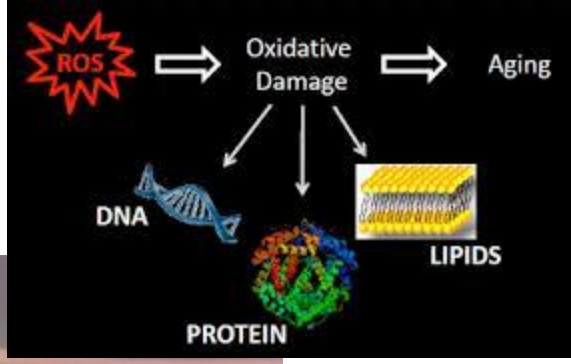
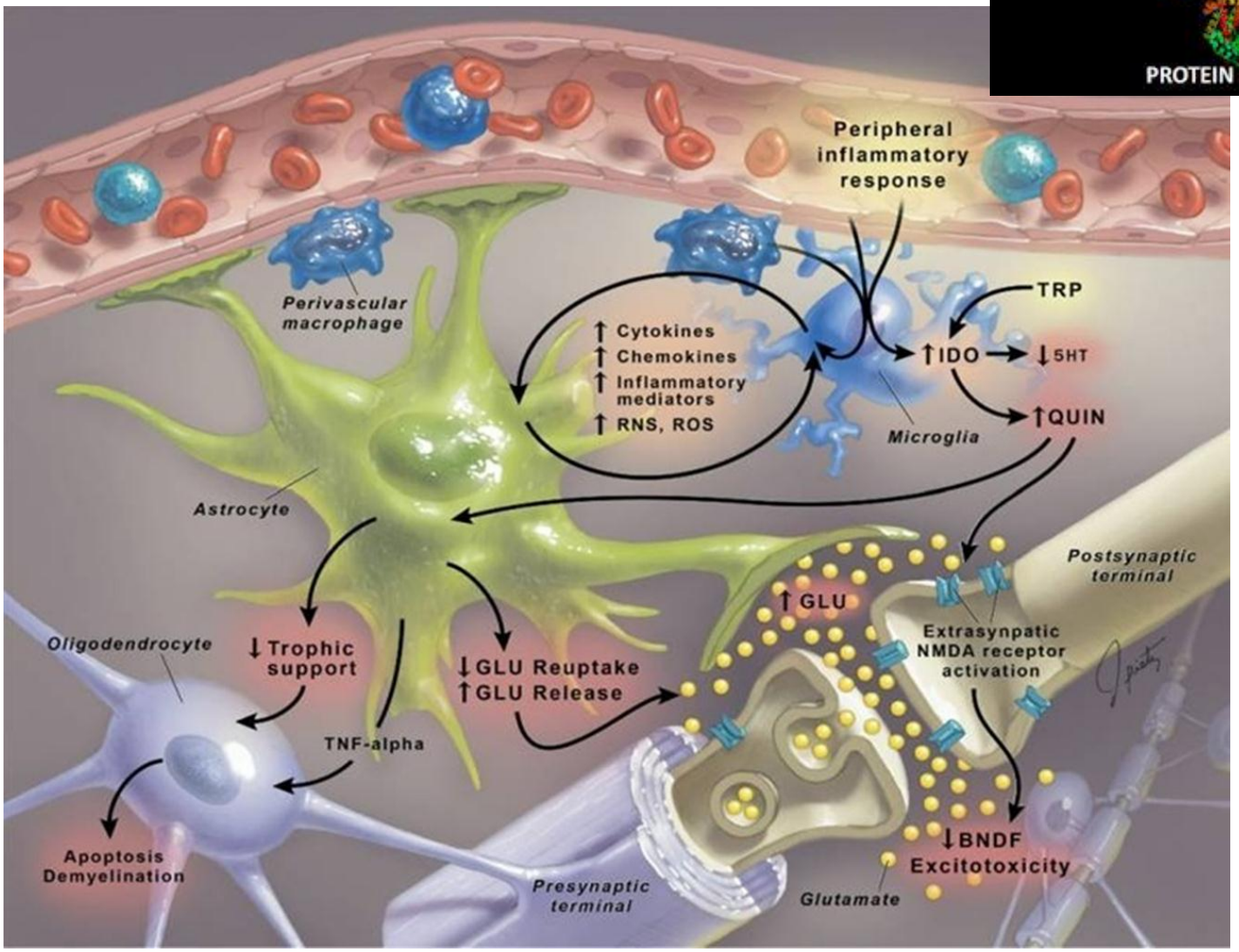
