

**BRM/Biomere**

**Diabetic Models of Alzheimer  
Diseases (AD)**

# Clinical Symptoms of AD

- Memory loss that disrupts daily life
- Changes in planning of solving problems
- Difficulty completing familiar tasks at home, at work or at leisure
- Confusion with time or place
- Trouble understanding visual images and spatial relationships
- New problems with words in speaking or writing
- Misplacing things and losing the ability to retrace steps
- Decreased or poor judgment
- Withdrawal from work or social activities
- Changes in mood and personality

# Risk Factors of AD

- Risk Factors
  - Age
  - Genetics
  - Insulin resistance
  - Hyperglycemia
  - Inflammation
  - Oxidative stress

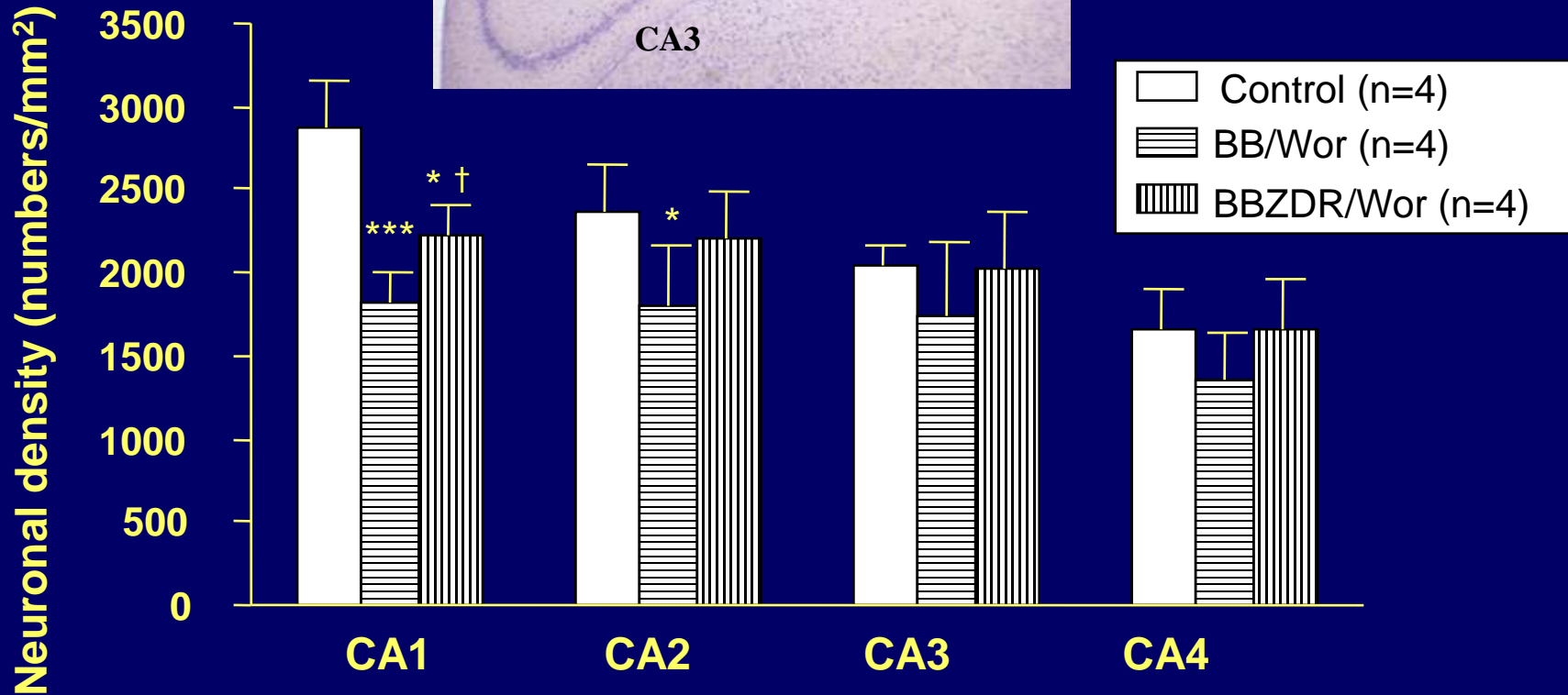
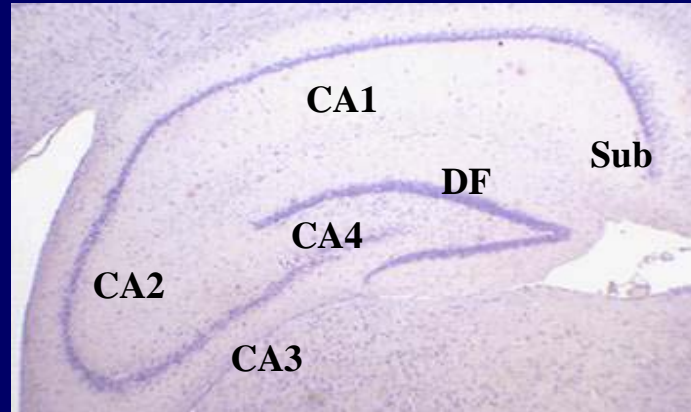
# 7 Stages of Alzheimer's Disease

