

# Depression and Diabetes

Lauren B. Marangell, MD  
Distinguished Scholar  
Lilly USA, LLC

# Disclosure

- Dr. Marangell is a full-time employee of Lilly USA, LLC (a wholly owned subsidiary of Eli Lilly and Company) and owns stock in Eli Lilly and Company
- Lilly USA, LLC has provided for Dr. Marangell's expenses for this presentation, including travel
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# Overview

- Understand the relationship between depression and diabetes
  - Depression occurs more often in those with diabetes
  - Depression negatively impacts diabetes outcomes
- Understand that Major Depression (MDD) is a complex disorder that involves the brain, endocrine and immune systems and is not the same as expected sadness
- Be able to assess patients for depression
  - Improving depression leads to improved outcomes in diabetes

# Depression and Diabetes: the classic viscous circle



# Having One Disorder Increases the Likelihood of Having the Other

- Nearly a third of persons with diabetes suffer from clinically relevant depressive disorders <sup>1</sup>
- Persons with depressive disorders are twice as likely as the rest of the population to also suffer from diabetes <sup>2</sup>

1. Anderson and Freedland, 2001

2. Bjorntorp 2001

# Prevalence and Correlates of Depressed Mood among Youth with Diabetes: The Search for Diabetes in Youth Study

- 10-21 yr patients with type 1 or type 2 DM
  - N =2672
- Center for Epidemiologic Studies Depression Scale (CES-D)
  - 14% Mild Depressive Symptoms
  - 8% Moderate to Severe Depressive Symptoms
- ↑ HbA1c and ↑ ED visits

# Prognosis

- The prognosis of both diabetes and depression – in terms of severity of disease, complications, treatment resistance and mortality – is worse for either disease when they are co-morbid than it is when they occur separately.
- Comorbid depression is associated with poor adherence to diabetic medications, exercise, and diet.

Lustman et al., 2000; Egede, 2006

# The Association of Comorbid Depression With Mortality in Patients With Type 2 Diabetes

- 4,154 patients with type 2 diabetes were surveyed and followed for up to 3 years
  - No depression: 8.3% deaths
  - Minor depression: 13.6% deaths
  - Major Depression: 11.9 % deaths
- Proportional hazards model for mortality adjusted for age, sex, race/ethnicity, and education
  - minor depression: 1.67-fold increase ( $P = 0.003$ )
  - major depression: 2.30-fold increase ( $P = 0.0001$ )

# Depression as a risk factor for the onset of type 2 diabetes mellitus. A meta-analysis

- While the prevalence of depression is doubled in individuals with type 2 diabetes compared with those without diabetes, the temporal or causal relationship between remains
- Goal of the current study was to examine the relationship between depression and the risk of onset of type 2 diabetes by conducting a meta-analysis of longitudinal studies

# Results

- Depressed adults have a 37% increased risk of developing type 2 diabetes mellitus.
- The pooled relative risk (95% CI) of studies that relied on self-reported diabetes to exclude prevalent diabetes at baseline was 1.32 (1.04–1.66)
- The pooled relative risk (95% CI) of studies that did control for undetected diabetes by screening all subjects for high blood glucose was 1.54 (1.07–2.22).

