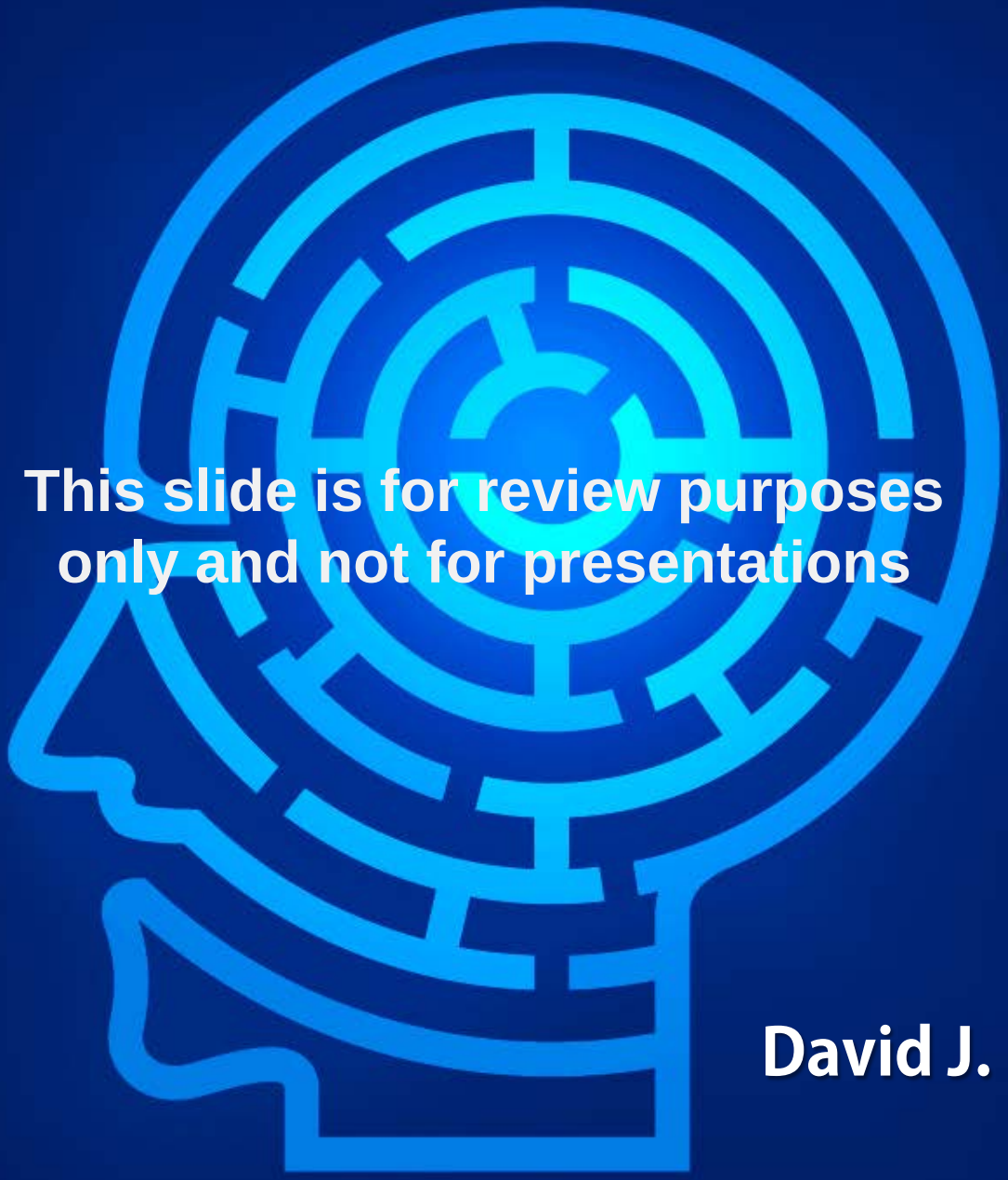

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Diabetes & Mental Health

David J. Robinson MD, FRCPC
CMHA - London, ON

In the past 2 years, I have received speaking honoraria from, and participated in advisory boards sponsored by:

- CPA
- Janssen
- Lundbeck
- Otsuka
- Pfizer

Objectives

- Shared Pathophysiology
- Bi-Directional Risks
- Diabetes-Specific Conditions
- Treatment Recommendations

Reference

Contents lists available at SciVerse ScienceDirect

Canadian Journal of Diabetes

journal homepage:
www.canadianjournalofdiabetes.com

Clinical Practice Guidelines

Diabetes and Mental Health

Canadian Diabetes Association Clinical Practice Guidelines Expert Committee

The initial draft of this chapter was prepared by David J. Robinson MD, FRCPC, FAPA, Meera Luthra MD, FRCPC, Michael Vallis PhD, RPsych

KEY MESSAGES

- Psychiatric disorders, particularly major depressive disorder (MDD), generalized anxiety disorder and eating disorders, are more prevalent in people with diabetes compared to the general population.
- People diagnosed with serious mental illnesses, such as MDD, bipolar disorder and schizophrenia, have a higher risk of developing diabetes than the general population.
- All individuals with diabetes should be regularly screened for the presence of depressive and anxious symptoms.
- Compared to those with diabetes only, individuals with diabetes and mental health disorders have decreased medication adherence, decreased compliance with diabetes self-care, increased functional impairment, increased risk of complications associated with diabetes, increased healthcare costs and an increased risk of early mortality.
- The following treatment modalities should be incorporated into primary care and self-management education interventions to facilitate adaptation to diabetes, reduce diabetes-related distress and improve outcomes: motivational interventions, stress management strategies, coping skills training, family therapy and collaborative case management.
- Individuals taking psychiatric medications, particularly atypical antipsychotics, benefit from regular screening of metabolic parameters.

approximately 60% increased risk of developing type 2 diabetes (9). The prognosis for comorbid depression and diabetes is worse than when each illness occurs separately (10). Depression in patients with diabetes amplifies symptom burden by a factor of about 4 (11). Episodes of MDD in individuals with diabetes are likely to last longer and have a higher chance of recurrence compared to those without diabetes (12).