- 7 Stages of AD
  - 1 – no impairment
  - 2 – very mild decline
  - 3 – mild decline
  - 4 – moderate decline (mild to early stage)
  - 5 – moderately severe decline (moderate to mid-stage)
  - 6 – severe decline (moderately severe to mid-stage)
  - 7 – very severe decline (severe or late state)

# **Comparison between BB/Wor- and BBZDR/Wor-Diabetic Rats**

- 1. Neuronal loss**
- 2. Neuronal apoptosis**
- 3. Alterations of various factors mediating apoptotic activity:**
  - Apoptosis-regulating proteins**
  - Perturbation of IGF system**
  - Activation of Fas/NGF-R.p75**
  - Oxidative stress: PARP, 8-OHdG**
  - Caspase activation**

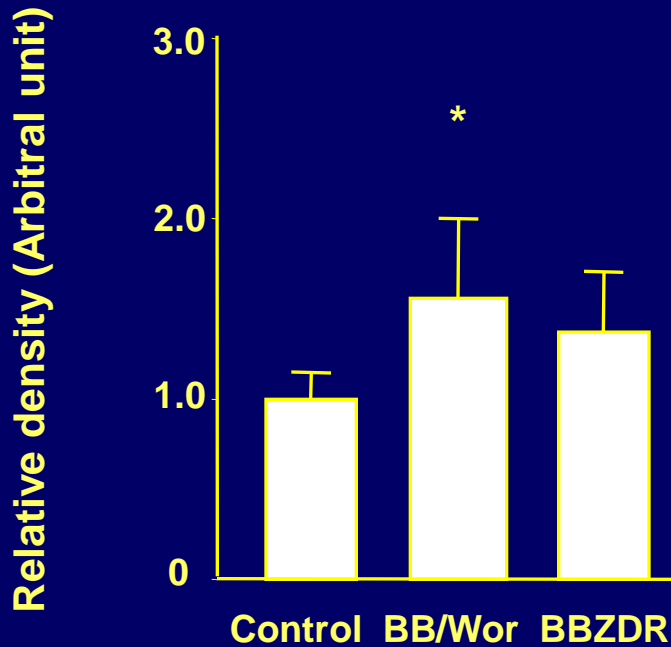
# Neuronal densities in type 1 vs. type 2 diabetic BB/Wor rats