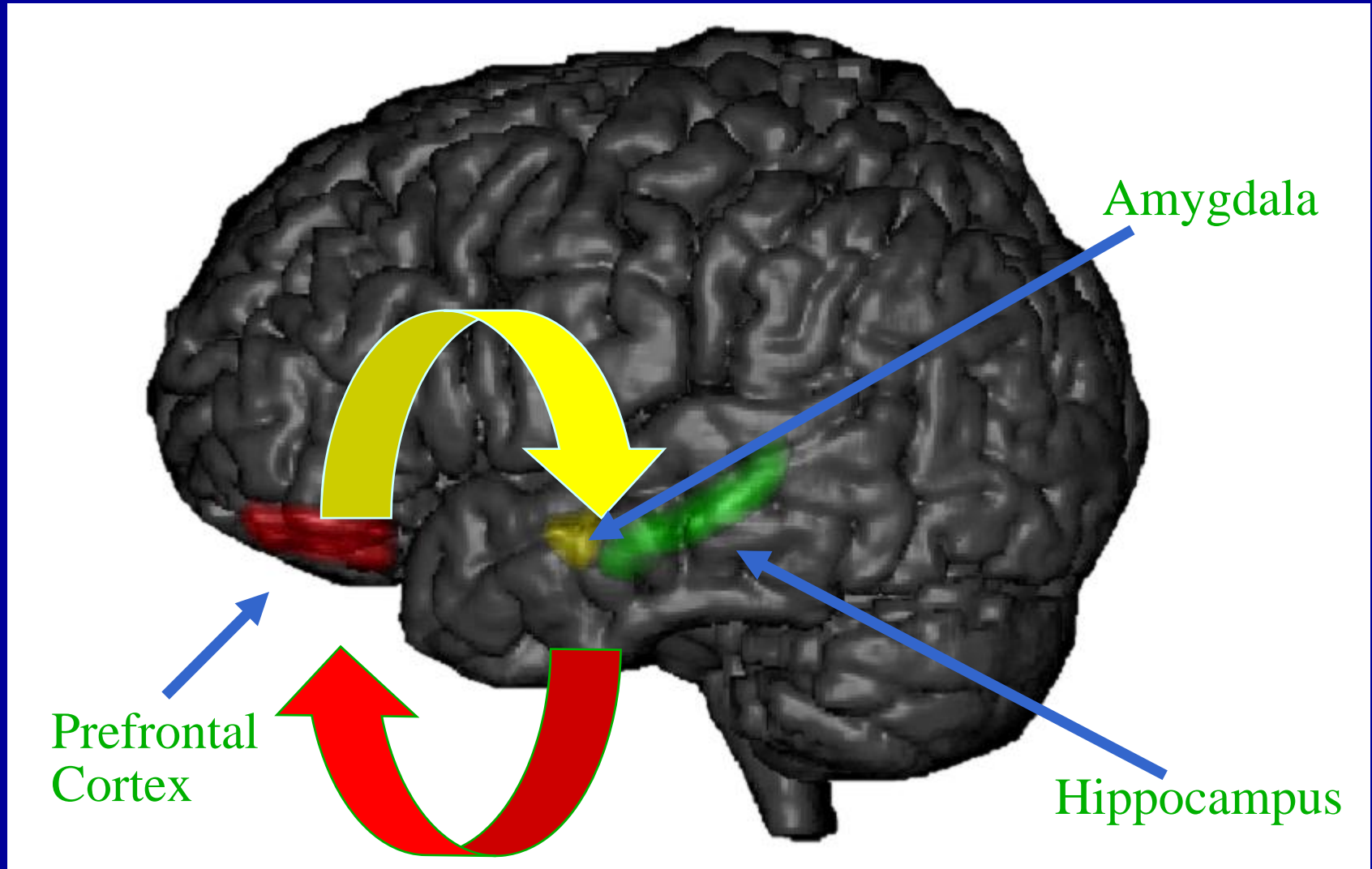
# Treating depression may improve insulin resistance in patients at risk for type 2

- 55 people considered at risk for type 2 diabetes enrolled in a diabetes-prevention program
- One in three study participants was “clinically depressed”, and about one in five of these patients was taking antidepressant
- Depressed patients who were not being treated had significantly greater insulin resistance than study participants who were not depressed.
- Treatment for depression appeared to improve insulin sensitivity, with depressed participants on antidepressant therapy having similar insulin sensitivity to non-depressed participants.