Studies examining differential rates for the prevalence of depression in type 1 vs. type 2 diabetes have yielded inconsistent results (4,13). One study found that the requirement for insulin was the factor associated with the highest rate of depression, regardless of the type of diabetes involved (14).

Risk factors for developing depression in individuals with diabetes are as follows:

- Female gender
- Adolescents/young adults and older adults
- Poverty
- Few social supports
- Stressful life events

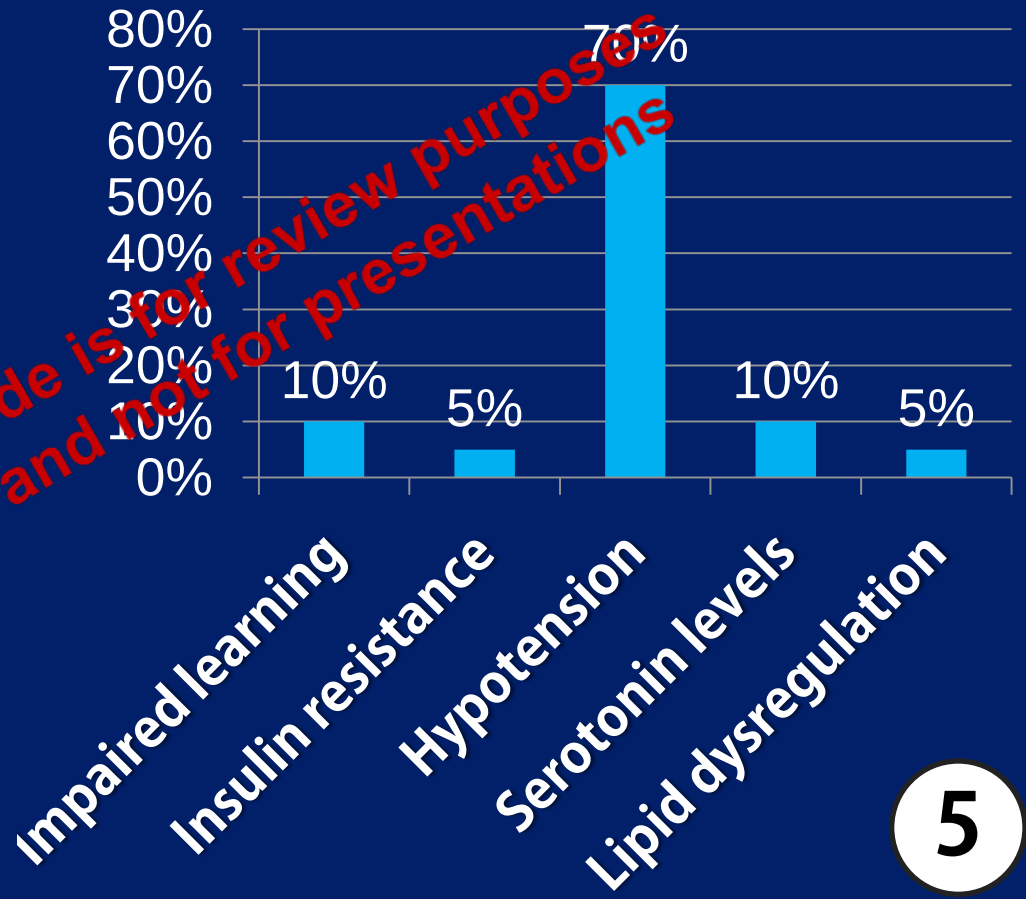
Diabetes is caused by sadness or long sorrow