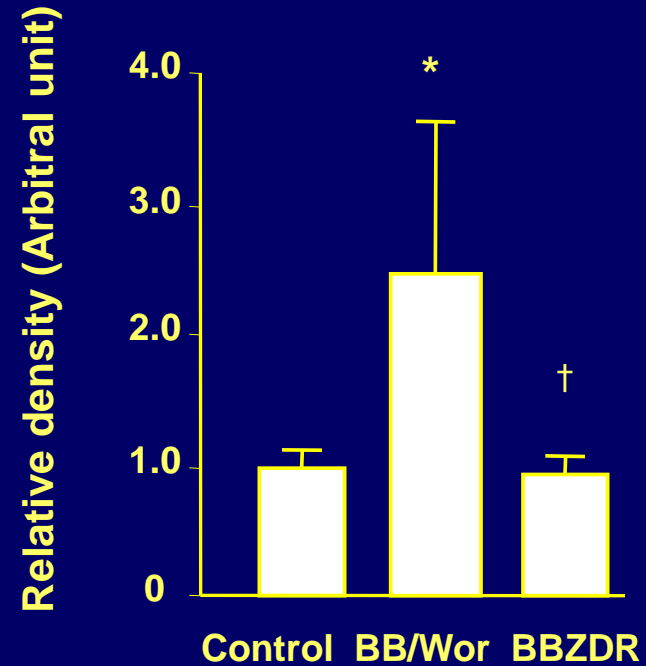
\*  $p < 0.05$ , \*\*\*  $p < 0.001$  vs. control, †  $p < 0.05$  vs. BB/Wor

# Expression of caspases in type 1 vs. type 2 diabetic BB/Wor rats

## a). Active caspase-3



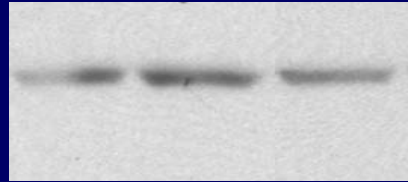
## b). Caspase 12



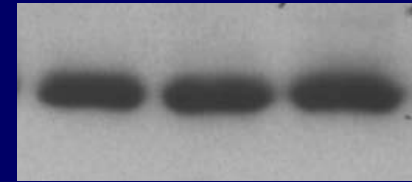
\*  $p < 0.05$  vs. control; †  $p < 0.05$  vs. BB/Wor

# Apoptosis- regulating proteins in type 1 vs. type 2 diabetic BB/Wor rats (hippocampus, 8 months)

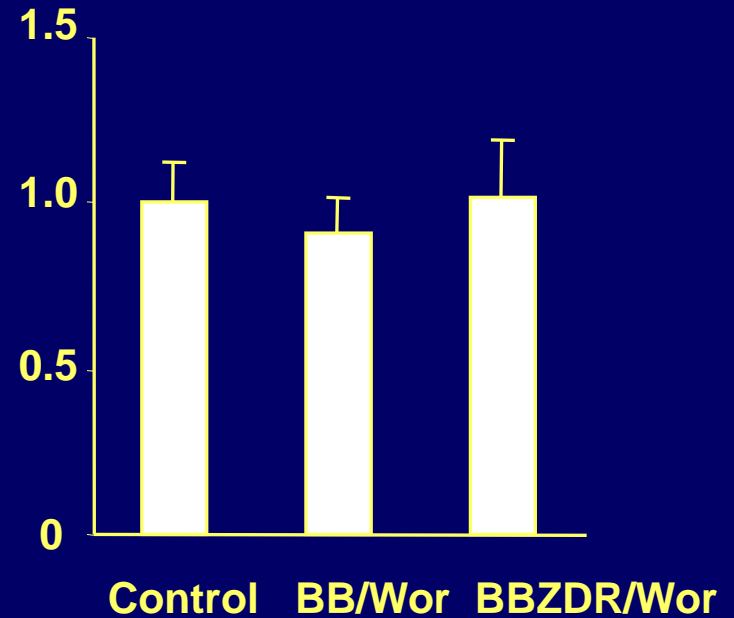
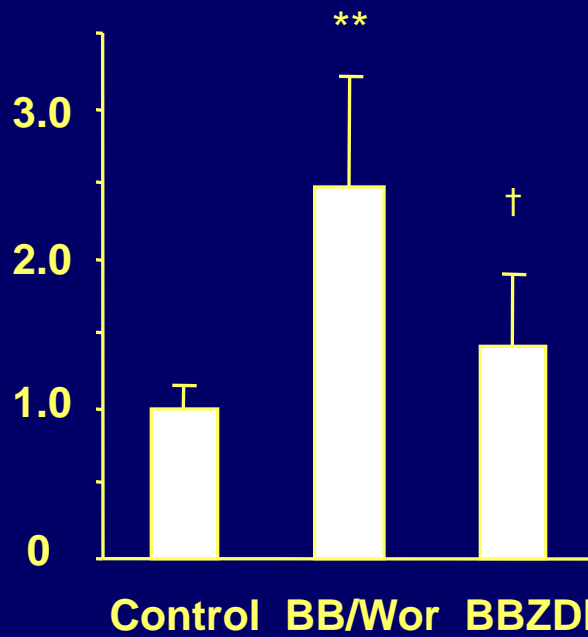
Bax



