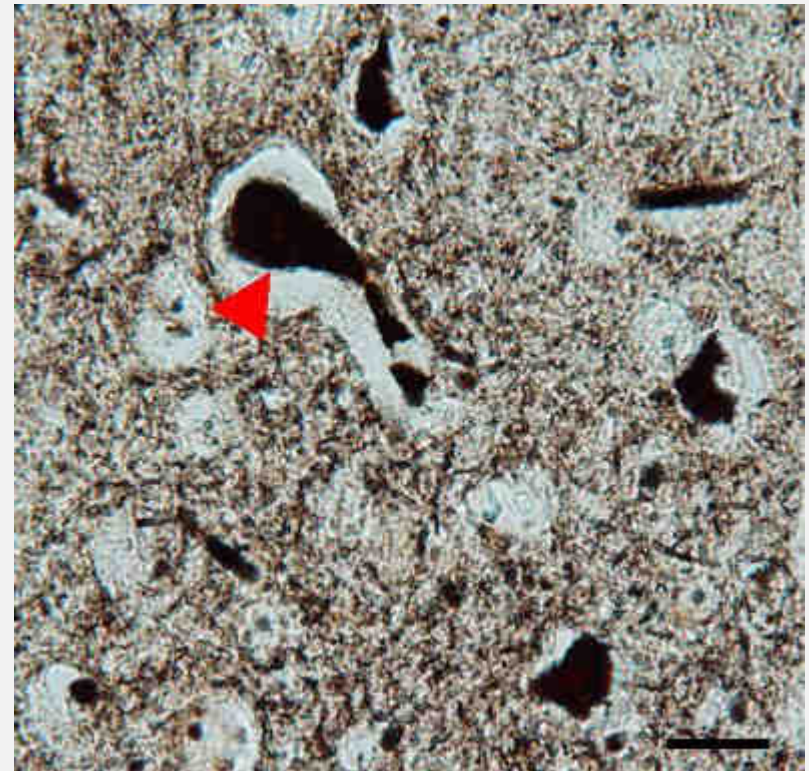
## Historical details of chronic cell disease

- slow progressive neuronal damage & neuronal shrinkage



Aging engenders profound changes in neuronal architecture. Patrick Hof.