Thomas Willis
English Physician
1621–1675

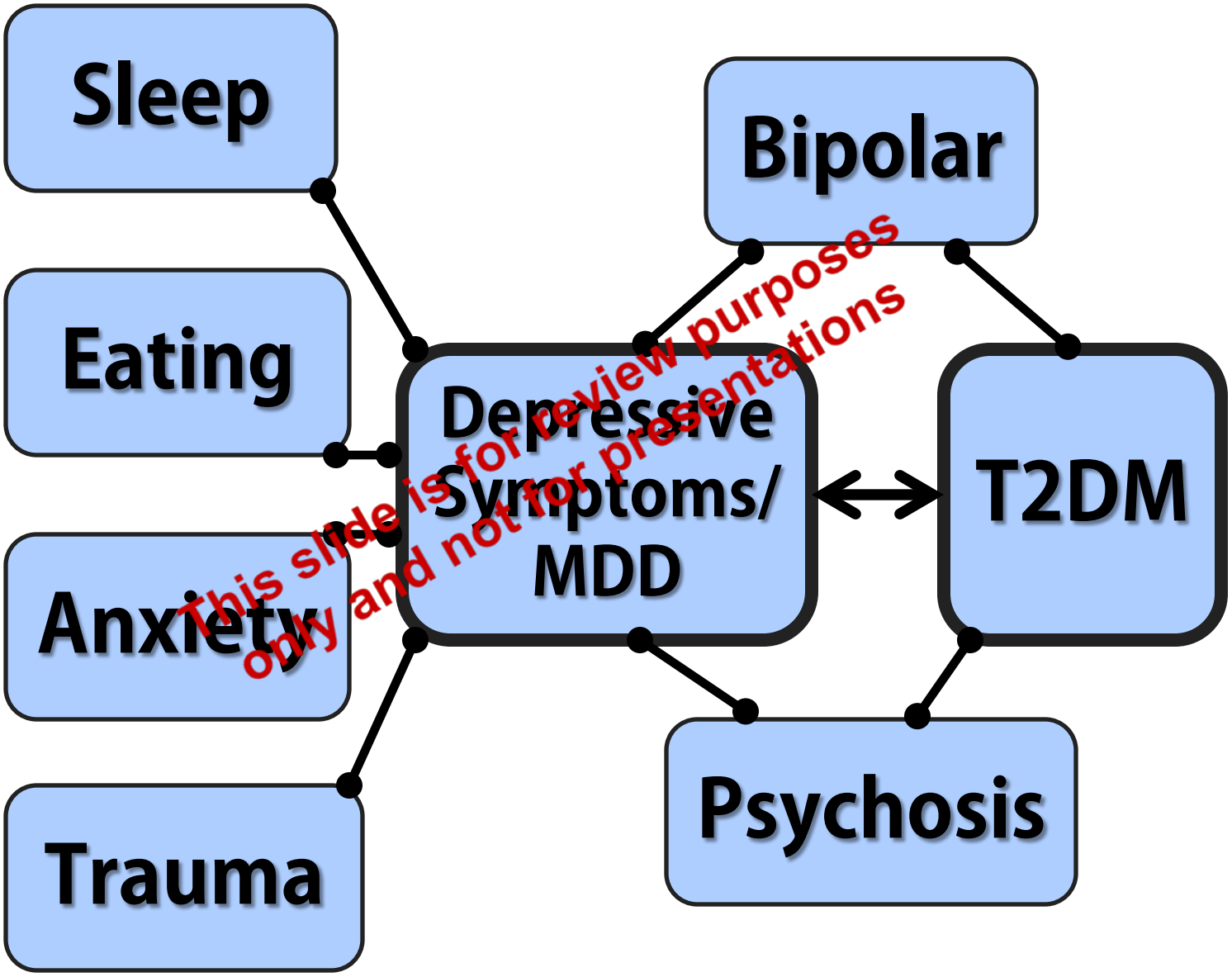
Question 1: Pre-Test

Which of the following is <u>not</u> an effect of sustained cortisol elevation?

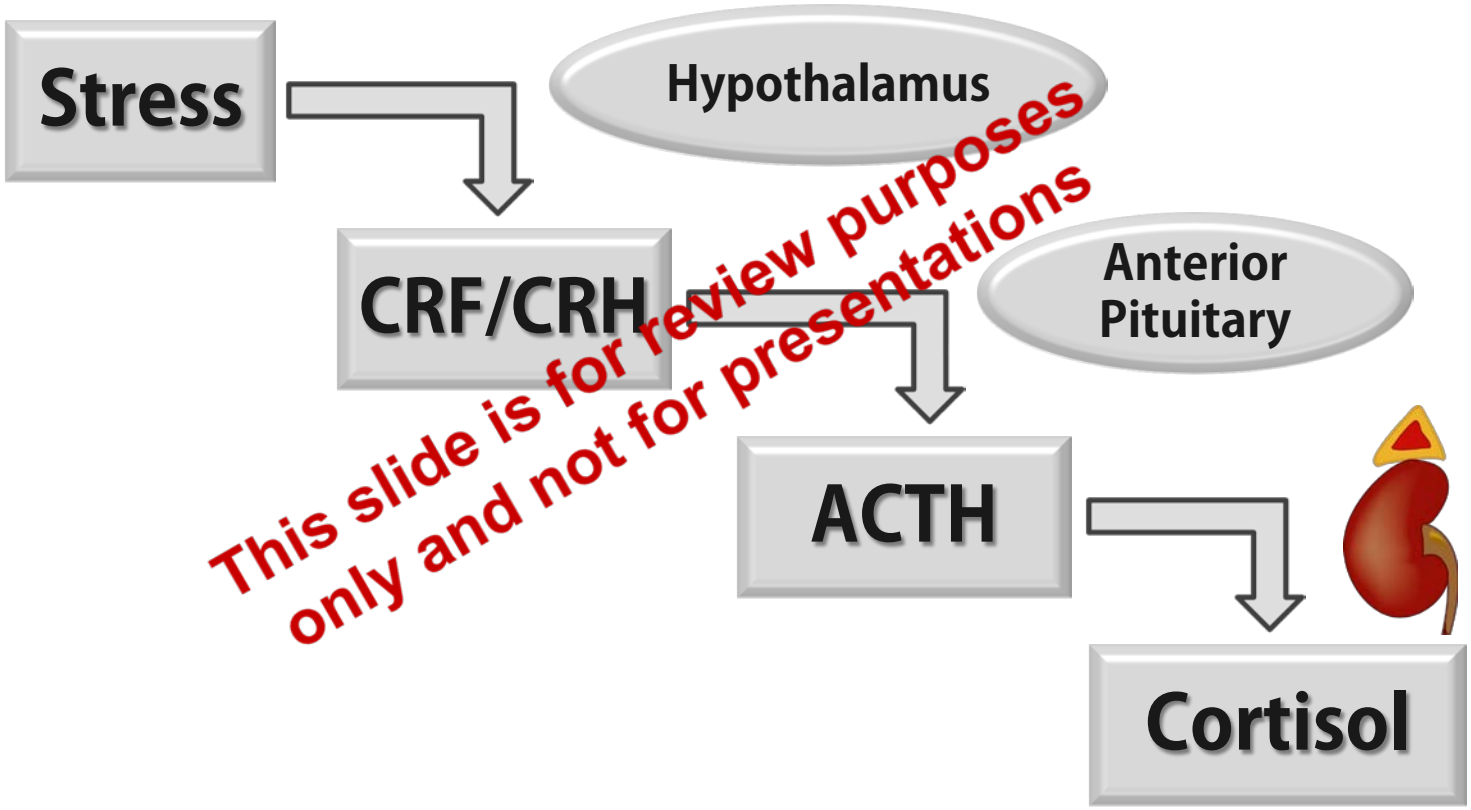
1. Impaired learning
2. Insulin resistance
3. Hypotension
4. ↓ Serotonin levels
5. Lipid dysregulation



Who Is At Risk?