Bcl-xL



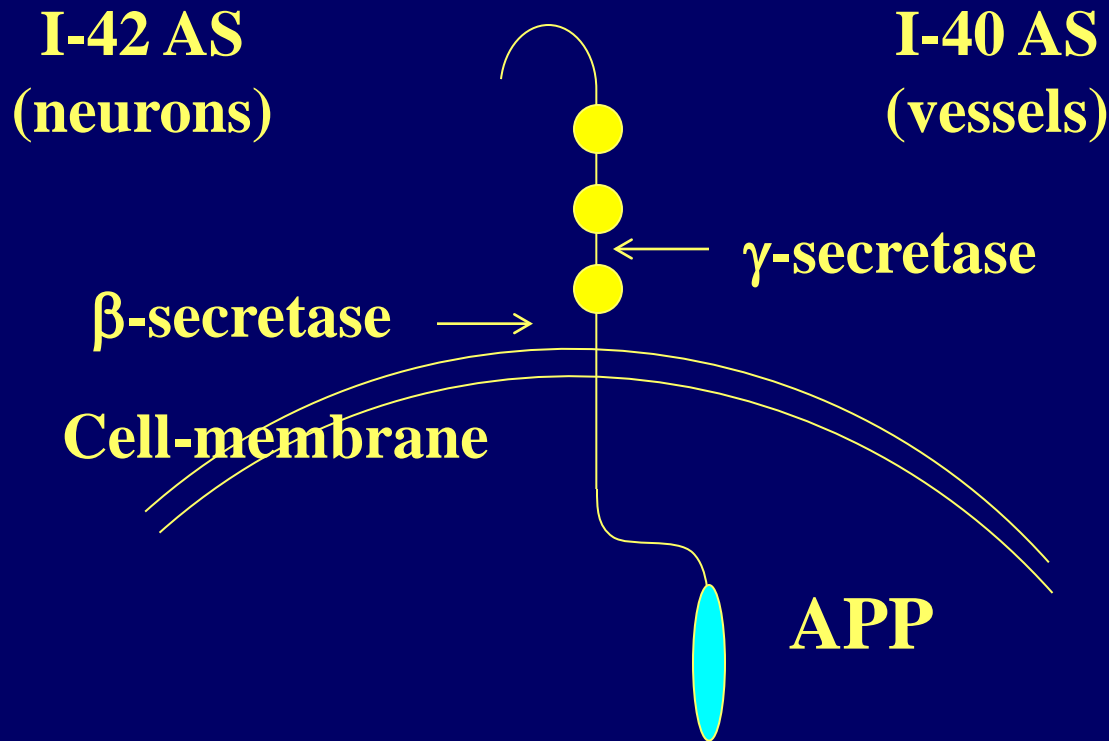
Relative density (Arbitrary unit)



\*  $p < 0.05$ , \*\*  $p < 0.01$  vs. control.

