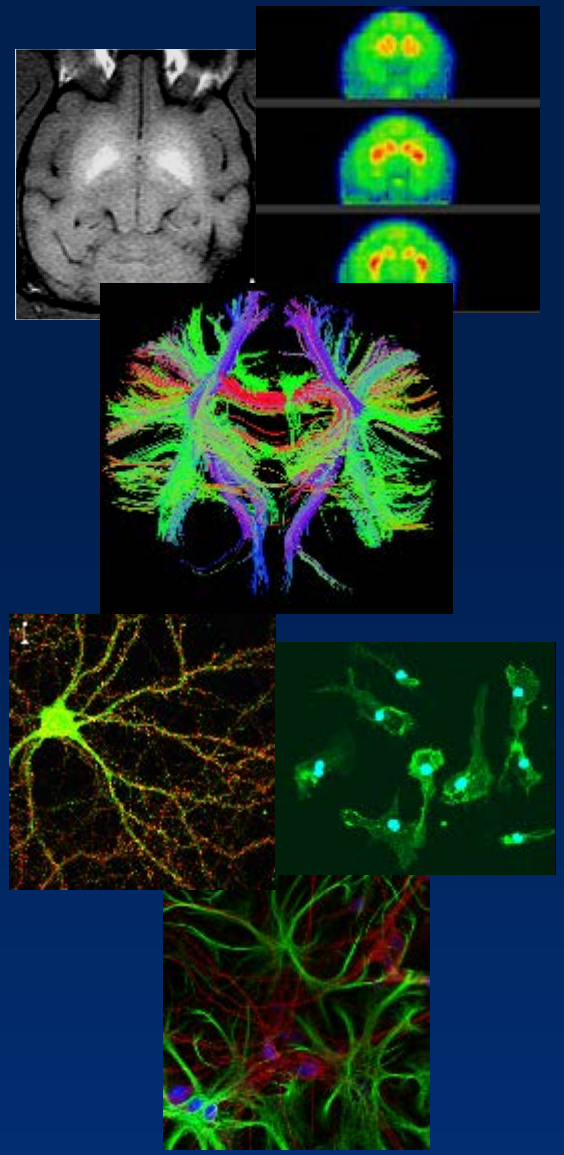
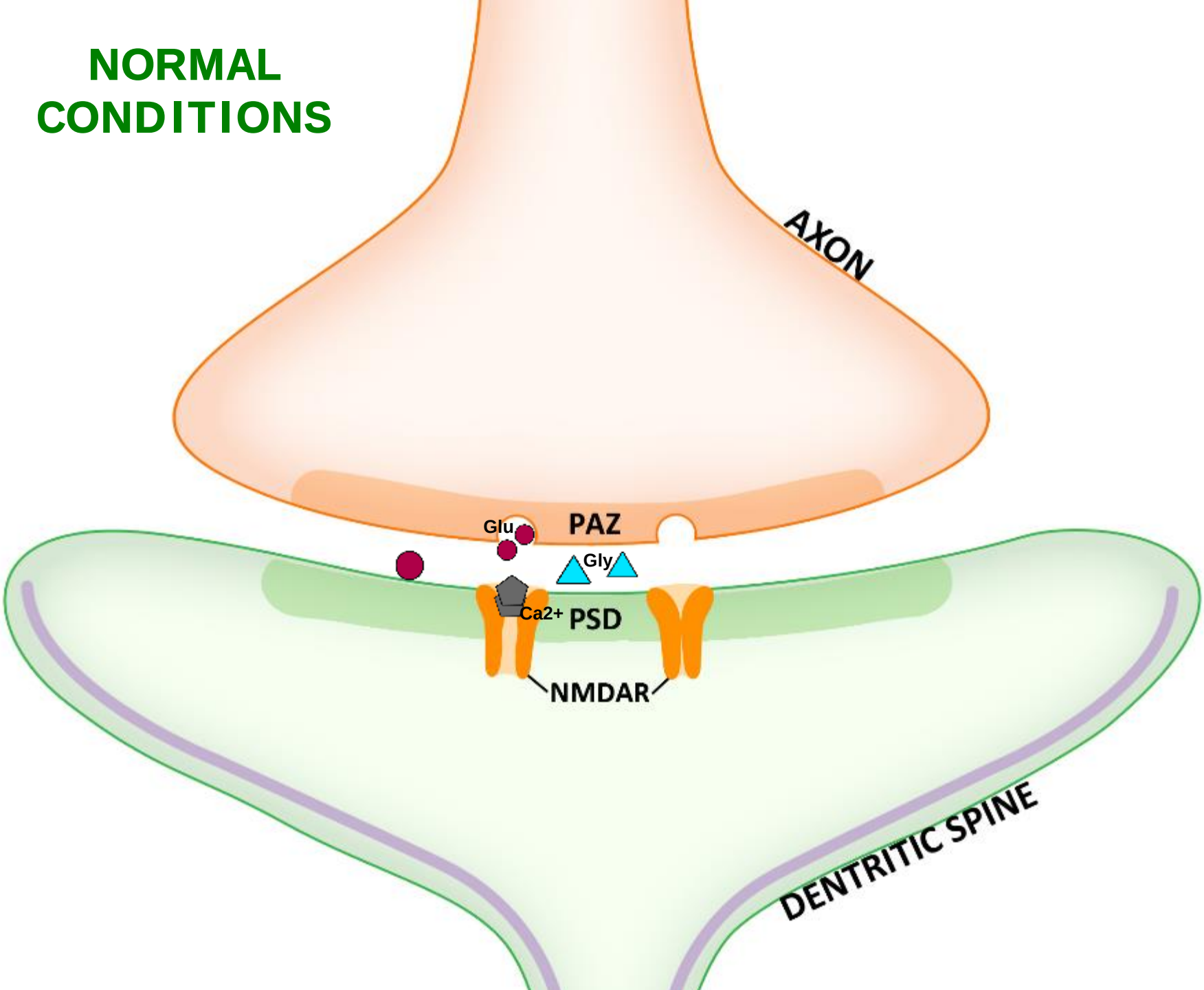