HPA Axis


Stress
Hypothalamus
CRF/CRH
Anterior Pituitary
ACTH
Cortisol
This slide is for review purposes only and not for presentations

HPA Axis, Part Deux

Stress

Hypothalamus

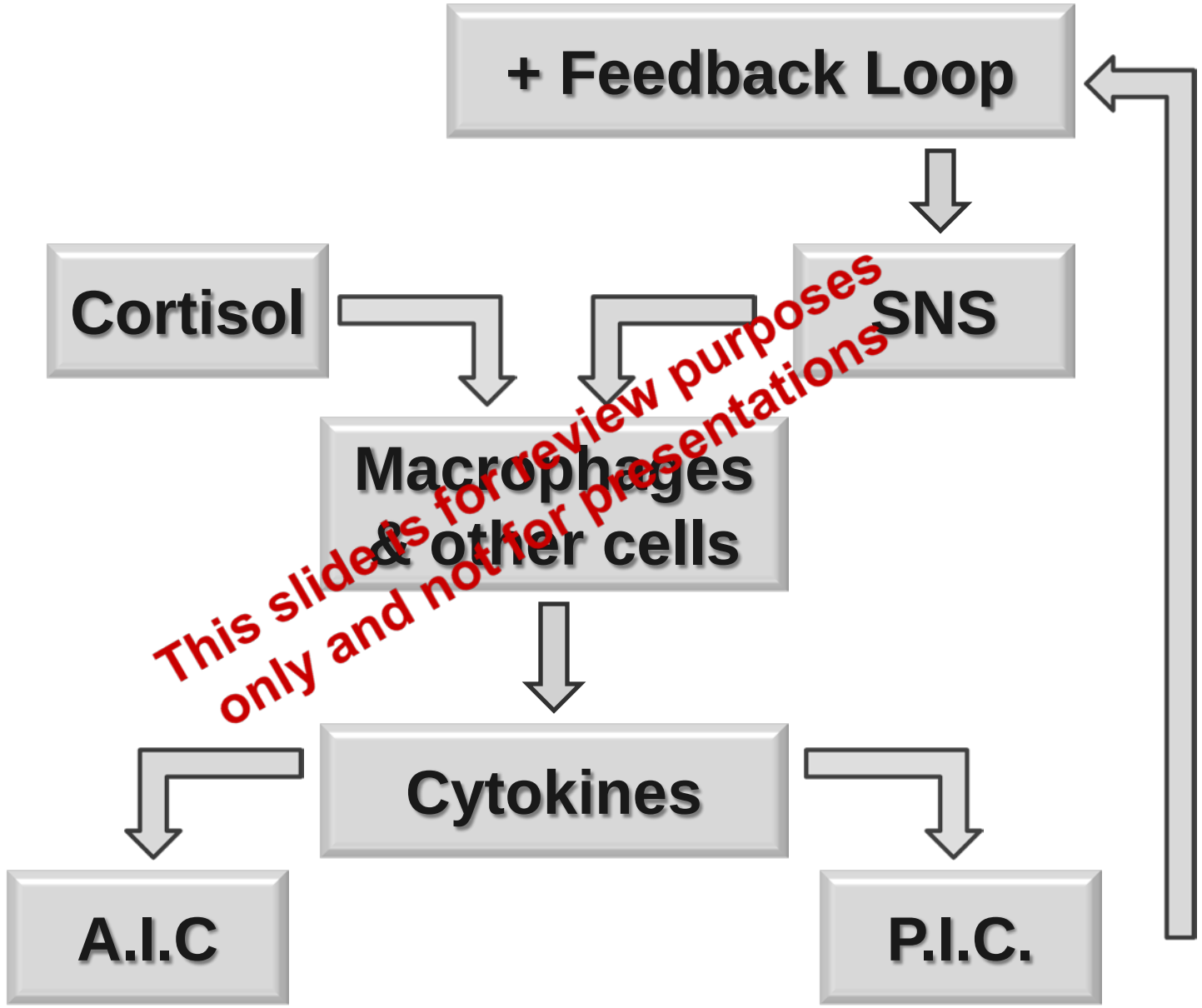
CRF/CRH

Locus Coeruleus

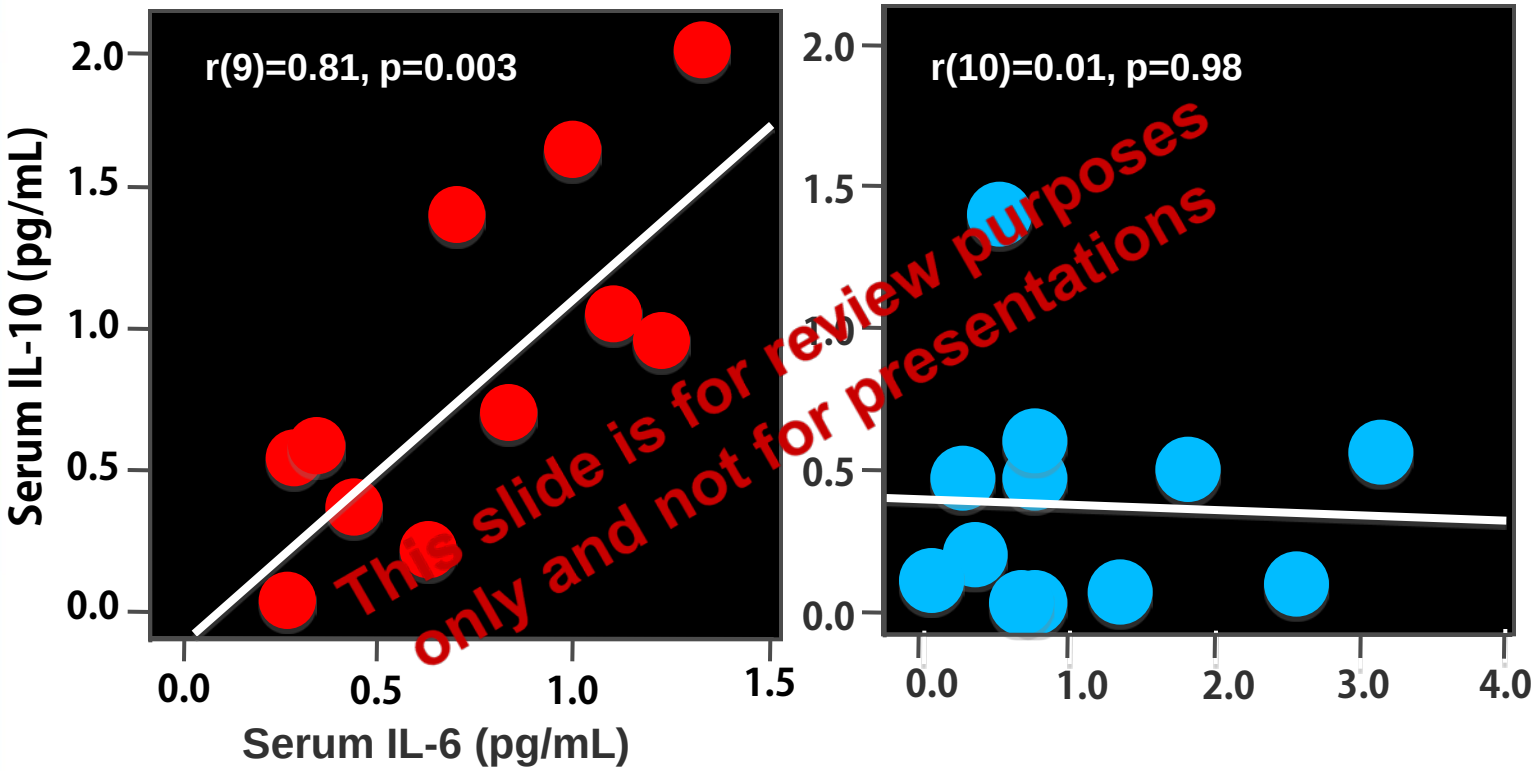
Norepin-ephrine

Symp-athetic Chain