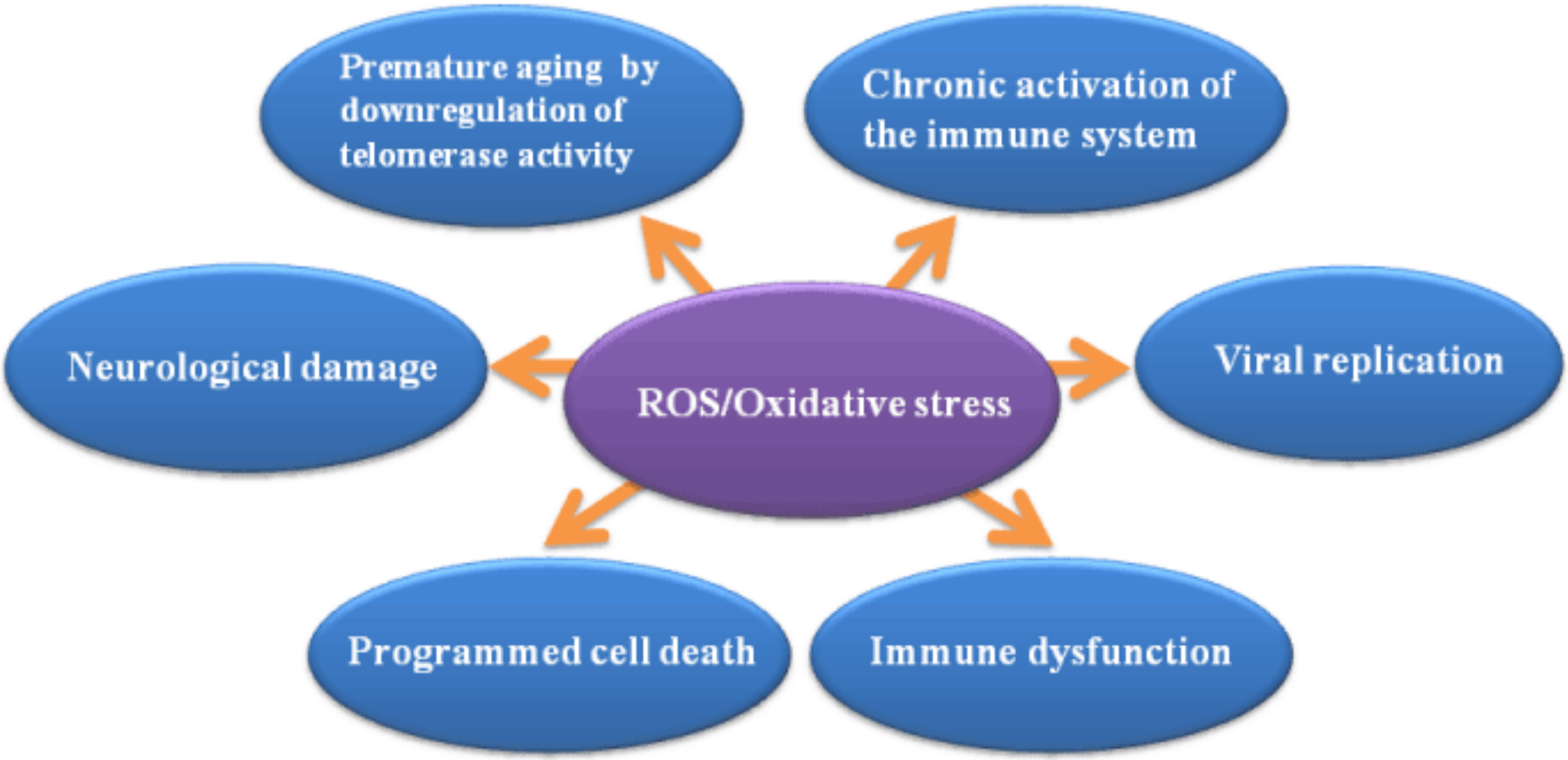
Inflammatory Model