Heavy Metals: Environmental Determinants of Developmental & Neurological Disorders

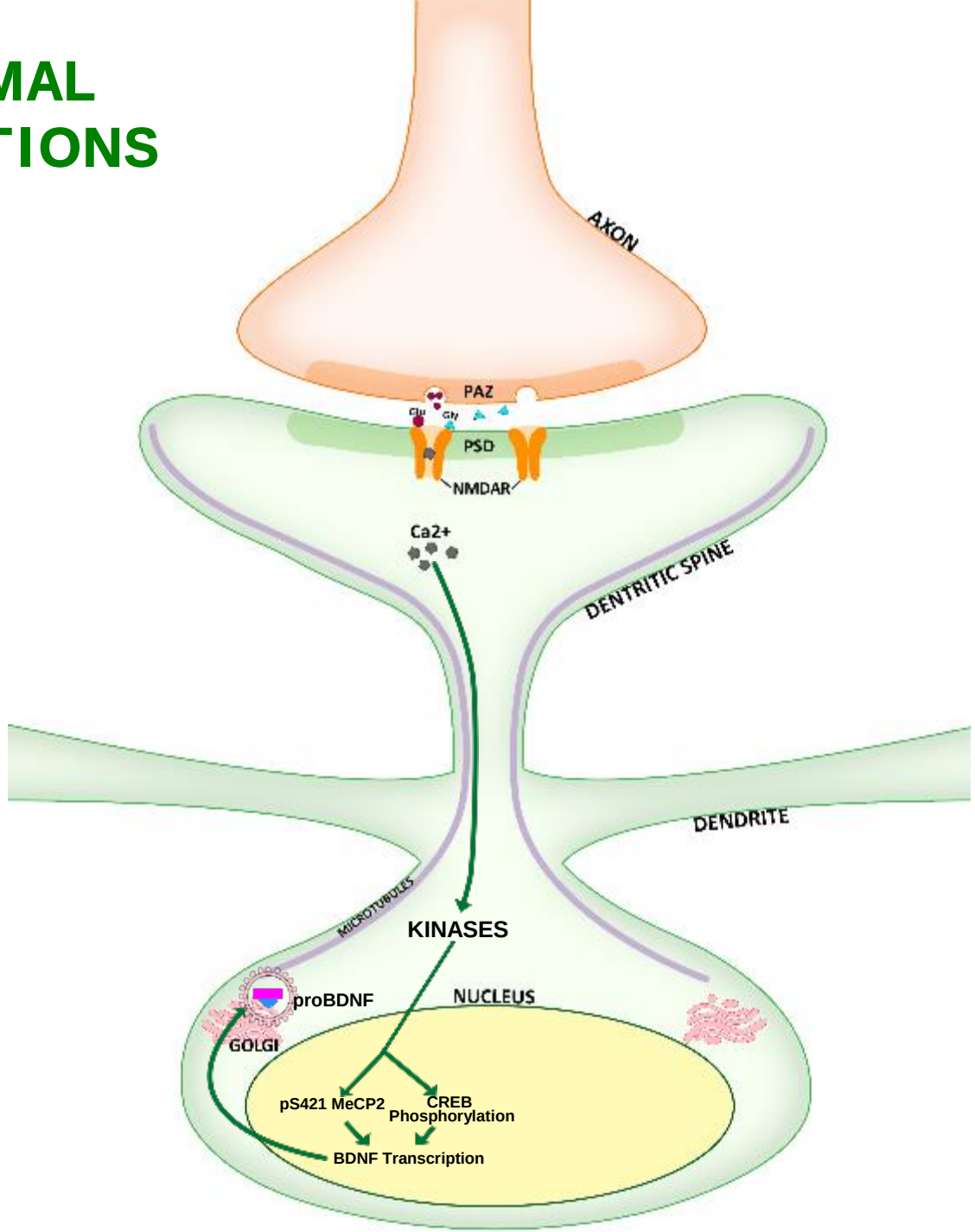
Tomás R. Guilarte, PhD
Dean, Robert Stempel College of Public Health & Social Work
Professor, Environmental Health Sciences
Professor, Cognitive Neuroscience & Imaging
Director: Brain, Behavior & Environment Program
Florida International University
Miami, FL 33139
tguilart@fiu.edu