HPA Axis, Part Trois



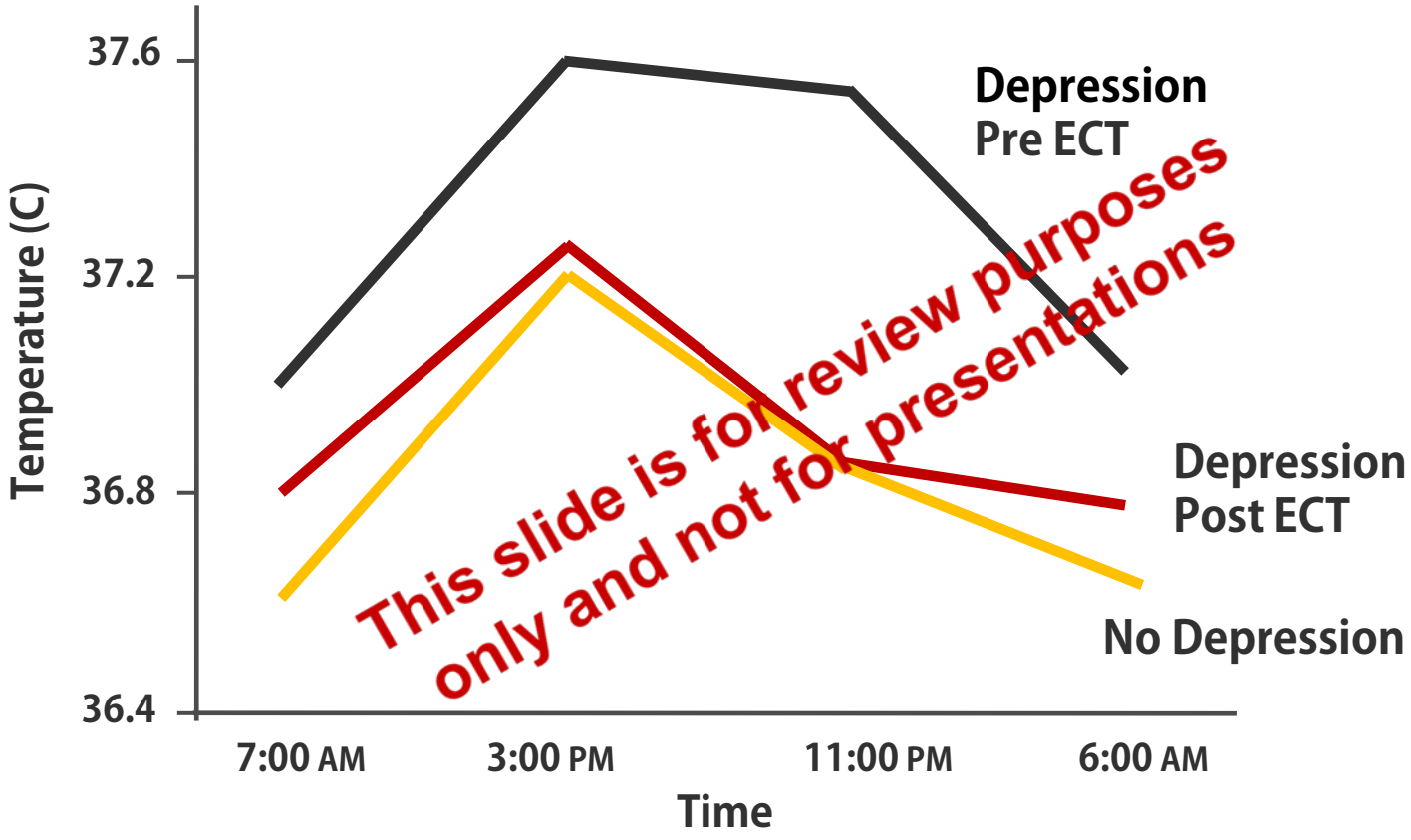
Regulatory Loss



Study comparing resting-state serum cytokine levels in 11 healthy control subjects and 12 unmedicated patients with MDD. IL = Interleukin; MDD = Major Depressive Disorder

Dhabhar et al. *J Psychiatric Res* 2009;43(11):962-69.