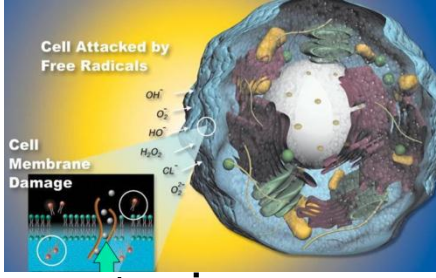
Adapted from Miller et al., 2009. Biol. Psychiatry



Adapted from Psychoneuroimmunology: Clinical application of an emerging field in medicine, May 21, 2013, APA

Adapted from Psychoneuroimmunology: Clinical application of an emerging field in medicine, May 21

Oxidative Stress



- Oxidative Stress is defined as an imbalance between toxic reactive species or ROS (free radicals) and antioxidant systems

- It is relevant to the pathophysiology of schizophrenia

- Free radicals are counteracted by several cytoprotective antioxidant enzymes that limit their damage such as:
  - Superoxide dismutase
  - Glutathione peroxide
- **Mitochondria dysfunction** has been reported in schizophrenia and may account for the low levels of the powerful antioxidant **glutathione**
- **Atypical antipsychotics have been reported to normalize the abnormal free radical metabolism but the first generation antipsychotics like Haloperidol increase oxidative stress.**

Adapted from Recent Advances in Neurobiology of Schizophrenia, Addressing the Major Unmet needs, Henry Nasrallah, May 18th, 2013 APA

Neuroinflammation

Evidence-Based Mental Health
Review

Non-steroidal Anti-inflammatory Drugs May Reduce Schizophrenia Symptom Severity in the Short Term When Added to Antipsychotics

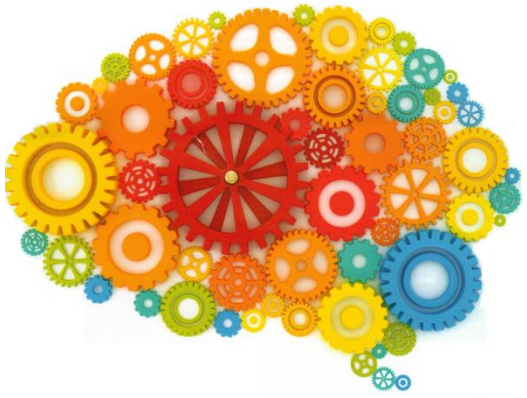
Xiaoduo Fan, Xueqin Song | Disclosures

Evid Based Ment Health. 2013;16(1):10

- There are many lines of evidence for immune dysregulation and neuroinflammation in schizophrenia
- Elevated inflammatory cytokines in schizophrenia **(TNF-α, 1FN-Ɣ)** Microglia are the primary reservoirs of **proinflammatory cytokines**, which act as antigens in the CNS and play a major role in innate immunity.
- **Some antipsychotic drugs (second generation) reduce inflammation and oxidative stress while others (first generation) increase inflammation and oxidative stress**
- Adding anti-inflammatory agents to antipsychotic drugs potentiate response, e.g. **Minocycline, Cox-2 inhibitors, Omega-3 fatty acid.** ESPECIALLY in **first episode!**

Adapted from Recent Advances in Neurobiology of Schizophrenia, Addressing the Major Unmet needs, Henry Nasrallah, APA 2013

Older Antipsychotics May Cause Additional Brain Tissue Loss: Neurotoxicity of Typical Antipsychotics



1. Increased apoptosis
2. Oxidative stress/increase in free radicals
3. Via NMDA pathways and glutamate toxicity
4. Neurotoxic metabolities
5. Potent D2 receptor blockade: suppresses BDNF