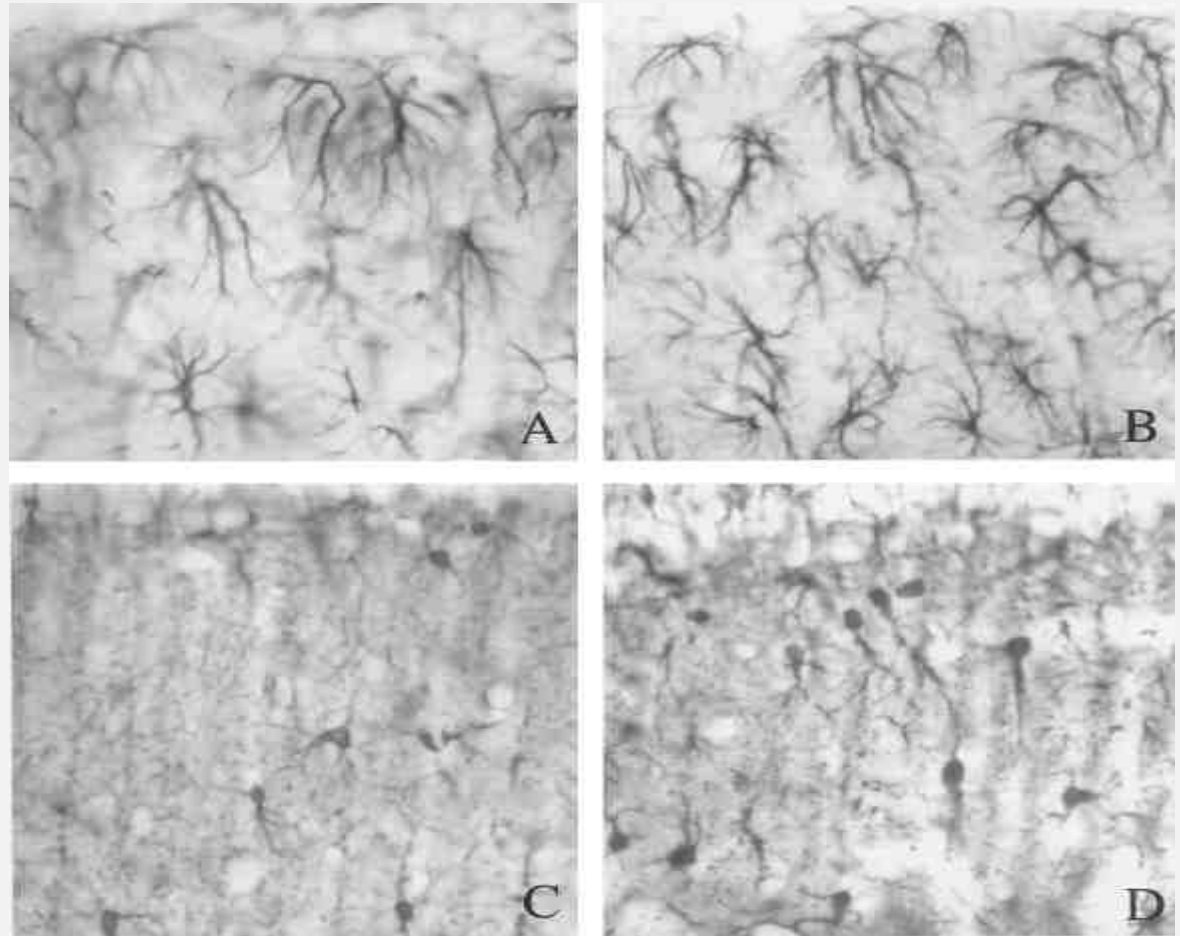
- Presence of so-called ‘dark neurons’ evident via histological examination.
- Interpreted as representing dying or degenerating neurons.
- Assigning inappropriate neurotoxic potential to the compounds?



## Studies of alcohol consumption:

Astrocytes immunostained for GFAP (*upper row*) & S-100 $\beta$  protein (*lower row*) from control (**A** and **C**) and treated (**B** and **D**) rats.

Tagliaferro et al., 2002





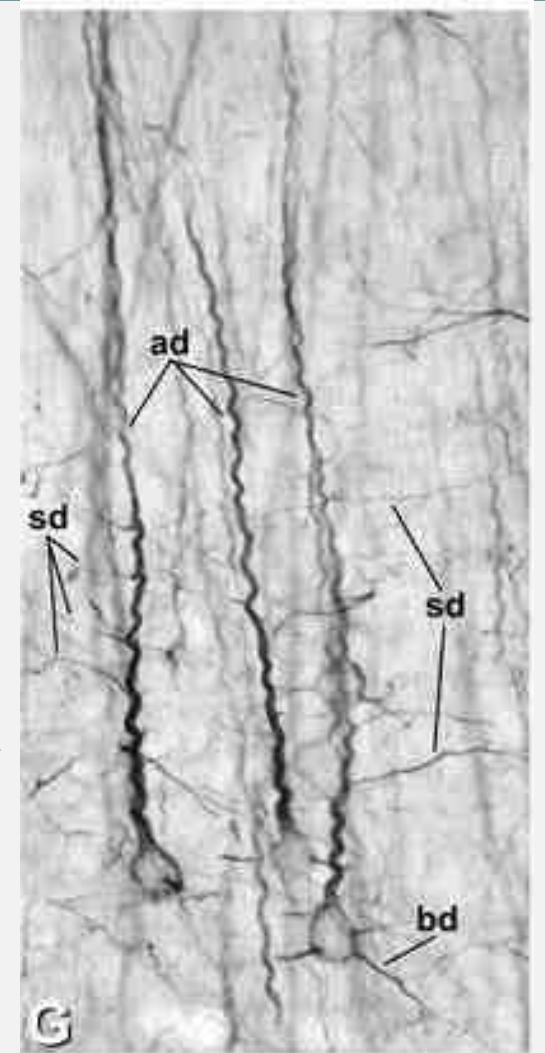
‘Morphological irregularity in both dendrites & axons as a sinuous, waving, **corkscrew-like shape**’ -often accompanied by immunostaining irregularities.