FIU Stempel

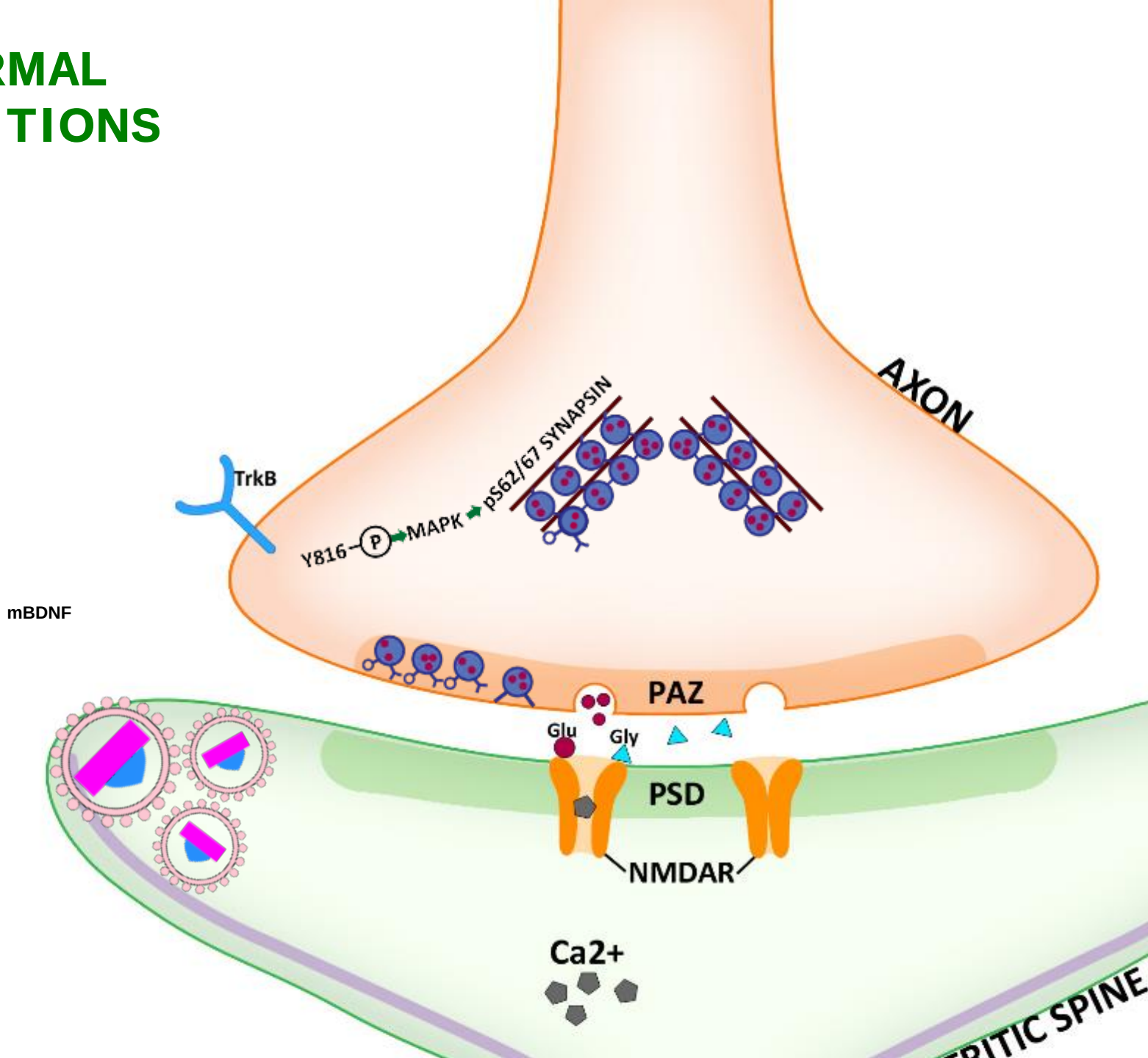
NORMAL CONDITIONS



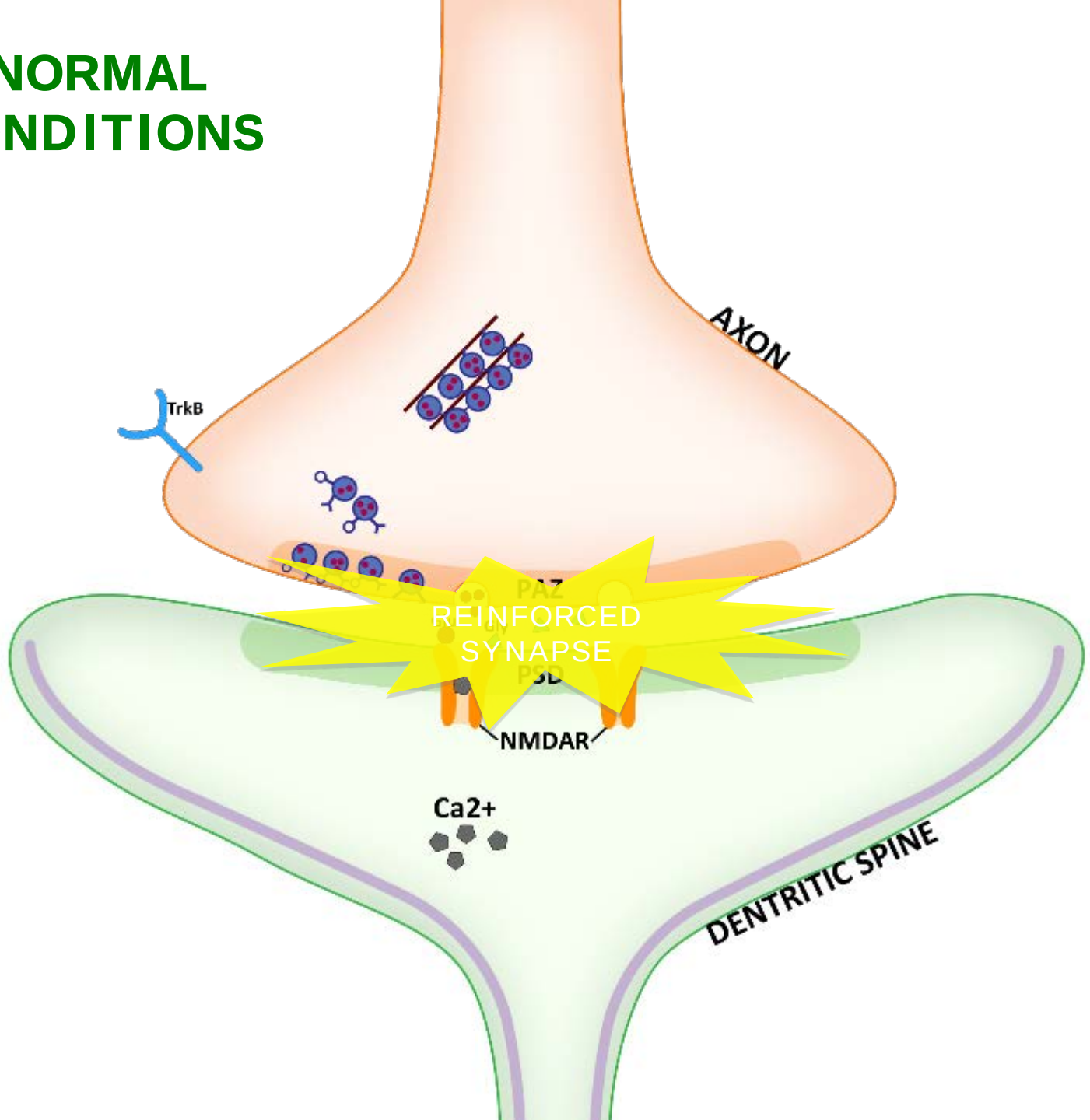
NORMAL CONDITIONS



NORMAL CONDITIONS

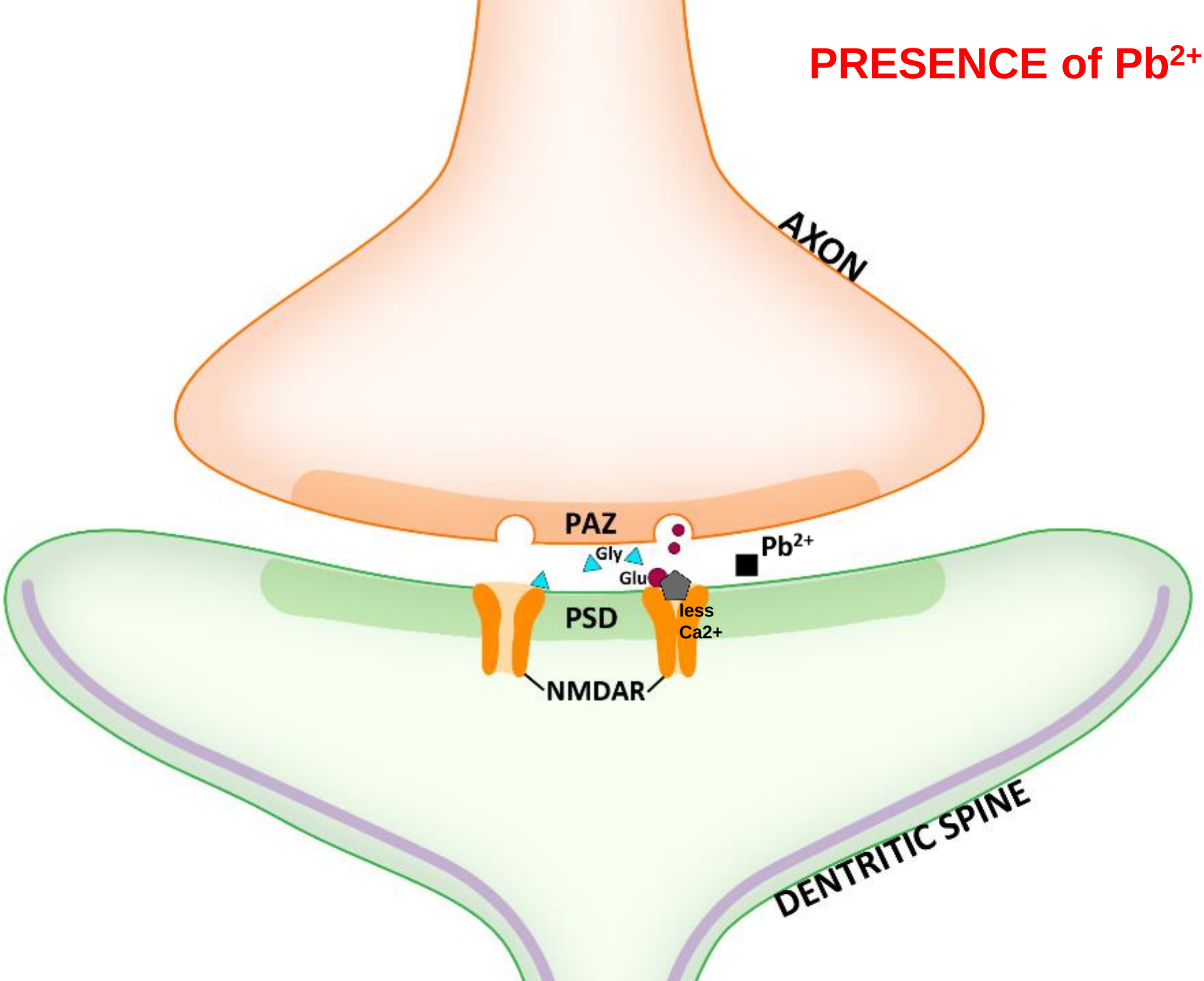


NORMAL CONDITIONS

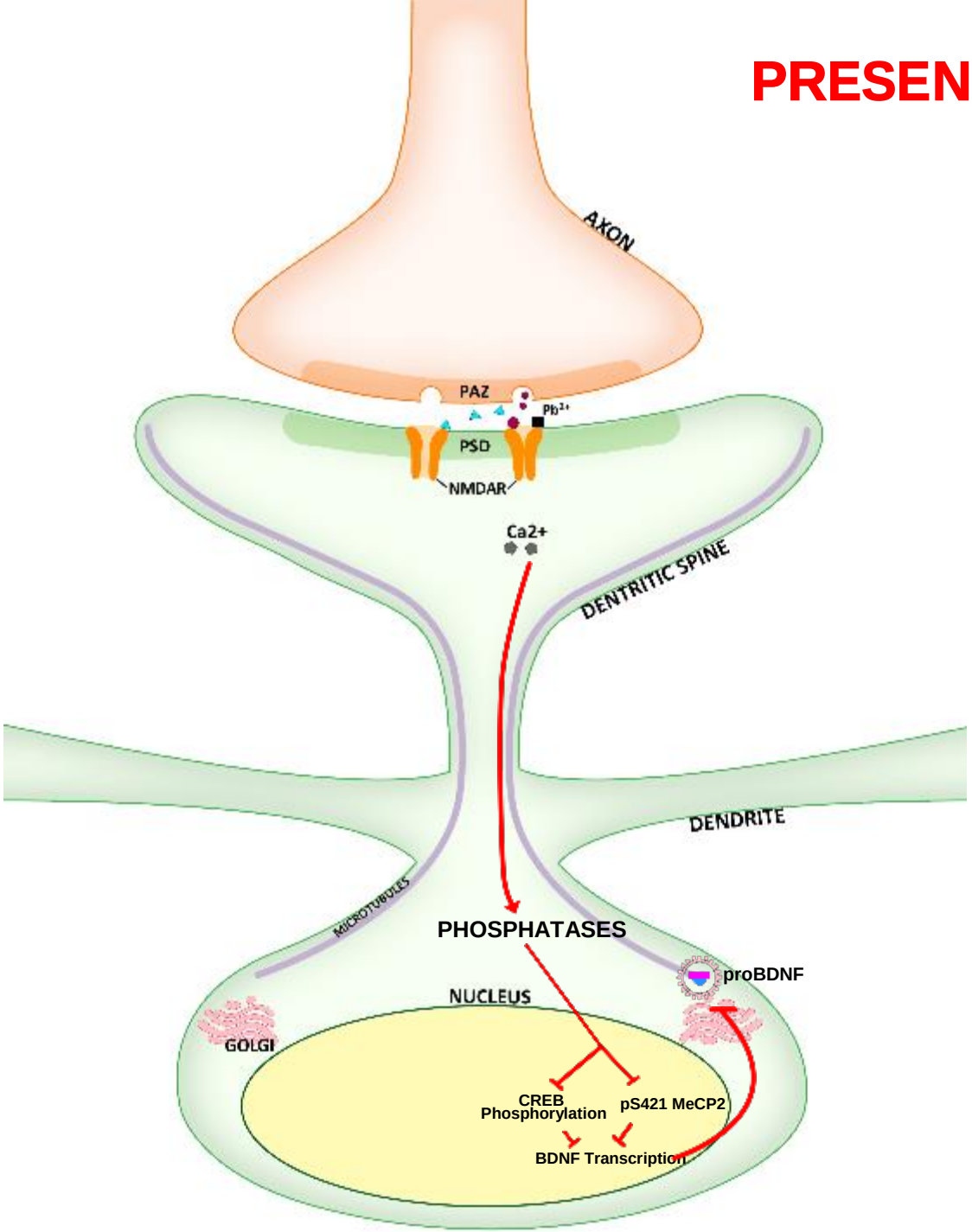


PRESENCE OF Pb^{2+}

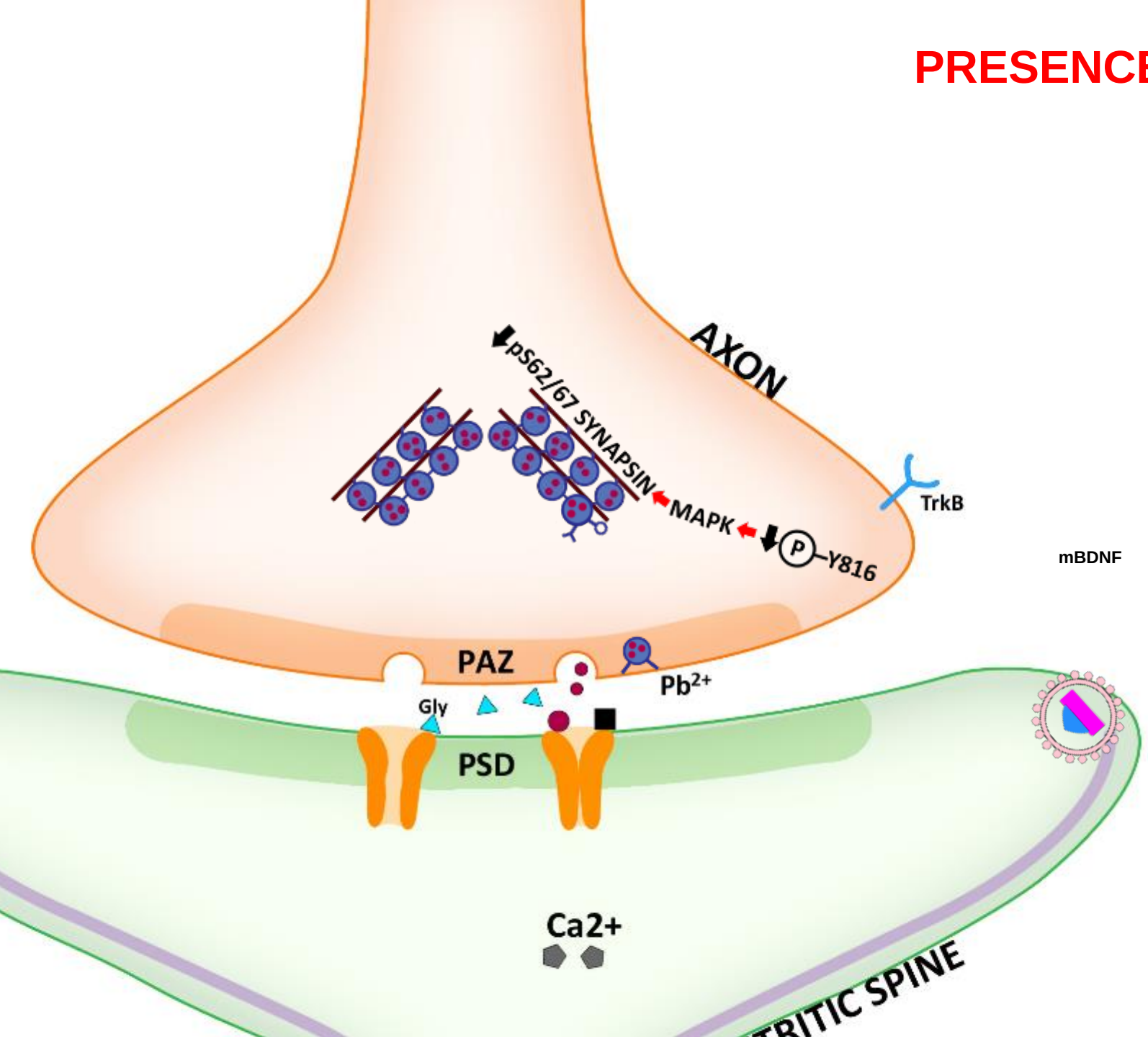
PRESENCE of Pb^{2+}