International Journal of Neuropsychopharmacology (2013), **16**, 121–135. © CINP 2011
doi:10.1017/S1461145711001775

Risperidone normalizes increased inflammatory parameters and restores anti-inflammatory pathways in a model of neuroinflammation

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[2] *Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM)*
[3] *Instituto de Investigación Sanitaria Hospital 12 de Octubre (I+12), Madrid, Spain*
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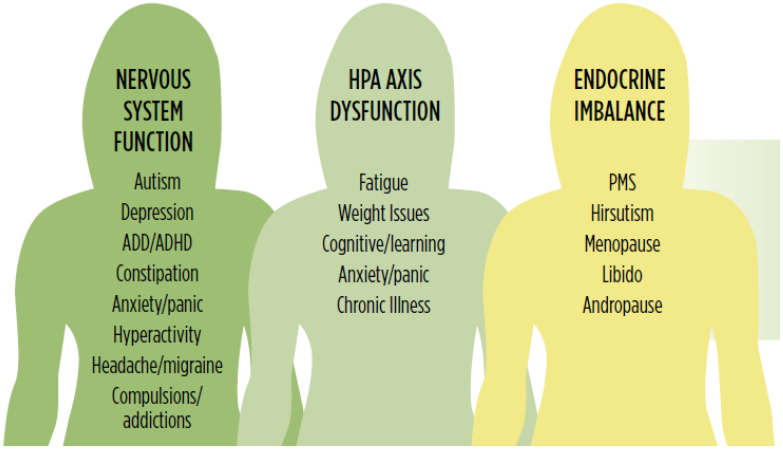
[5] *Department of Pharmacology, Faculty of Medicine, University of Cádiz, Spain*

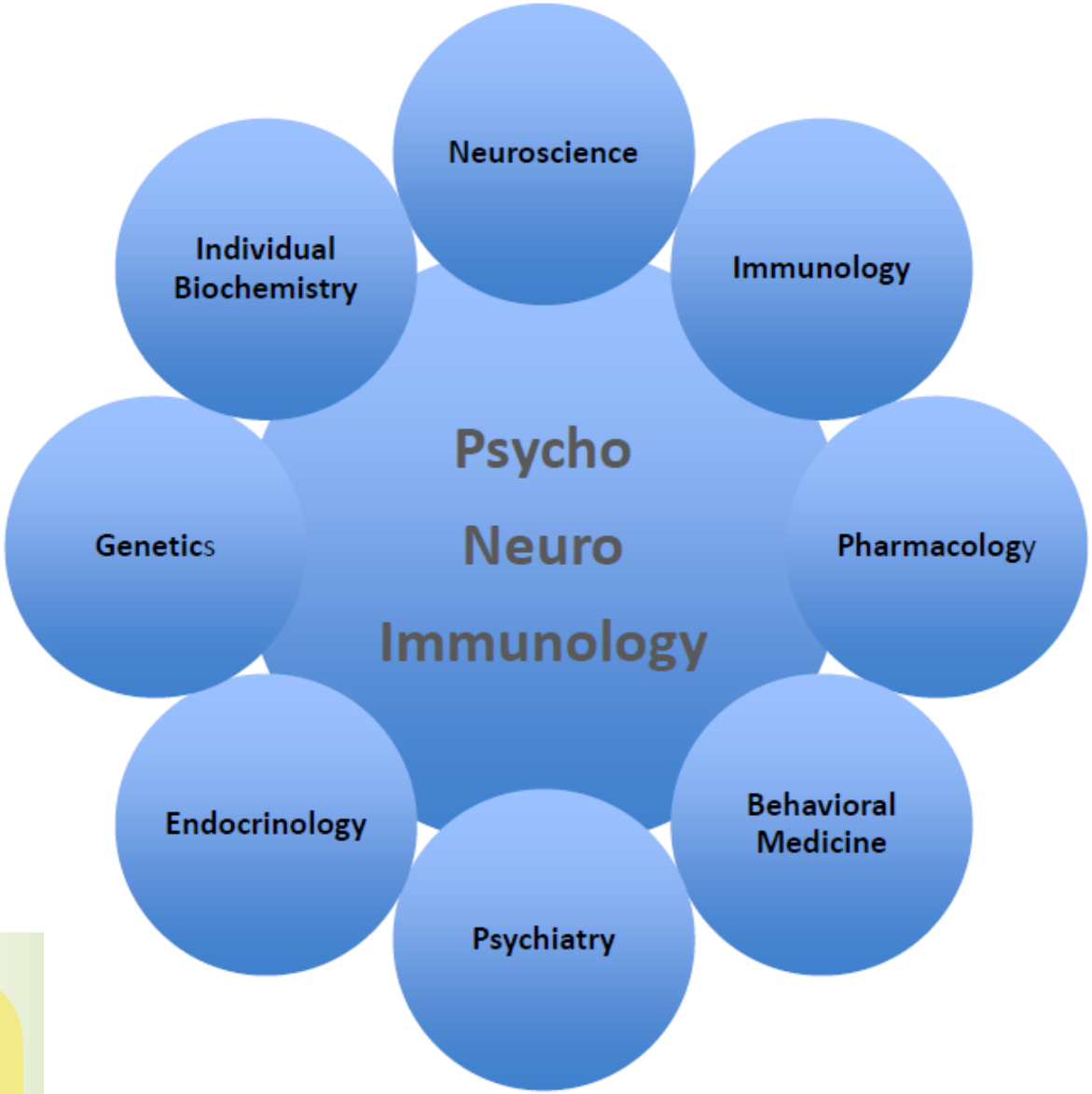
Inflammation, caused by both external and endogenous factors, has been implicated as a main pathophysiological feature of chronic mental illnesses, including schizophrenia. An increase in pro-inflammatory cytokines has been described both in experimental models and in schizophrenia patients.