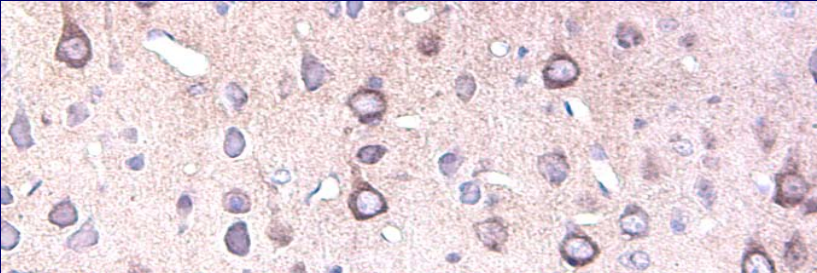
†  $p < 0.05$  vs. BB/Wor

# Splicing of the transmembranous APP-molecule

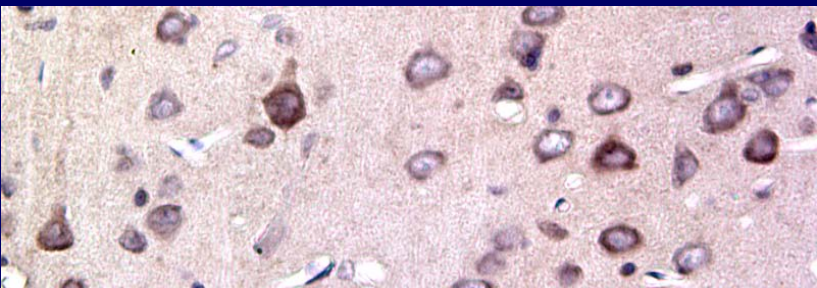


# APP Frontal Cortex

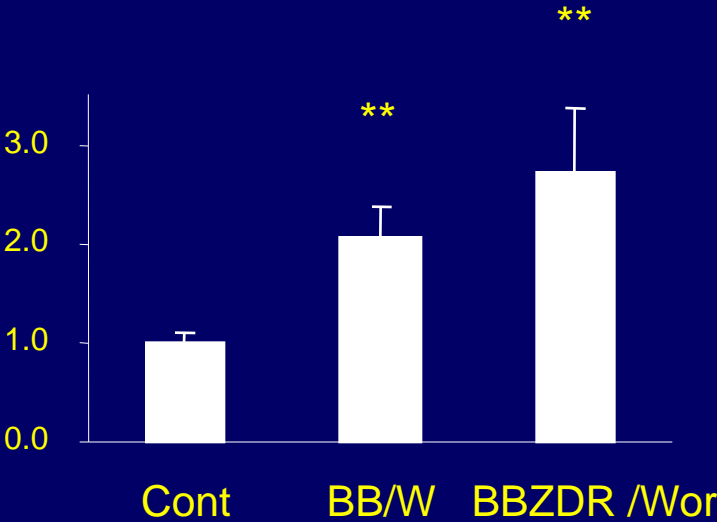
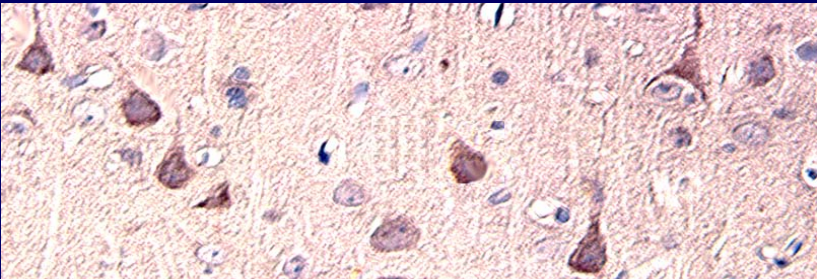
Control