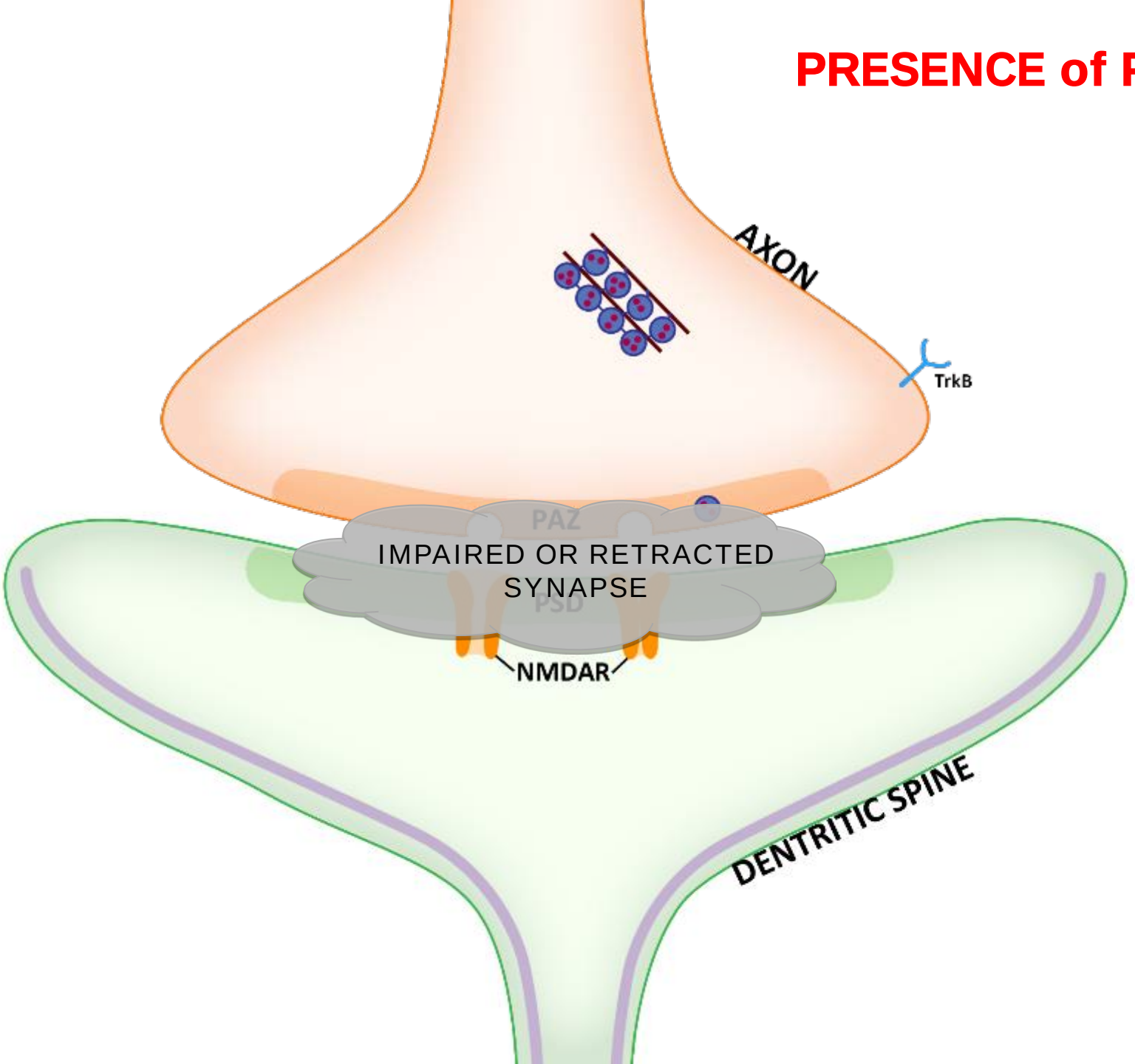


PRESENCE of Pb^{2+}

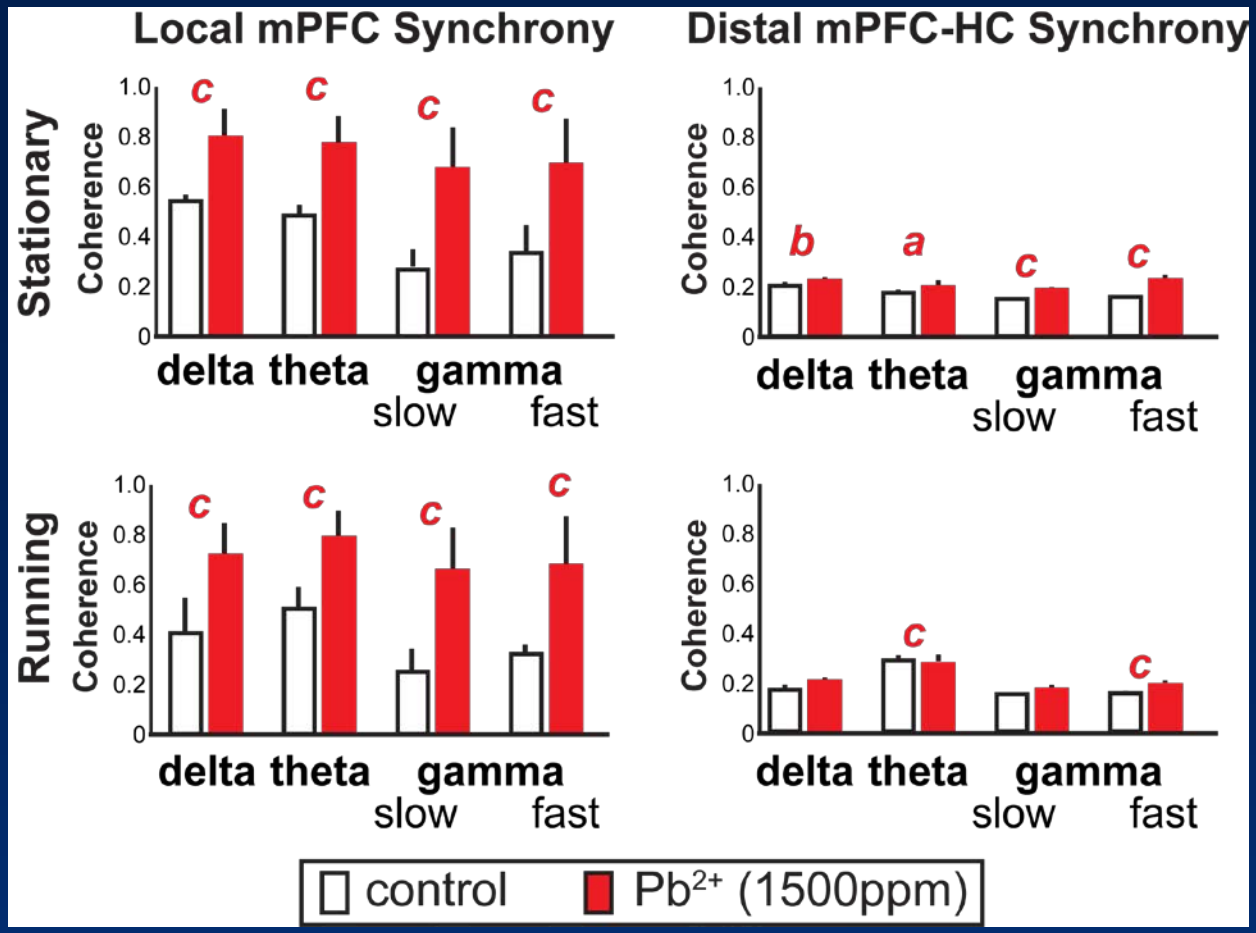


PRESENCE of Pb^{2+}




PRESENCE of Pb^{2+}
AXON
TrkB
PAZ
IMPAIRED OR RETRACTED SYNAPSE
PSD
NMDAR
DENTRITIC SPINE

Hippocampal-Prefrontal Network Dysfunction caused by Early-Life Lead Exposure



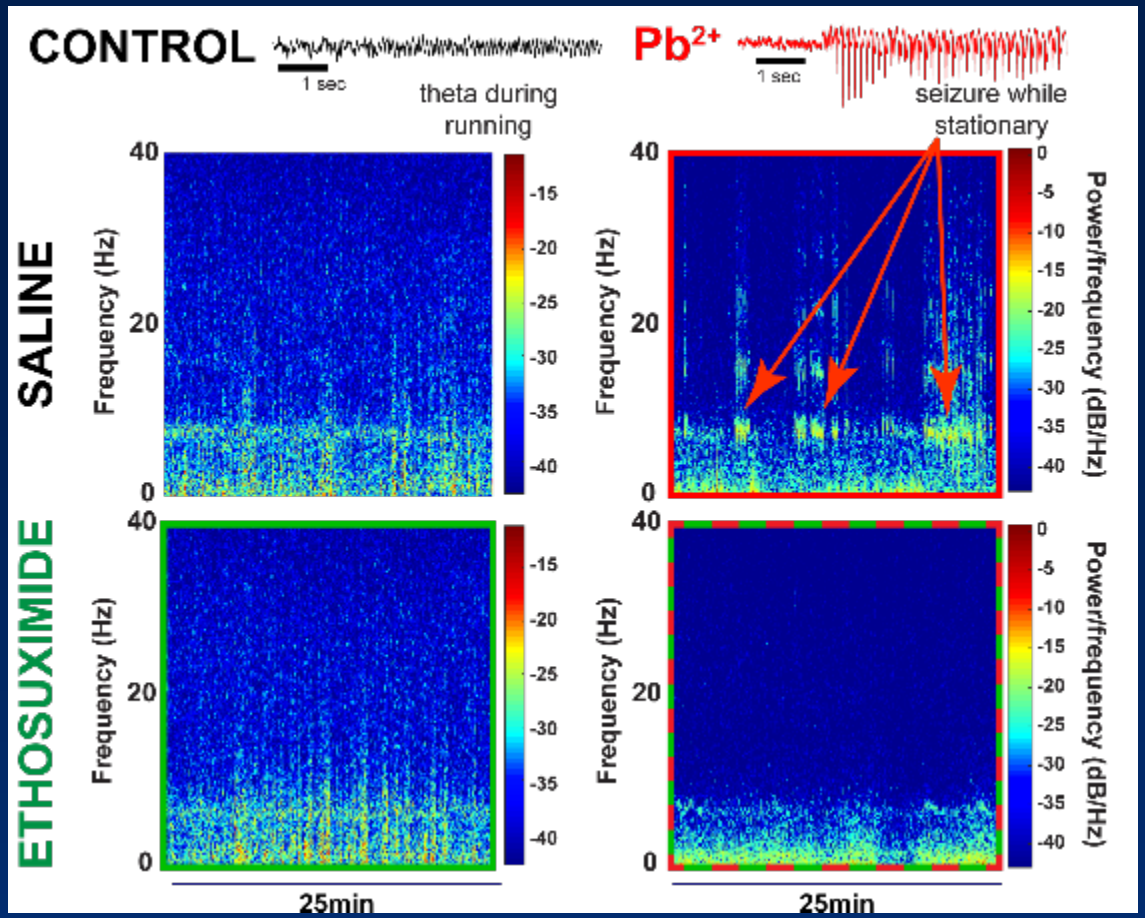