Risperidone prevented increased inflammatory parameters induced by LPS Challenge in rats' brain cortex

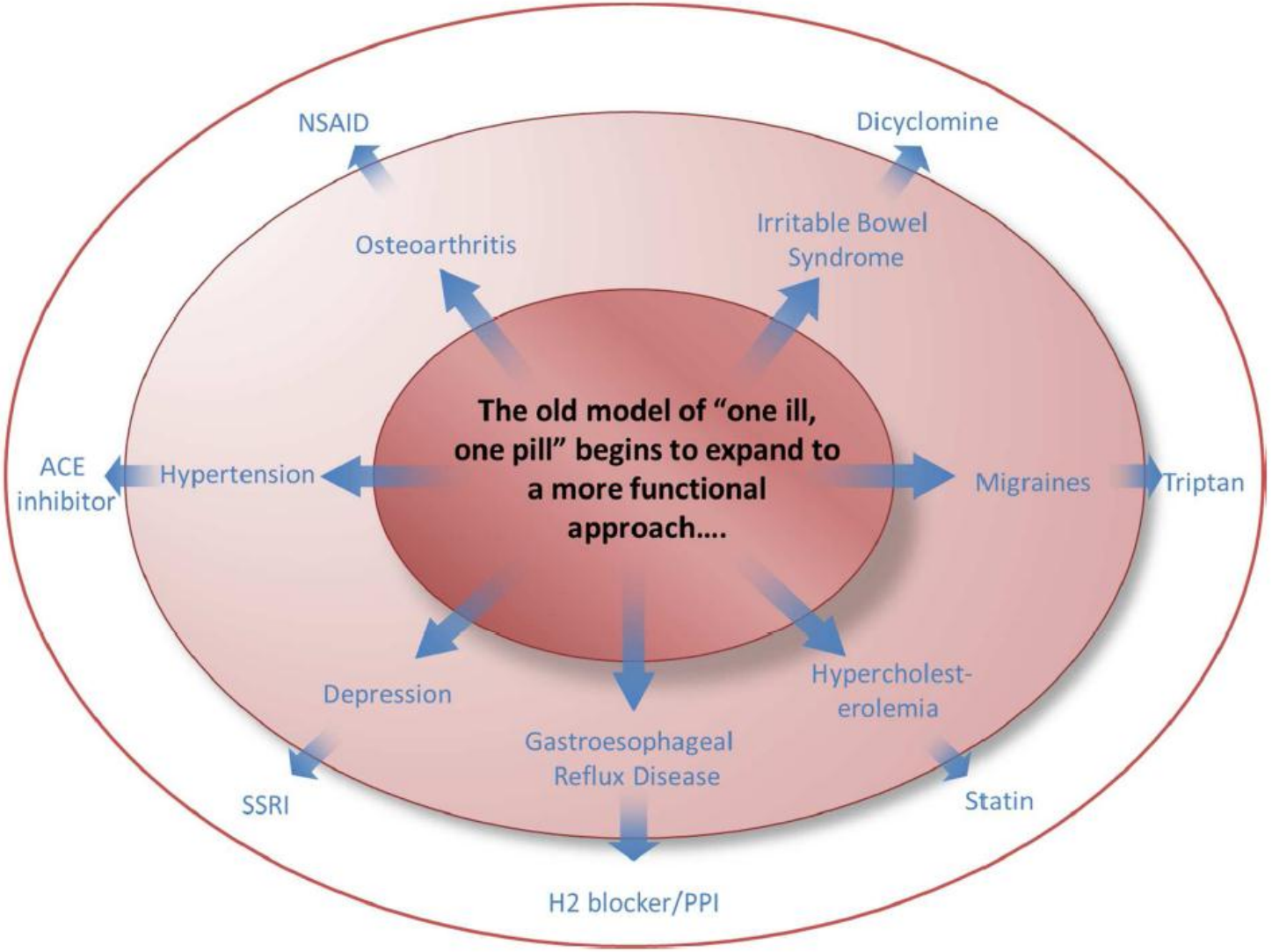
but also at intra- and intercellular inflammatory pathways. The present study was conducted in a model of mild neuroinflammation using a lipopolysaccharide (LPS) challenge that was not an endotoxaemic dose (0.5 mg/kg i.p.) in young adult rats. Main results: single doses of risperidone (0.3–3.0 mg/kg i.p.) prevented increased inflammatory parameters induced by LPS in brain cortex [expression of inflammatory cytokines, interleukin (IL)-1β and tumour necrosis factor (TNF)-α, activity of the inducible inflammatory enzymes nitric oxide synthase and cyclooxygenase, p38 mitogen-activated protein kinase (MAPK) and inflammatory nuclear transcription factor κB] and restored anti-inflammatory pathways decreased by LPS challenge (deoxyprostaglandins and peroxisome proliferator activated receptor γ). This is the first study demonstrating that risperidone elicits a preventive effect on the anti-inflammatory arm of the homeostatic mechanism controlling inflammation in a model of mild encephalitis in rats. Our findings suggest a possible protective effect of risperidone on brain cells.


fatigue
chronic
memory
changes
drowsines
listlessness
anxiousness
acute
irritability
low
weight
mood
energy
increased
gain sleep
lethargy
decreased
loss
malaise
nervousness
vague symptoms