BB/Wor



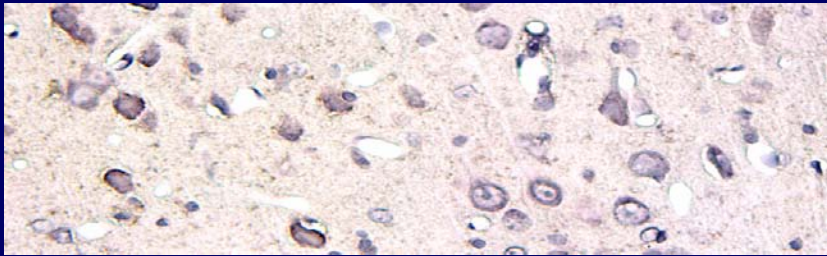
BBZDR/Wor



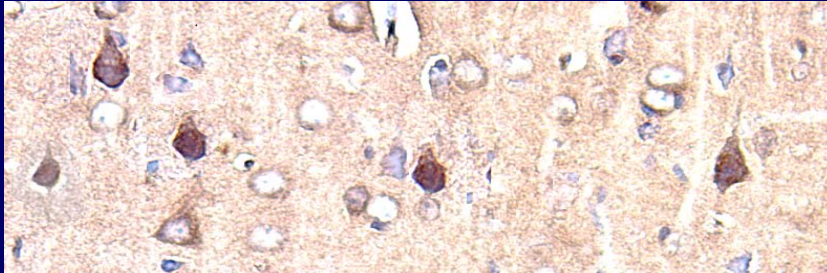
\*\* p < 0.005 vs. control

# $\beta$ – Secretase Frontal Cortex

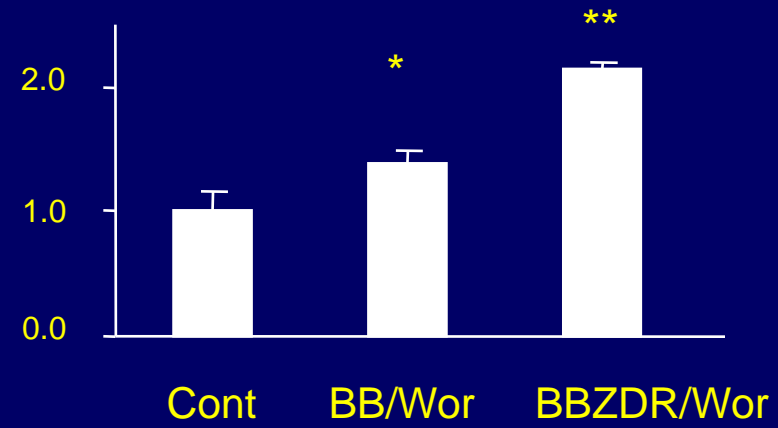
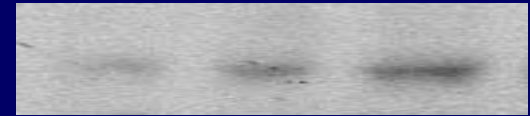
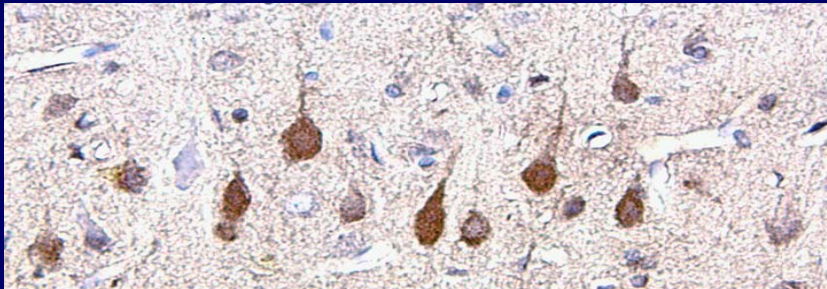
Control



