

Pro-inflammatory cytokines as modulatory factors in nervous system injury.

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NIEHS

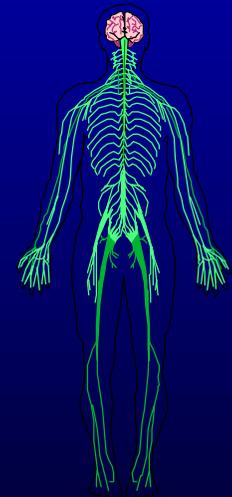
Data Gaps in Evaluation

Radiation

Factors determining target site



Mechanisms of damage and repair



EXPOSURE

DOSE TO
BIOLOGICAL TARGET

ADVERSE
HEALTH
EFFECT

CNS CELLS

- Neurons - functional unit of brain information processing
- Glia
 - Macroglia - astrocytes, oligodendrocytes
 - Microglia- immune-like cells of the brain

What role do microglia play in degeneration of the nervous system

Initial responders to adverse factors penetrating the brain from the circulation

Indicators of neuronal activity - injury

Responders to neuronal injury - phagocytosis

Contributors to the progression of injury via secretory factors and by-stander effects

Cytokines

- Diverse group of polypeptide intracellular signaling molecules
- Rapidly produced and secreted by multiple cell types in response to various stimuli
- Bind to specific cell surface receptors linked to multiple signal transduction pathways
- Critical role in initiation, propagation, regulation, and suppression of immune and inflammatory responses

Central Nervous System Elevation of Pro-inflammatory Cytokines

- Clinical

Multiple Sclerosis

Viral encephalitis

Cerebral malaria

Down's syndrome

Alzheimer's Disease

AIDs dementia
complex

- Experimental

Experimental allergic
encephalitis

Lipopolysacharide

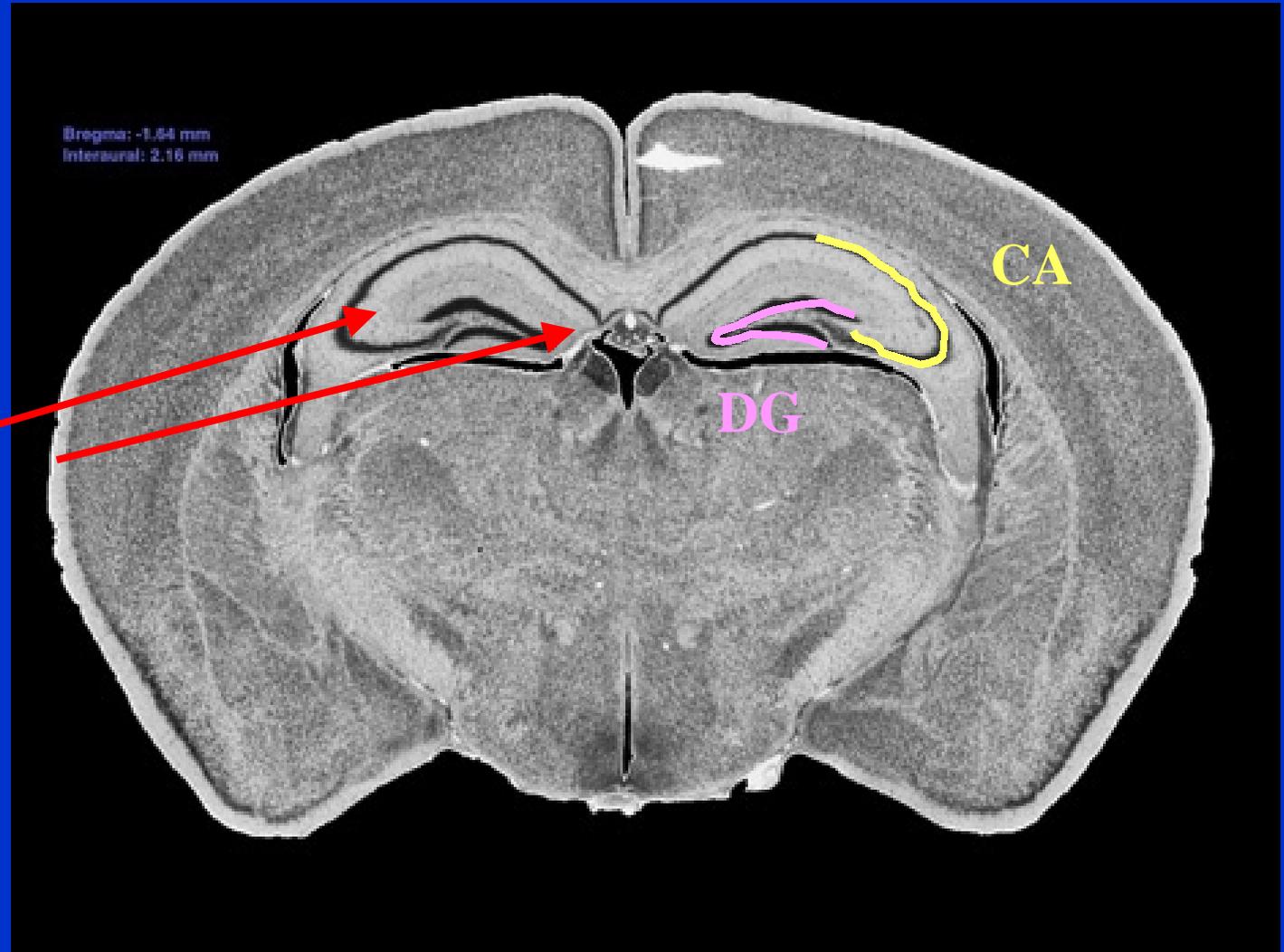
Scrapie

Brain ischemia

Physical injury

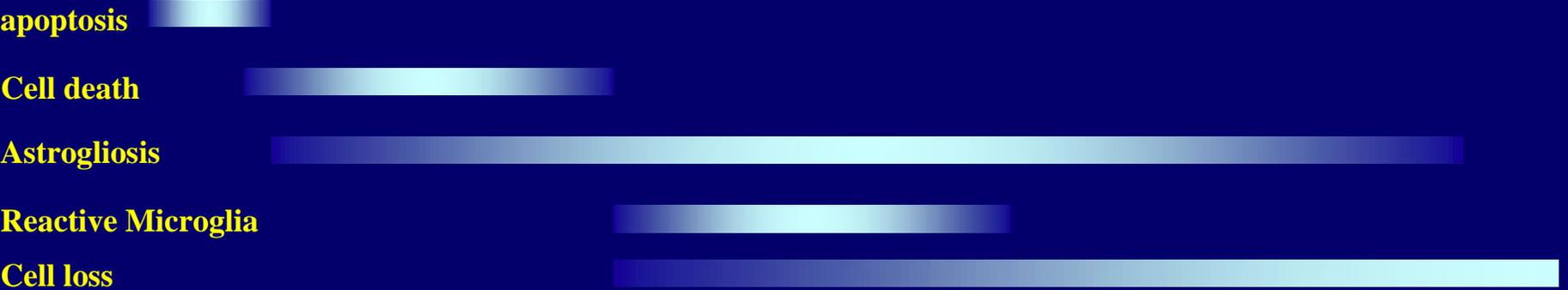
Excitotoxicity

Frontal section of the mouse brain



TMT induced neurodegeneration

Structural changes



Cytokine changes