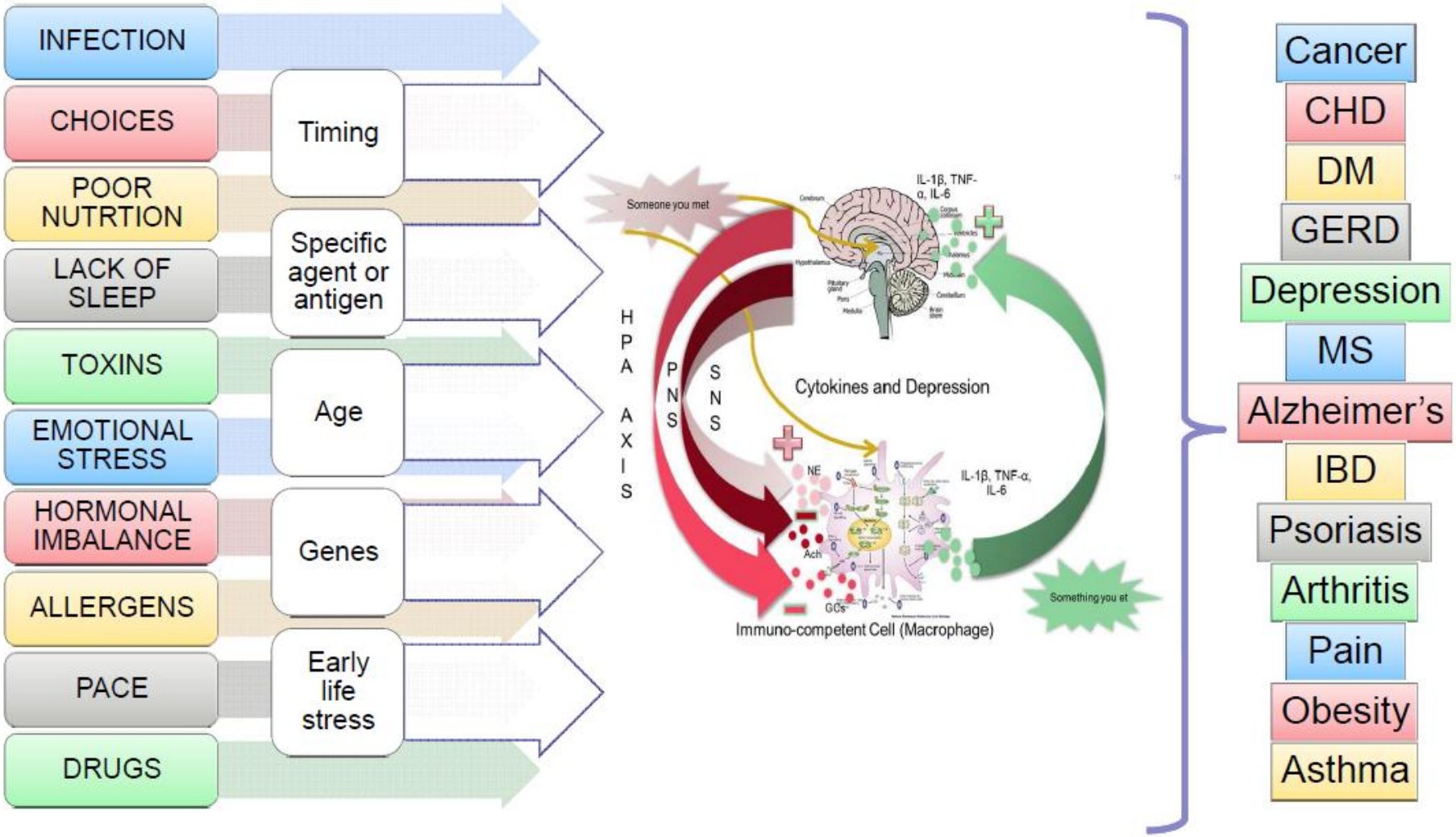

NERVOUS SYSTEM FUNCTION
Autism
Depression
ADD/ADHD
Constipation
Anxiety/panic
Hyperactivity
Headache/migraine
Compulsions/ addictions
HPA AXIS DYSFUNCTION
Fatigue
Weight Issues
Cognitive/learning
Anxiety/panic
Chronic Illness
ENDOCRINE IMBALANCE
PMS
Hirsutism
Menopause
Libido
Andropause


Neuroscience
Individual Biochemistry
Immunology
Psycho
Neuro
Immunology
Genetics
Pharmacology
Endocrinology
Behavioral Medicine
Psychiatry