Body Temperature



ECT=Electroconvulsive Therapy; MDD=Major Depressive Disorder

Adapted from: Szuba MP et al. *Biol Psychiatry* 1997;42:1130-37.

Long-Term Effects of Elevated Cortisol Production

- ☹ Anabolic (↑wt)*
- ☹ Hypertension
- ☹ Glucose dysregulation
- ☹ HDL decrease

} Metabolic Syndrome

- ☹ Osteoporosis, myopathy
- ☹ Neuropsychiatric symptoms
- ☹ Inhibits other hormones (e.g. gonadal, GH, thyroid)

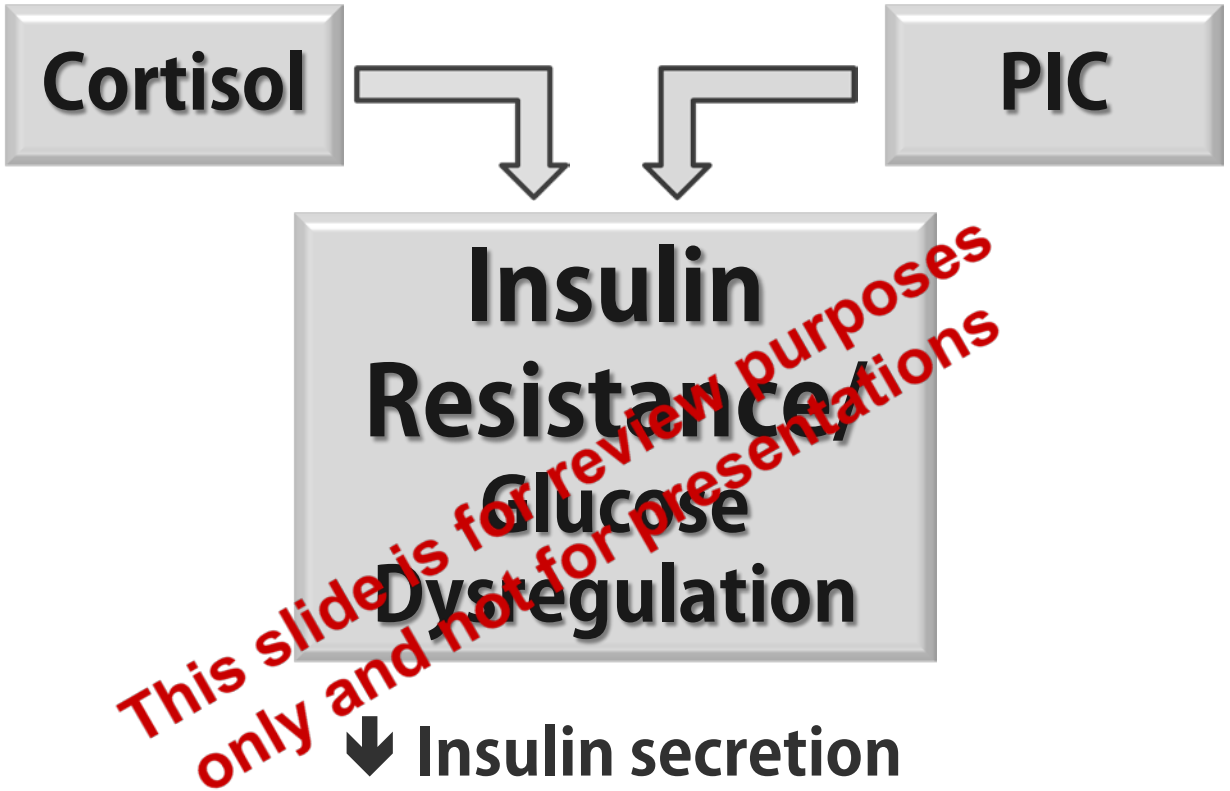
Fraser R, et al. Cortisol Effects on Body Mass, Blood Pressure, and Cholesterol in the General Population. Hypertension. 1999; 33:1364-1368.

P.I.C. Symptoms

- ☹ Fatigue[1-3]
- ☹ Aches and pains[1,2]
- ☹ Difficulty concentrating[1,3]
- ☹ Endocrine variations[1]
- ☹ Anxiety and irritability[1]
- ☹ Sleep, appetite + libido disturbances[1-3]

1. Raison et al. *CNS Drugs* 2005;19(2):105-23. 2. Dantzer et al. *Nat Rev Neurosci* 2008;9(1):46-56.
3. Kim et al. *Prog Neuropsychopharmacol Biol Psychiatry* 2007;31(5):1044-53.

HPA Axis



Affects free fatty acids ➔ tryptophan metabolism

Question 1: Post-Test

Which of the following is <u>not</u> an effect of sustained cortisol elevation?