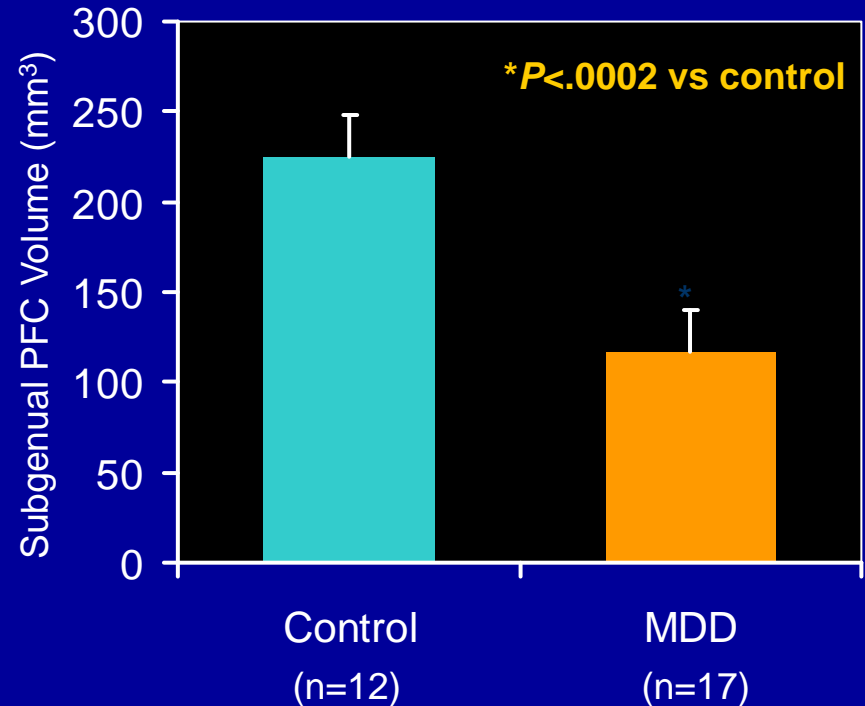
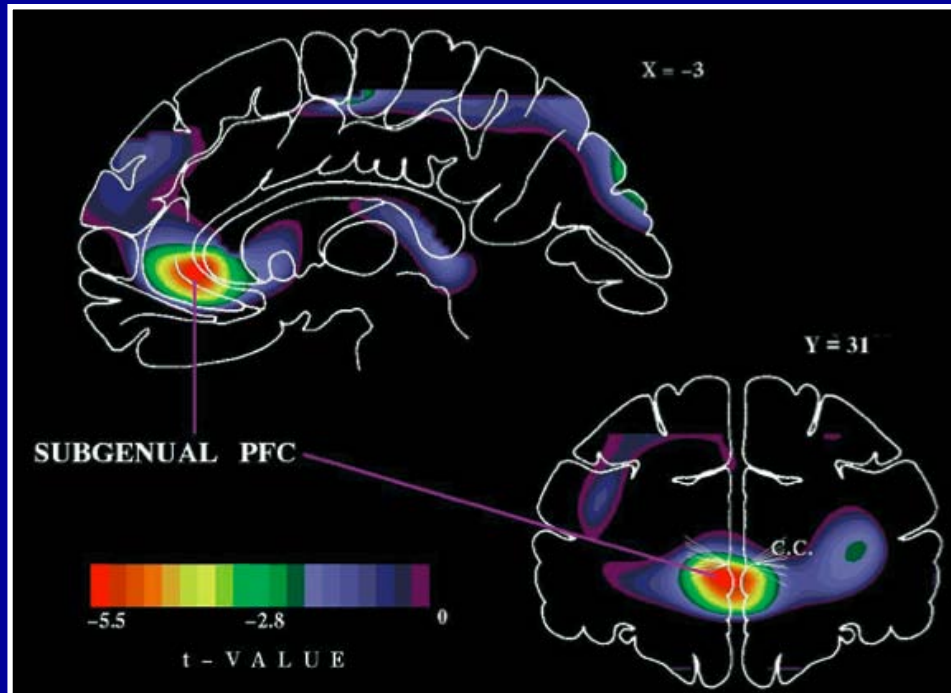
# Sadness vs. Major Depression