Outcomes:

1) Hypersynchrony in prefrontal cortex in delta, theta and gamma bands (poor local processing)

2) Impaired hippocampal-prefrontal coordination, particularly during stationary behaviors

FIU Stempel

Controlling ‘Absence Seizures’ caused by Early-Life Lead Exposure with Ethosuximide



Outcome:

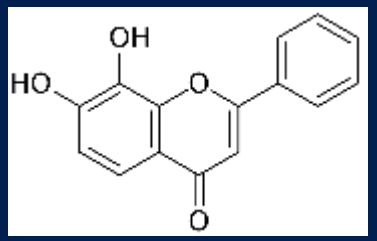
Prevalent ‘absence seizures’ during awake stationary behaviors—definitive of network dysfunction (CA1 recordings shown)

Treatment:

Ethosuximide as a first choice anticonvulsant for these seizures at doses that have no effect on control networks (50-200mg/kg)

FIU Stempel

7,8-DIHYDROXYFLAVONE



- Selective tyrosine kinase receptor B (TrkB) small molecule agonist
- Both orally-bioavailable and able to penetrate the blood-brain-barrier
- Signaling pathways associated with TrkB activation include those involving neuroprotection and memory
- Manifests the therapeutic effects of BDNF without the poor pharmacokinetic profile of BDNF, which limits it's therapeutic potential
- Therapeutic efficacy has been shown in animal models of central nervous system disorders including:

Depression
Schizophrenia (cognitive deficits)
Huntington's disease
Traumatic Brain Injury
Fragile X Syndrome
Alzheimer's disease
Parkinson's disease
ALS
Cerebral Ischemia
Rett Syndrome

FIU Stempel