BB/W



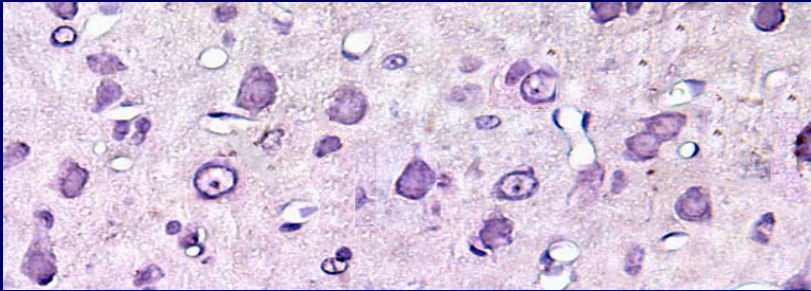
BB/ZDR



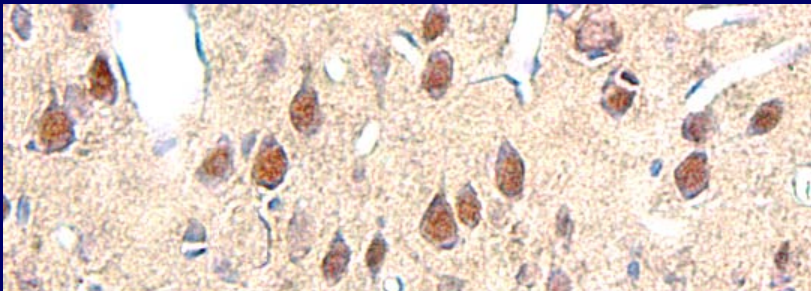
\*  $p < 0.05$ , \*\*  $p < 0.005$  vs. control

# $A_{\beta}$ 1-42 Frontal Cortex

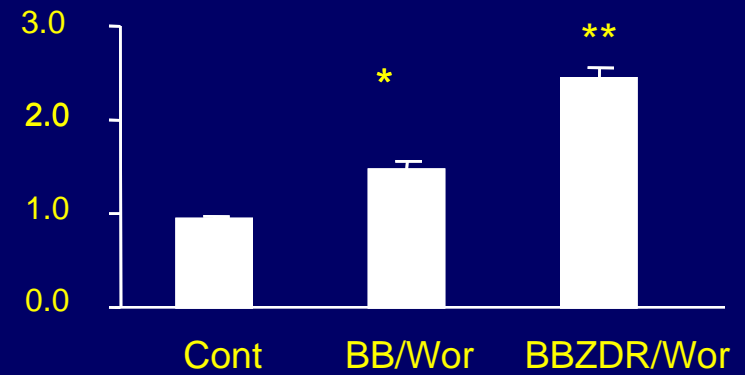
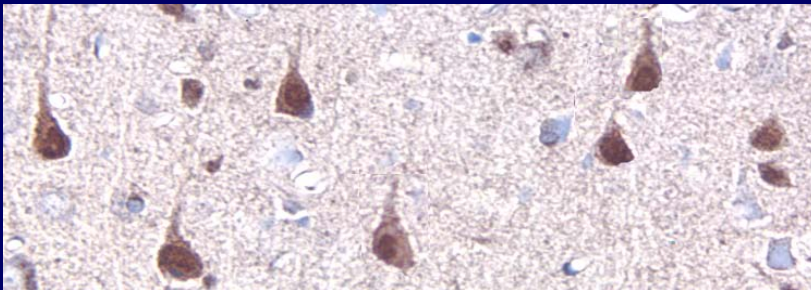
Control



BBW



BBZ



\*  $p < 0.05$ , \*\*  $p < 0.005$  vs. control

# Formation of Paired Helical Filaments (NFT)