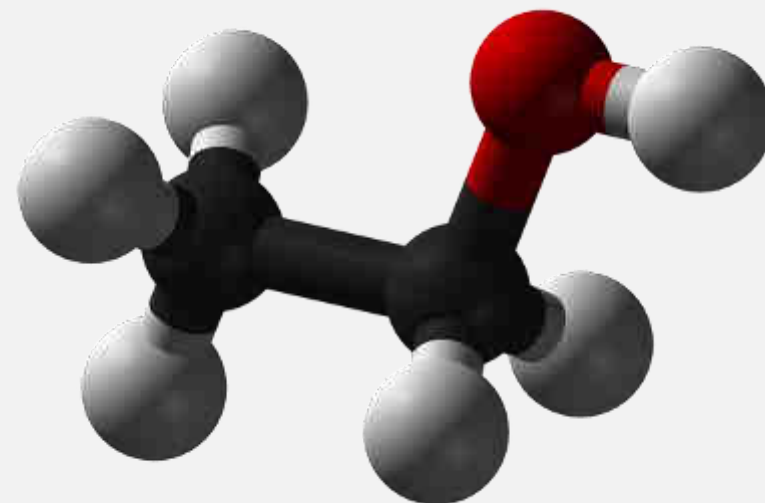
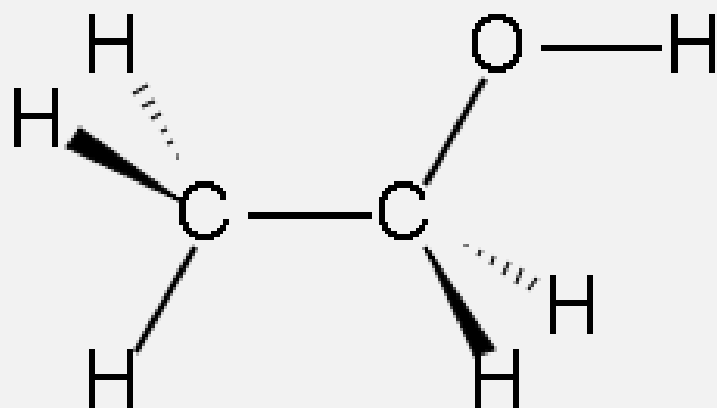
Evrard & Brusco – University of Buenos Aires, Argentina