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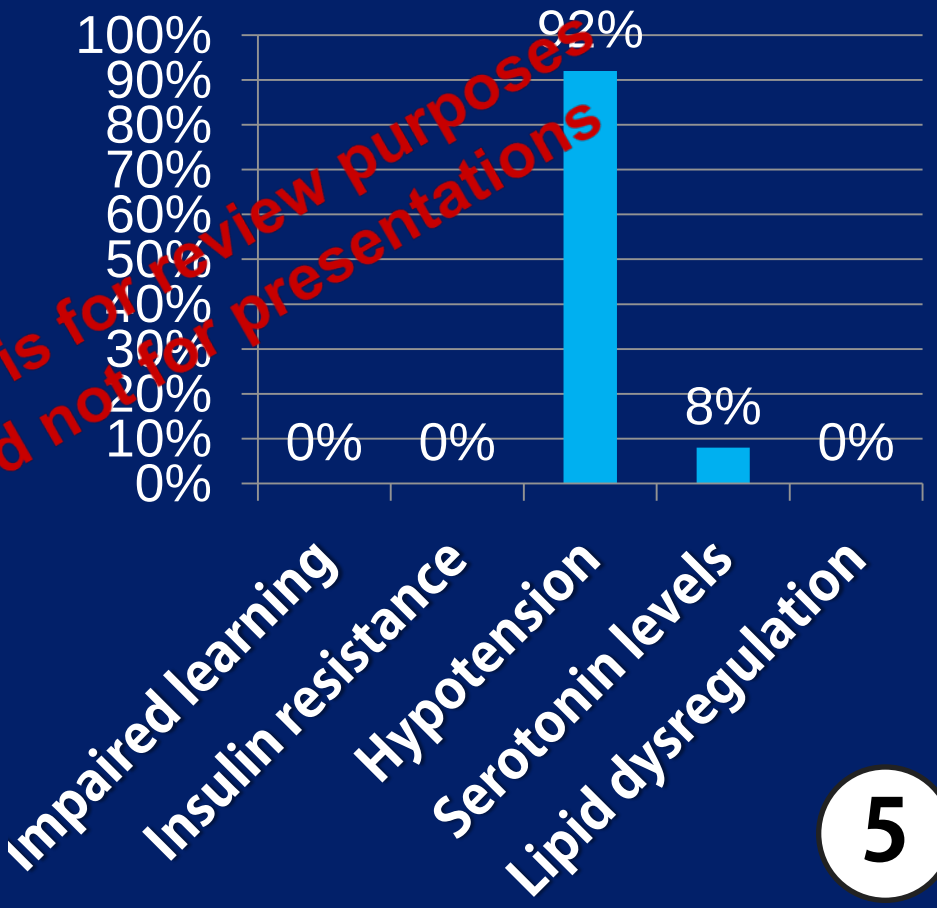
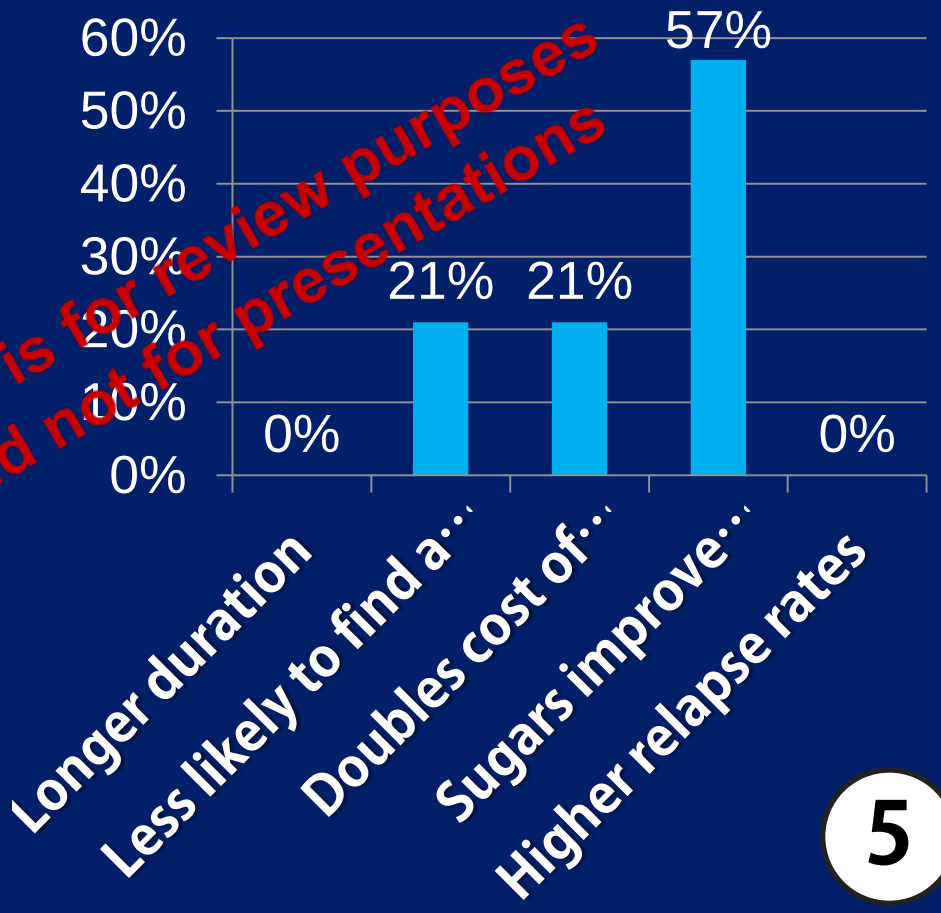


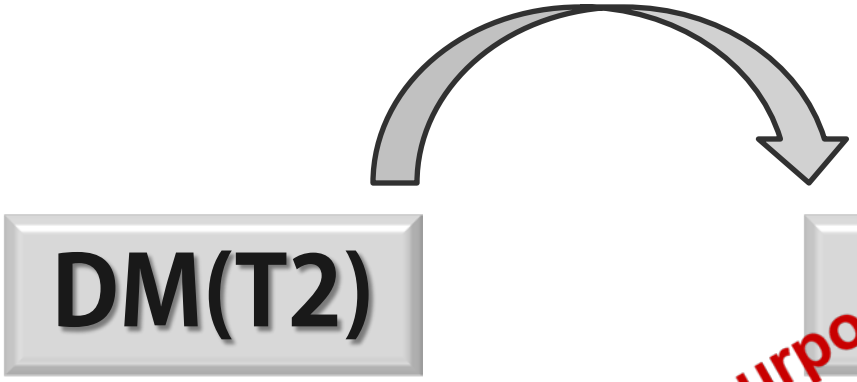
Question 2: Pre-Test

Which is <u>not</u> a feature of episodes of depression in patients with diabetes?