We Now Expand the Old Model



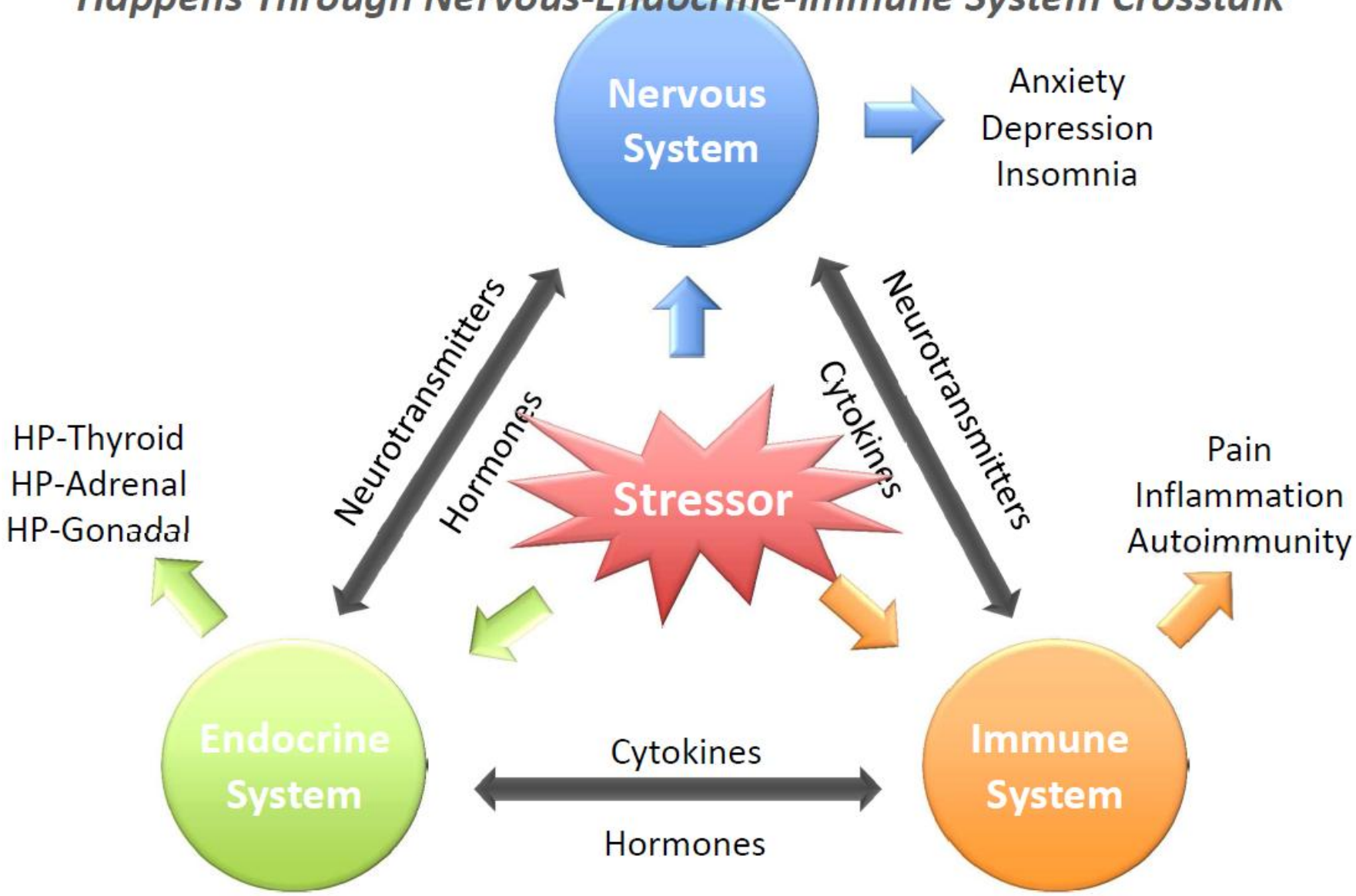
Chandra A, Lukaczer D. Functional Medicine: A Patient-Centered, Comprehensive Chronic-Care Model. http://courses.washington.edu/mhe501/Functional%20Medicine/UW_talk_3-2-09%5B1%5D.pdf. Accessed Oct. 2, 2012.



Adapted from Goldstein BI et al. *J Clin Psychiatry.* 2009;70(8):1078-1090; Szelényi J, Vizi ES. *Ann N Y Acad Sci.* 2007;1113:311-324.

Psychoneuroimmunology

Happens Through Nervous-Endocrine-Immune System Crosstalk



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