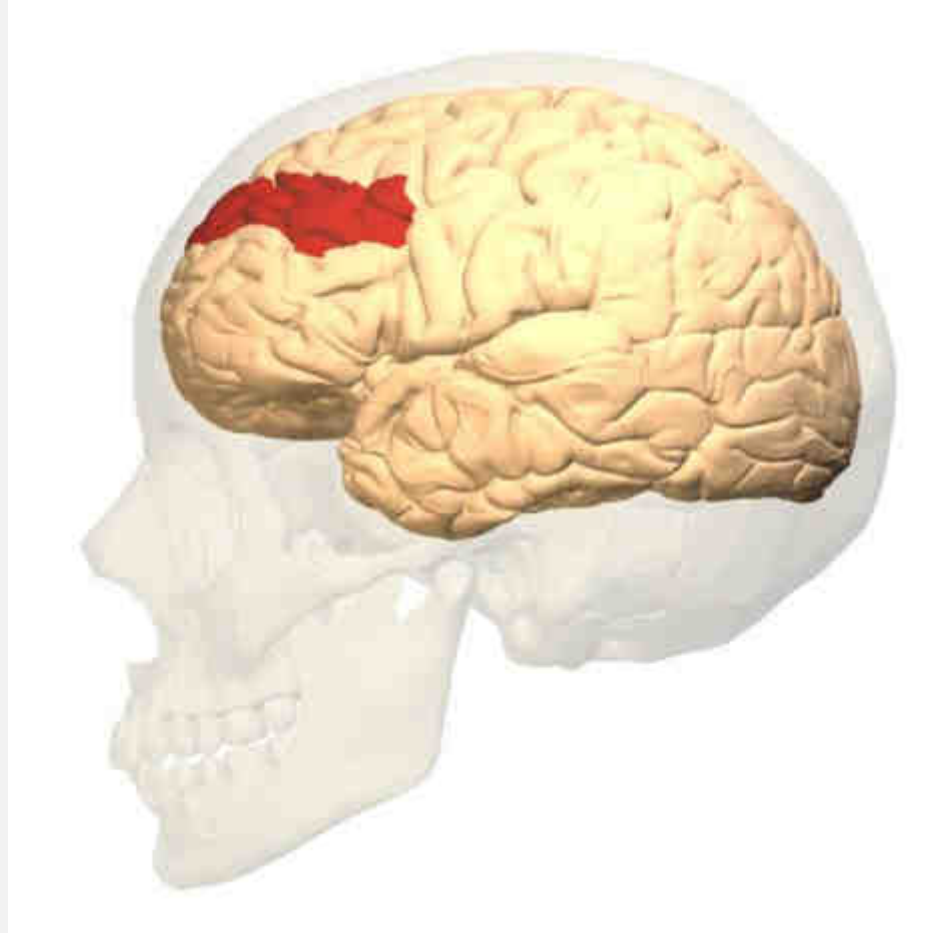
Pyramidal neurons from the frontal cortex after chronic (6 weeks) ethanol exposure

Evrard et al., 2006

- Reduced MAP-2 staining







**Brodmann's area 9 - PFC**



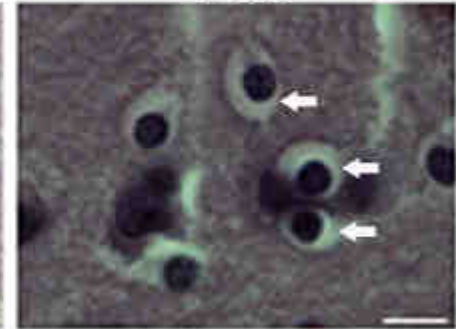
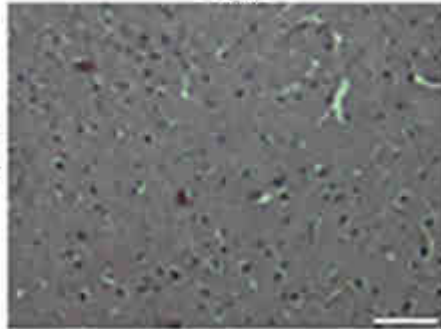
### H & E stained sections from prefrontal cortex

10x

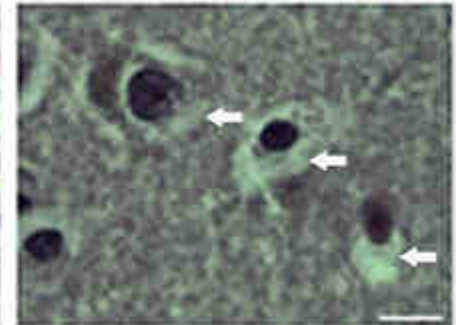
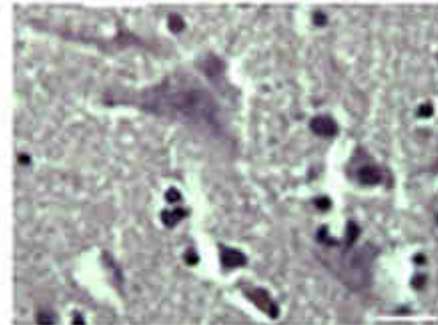
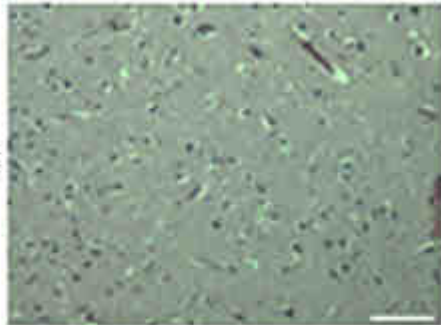
50x