- Adverse psychosocial circumstances are important and should be considered and addressed whenever possible
- Sadness in the face of adverse circumstances is not unusual
- However, Major Depression is a diagnosable and treatable disease. It is NOT expected sadness due to adverse circumstances

# Brain Regions Involved in Depression



# MDD May Impact Function and Structure of the Subgenual Anterior Cingulate

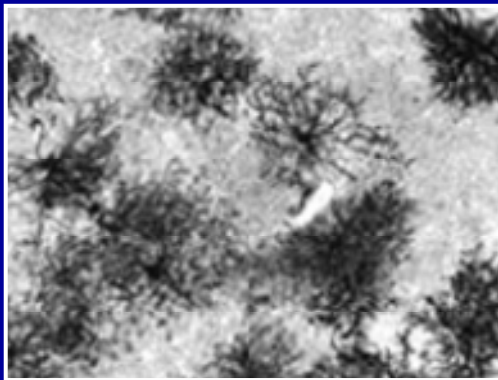


- Patients with MDD had a 48% lesser volume of the subgenual PFC

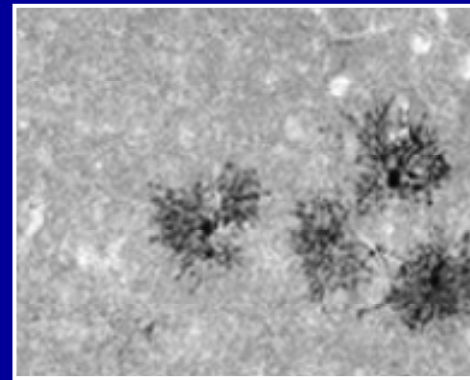
# Glial changes in the PFC of a depressed patient

Glial Immunoreactivity in the PFC<sup>1</sup>

Control (27 years old)



MDD (32 years old)

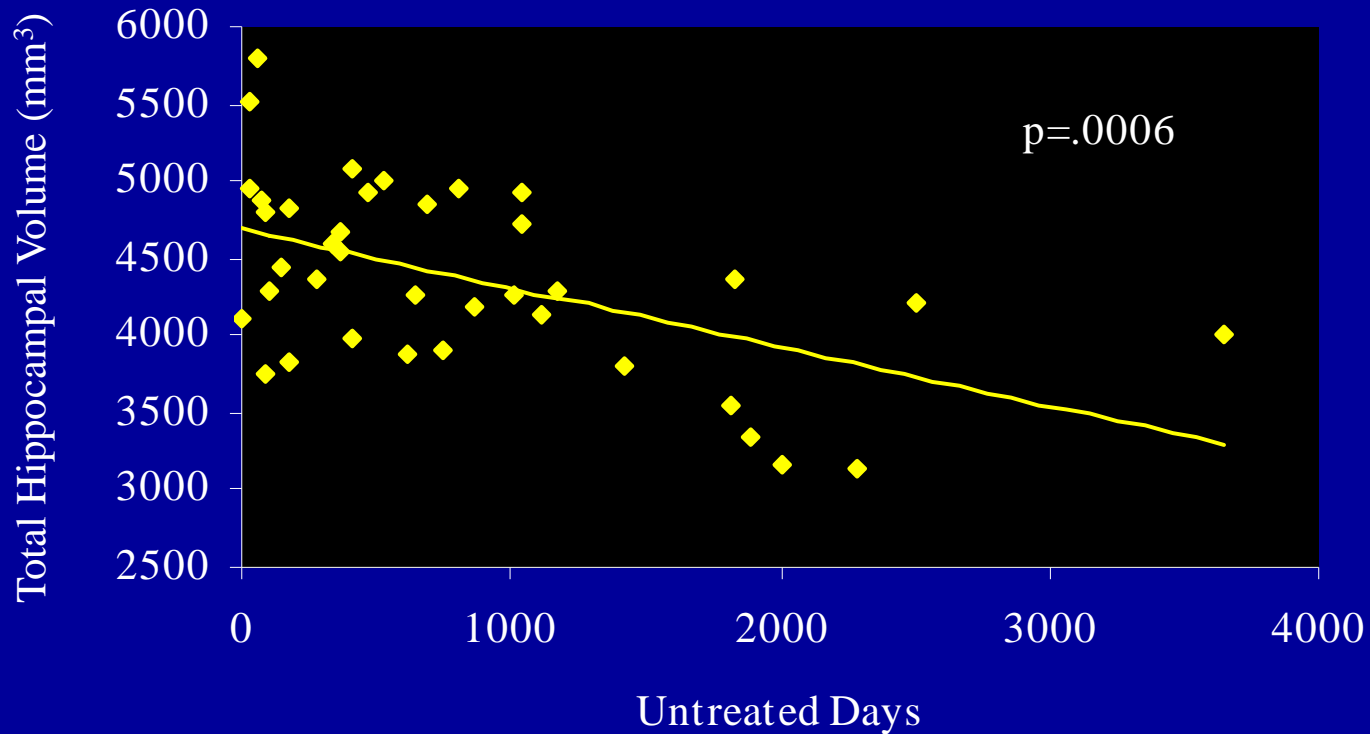


- Reduction in glial cell density and number is the most prominent feature of cell pathology in depression<sup>1-4</sup>

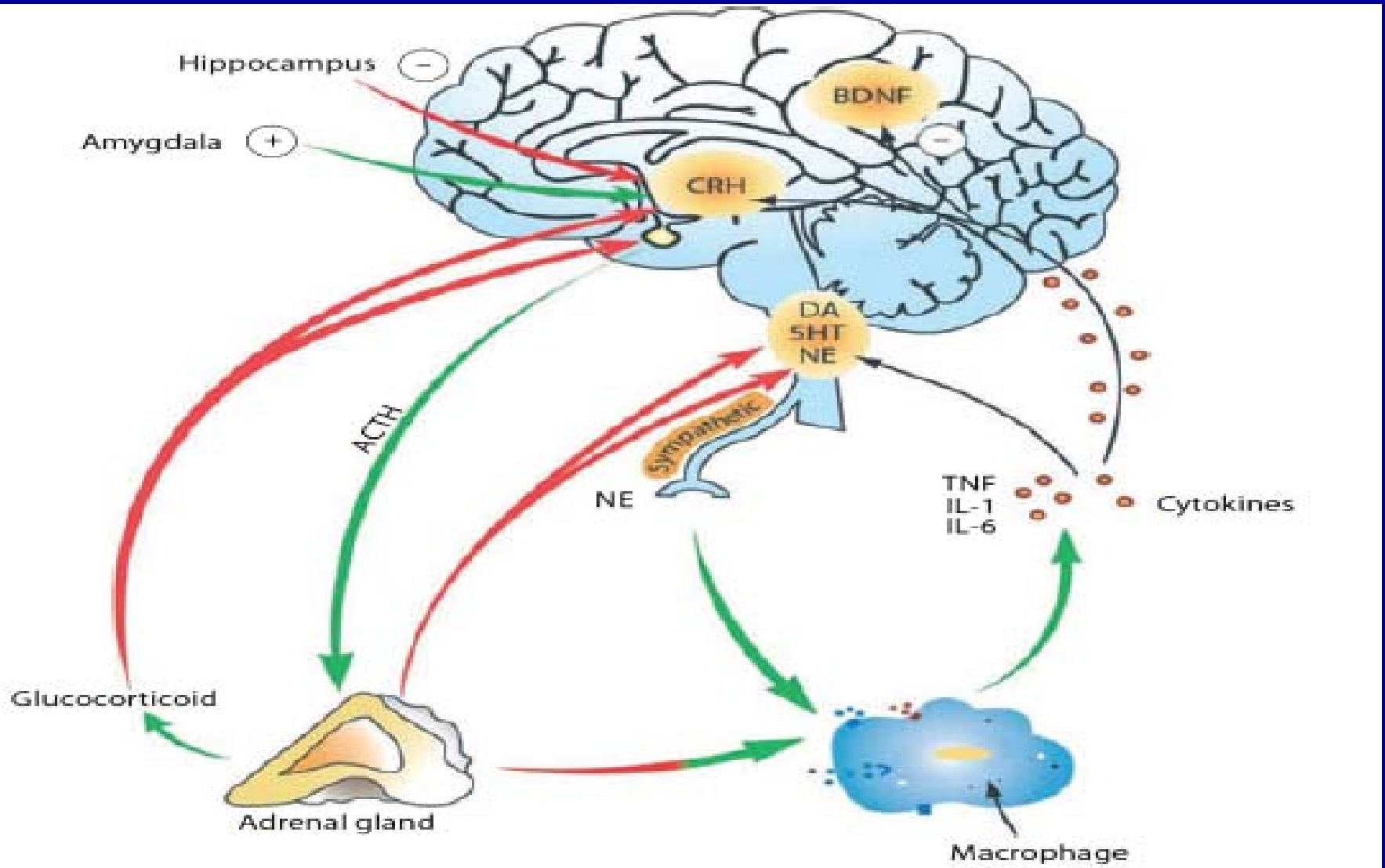
1. Rajkowska G, et al. *CNS Neurol Disord Drug Targets*. 2007;6:219-233.  
2. Rajkowska G, et al. *Biol Psychiatry*. 1999;45:1085-1098.  
3. Ongür D, et al. *Proc Natl Acad Sci USA*. 1998;95:13290-13295.  
4. Si X, et al. *Neuropsychopharmacol*. 2004;29:2088-2096.