100x

Control

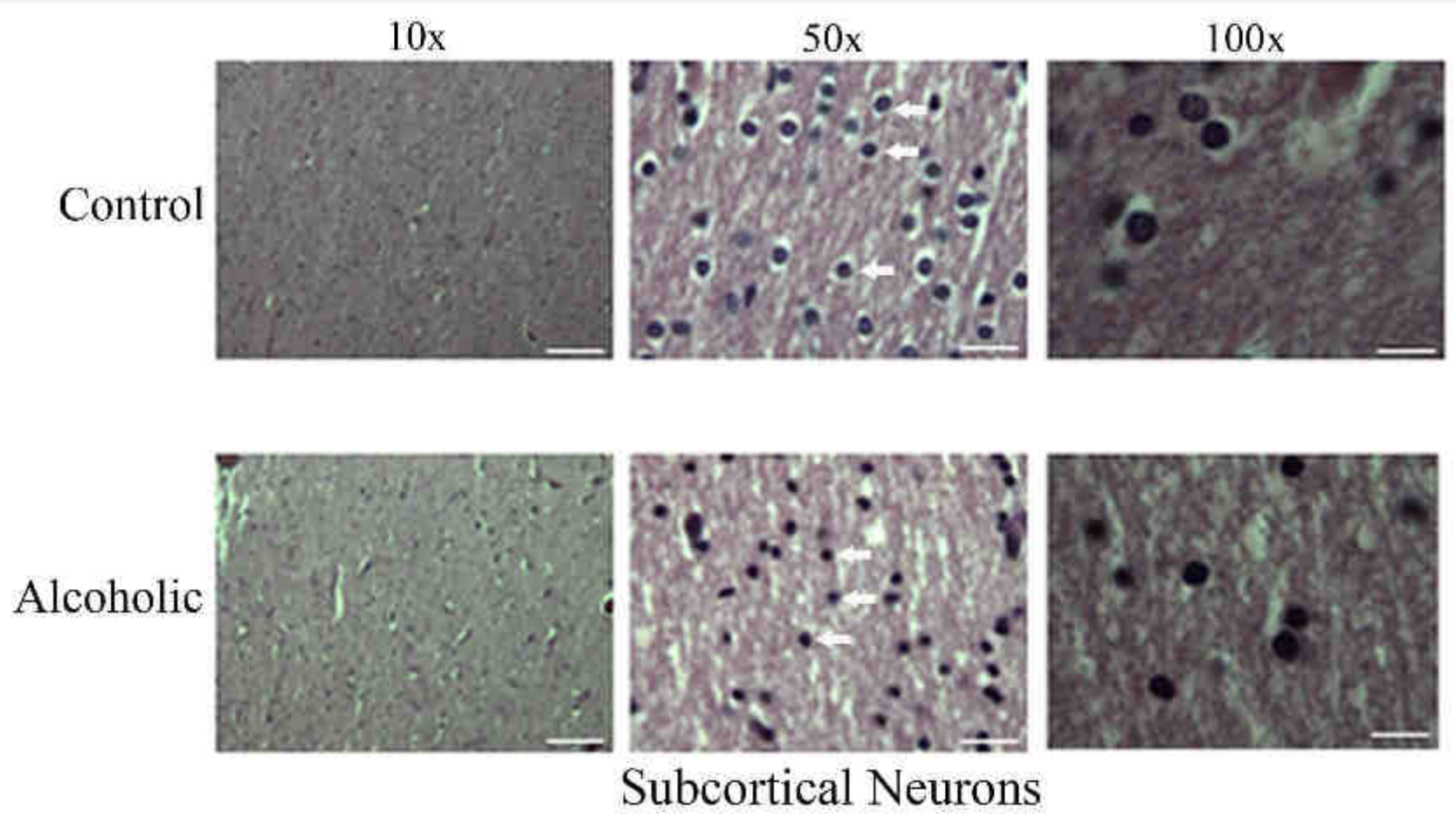


Alcoholic



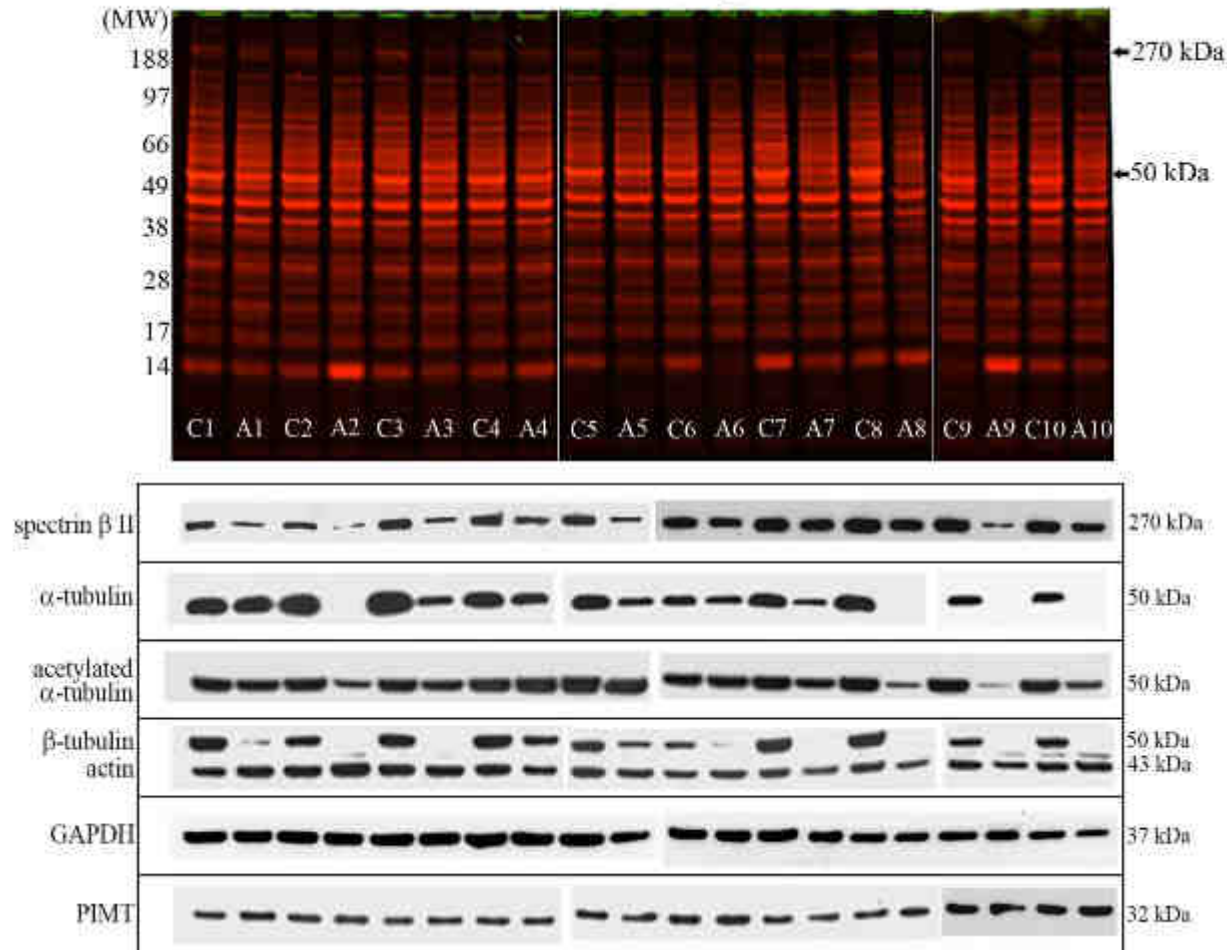
Cortical Pyramidal cells

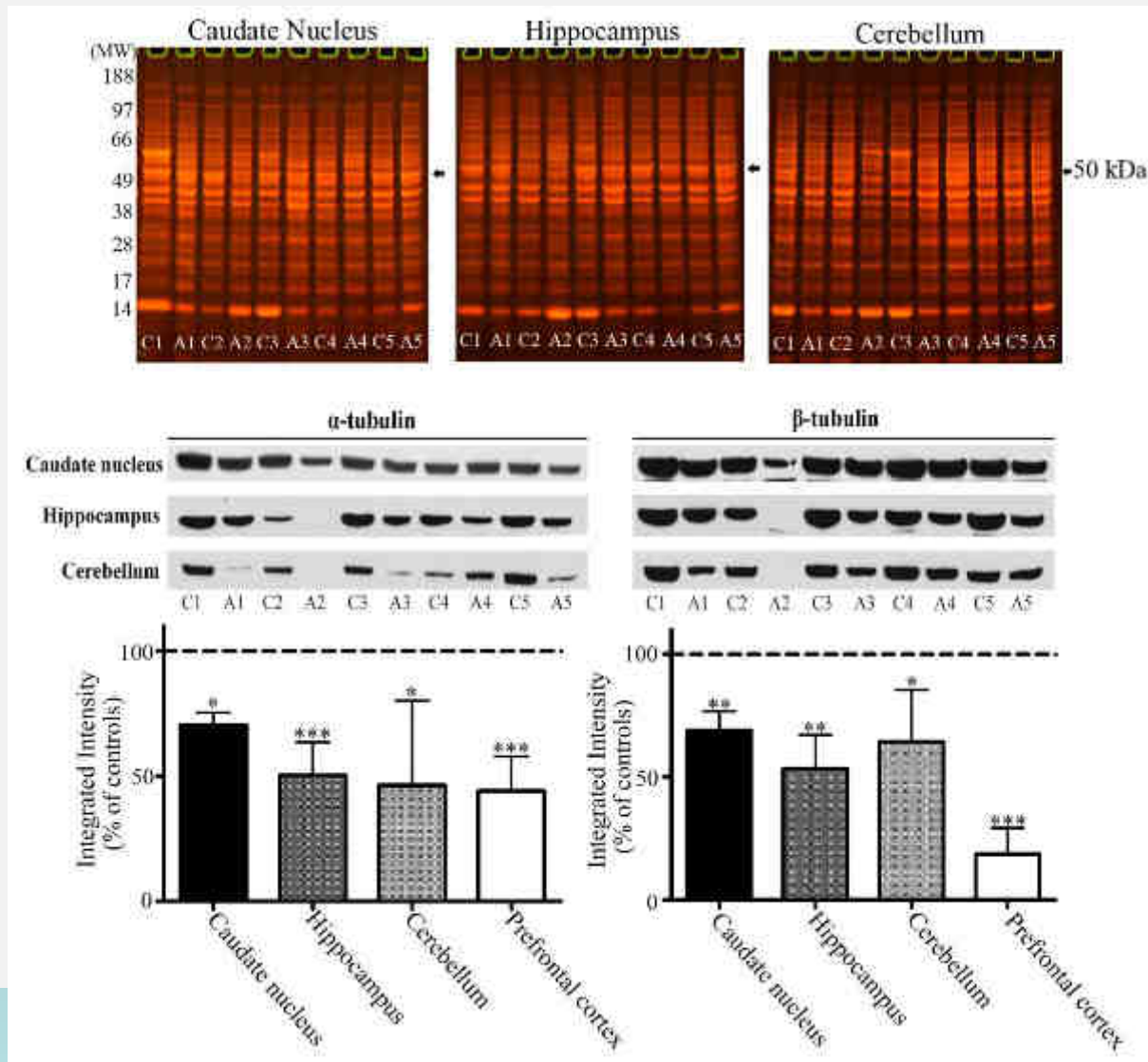