Images courtesy of Bentham Science Publishers

# Correlation between hippocampal volume and duration of untreated depression



# The Neurobiology of Depression Impacts the Pathophysiology of Diabetes



# DSM-IV Criteria for Major Depressive Episode

Pervasively depressed mood and/or loss of interest or pleasure for 2 weeks or more, along with a constellation of 5 or more total symptoms:

- Sleep impairment
- Interest/Pleasure loss
- Guilt/Self-blame
- Energy impairment
- Concentration impairment
- Appetite disturbance
- Psychomotor agitation
- Suicidal thoughts

**The “SIG: E-CAPS” of Depression**

# Major Depressive Disorder Management

- Diagnose
- Evaluate:
  - Symptoms
  - Functioning
  - Safety
  - Psychosocial factors
- Treat to full symptomatic and functional recovery
- Educate (patients, families,...)
- Monitor

# Hope for the Future

- The Dialogue on Diabetes and Depression (DDD): an international collaborative effort addressing problems related to the co-morbidity of diabetes and depression.

# Participating Professional Organizations

- American Association of Clinical Endocrinologists
- American Diabetes Association
- Asociacion Latinoamericana de Diabetes
- Chinese Diabetes Association
- Diabetes UK
- European Association for the Study of Diabetes / Psychosocial Aspects of Diabetes
- Global Alliance of Mental Illness Advocacy Network (GAMIAN) - Europe
- **International Council of Nurses**
- International Society for Affective Disorders
- International Society of Behavioral Medicine
- World Federation for Mental health
- World Organization of Family Doctors (Wonca)
- World Psychiatric Association

# Conclusions

- The prevalence of depression is 2 fold greater in patients with diabetes
- Better detection/screening is essential to improving diabetes outcomes
- Nurses have a unique opportunity to formulate and implement an effective strategy to prevent diabetes and reduce the burden of diseases and deaths worldwide