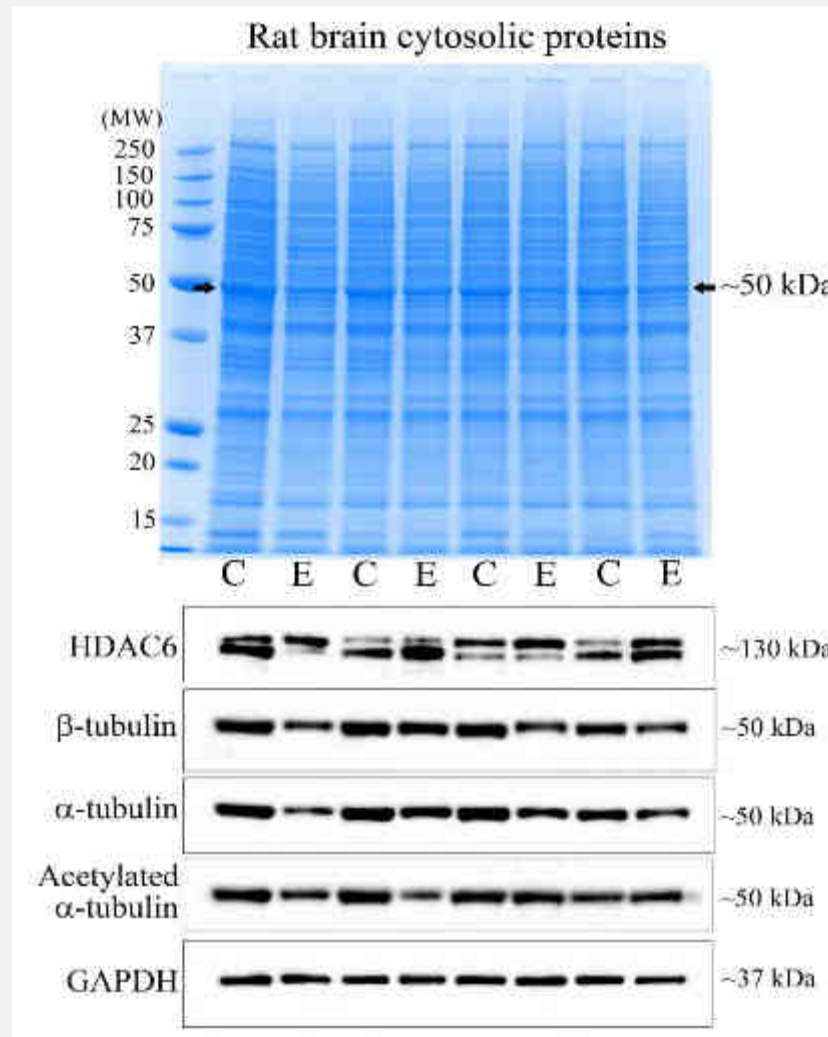




### Prefrontal Cortex (BA9) Cytosolic Proteins









## 'Tubulin code'

<b>Modification</b>
Acetylation
Detyrosination
Deglutamylation
Glutamylation
Polyamination
Glycosylation
Palmitoylation
Phosphorylation
Sumoylation
Ubiquitination
Isoaspartate formation
Succination





- Presence of irregularities of the cytoskeletal architecture with other neurotoxicants, & brain injury?
- Differences of immunostaining – dark neurons – an artifact?
- Tubulin protein level changes and modifications?



GROUP DISCUSSION