1. Longer duration
2. Less likely to find a precipitant
3. Doubles cost of treatment
4. Sugars improve with mood
5. Higher relapse rates



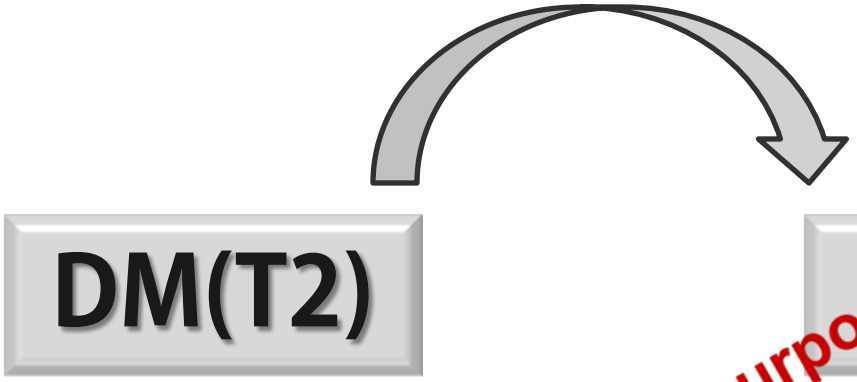
DM(T2) Causing MDD



Non-Specific Factors:

- ☹ Few social supports
- ☹ Lower socioeconomic status
- ☹ Adolescent/geriatric age group
- ☹ Critical life events
- ☹ Obesity
- ☹ Tobacco smoking

DM(T2) Causing MDD



- Cytokine release (as described)
- Diabetes-Specific Factors:
  - Perceived burden of illness
    - Demanding regimen/insulin treatment
      - Persistent poor control
        - Hypo/hyperglycemic episodes
          - Complications (severe, late)
            - Duration of disease

MDD Causing DM(T2)

DM(T2) MDD

- Obesity and physical inactivity lead to insulin resistance
- As severity of depression worsens, the correlation with glucose dysregulation is more robust
- More likely to report diabetic symptoms when depressed (amplified by a factor of 4)
- Treating depressive symptoms improves mood but not necessarily glycemic control

Shared Risks?

DM(T2) ⟺ MDD

- Genetics?
- Low birth weight (< 3 kg/6 lb 9 oz)
- Early nutrition (in utero/early childhood)
- Early adversity (3+ events; ↑ CRP in children)
- Level of education (high school)
- Socioeconomic stress

Dual Impact

- Up to 25% of patients with DM have MDD
- Up to 40% of patients with DM have depressive symptoms
- Odds ratio of developing MDD in patients with diabetes is ~2
- Extent of disability caused for comorbid [DM+MDD] is greater than their individual values (e.g. 2+2=6)
- MDD is the most problematic comorbidity if a person has diabetes

Question 2: Post-Test

Which is <u>not</u> a feature of episodes of depression in patients with diabetes?

1. Longer duration
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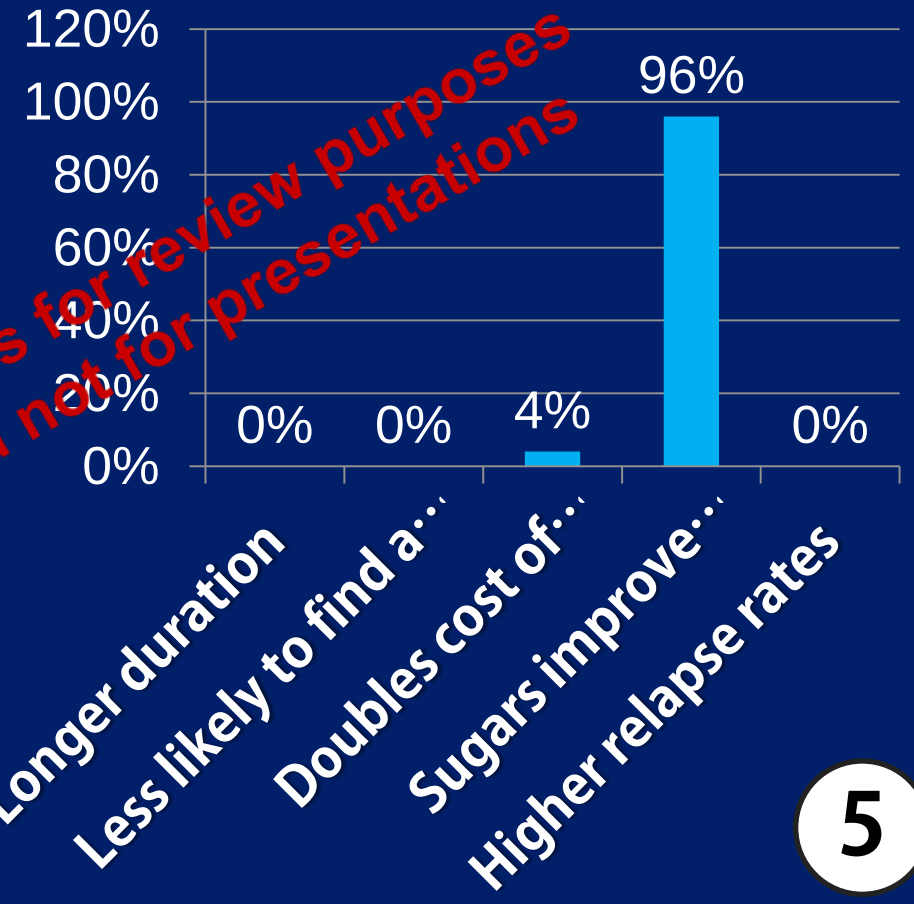
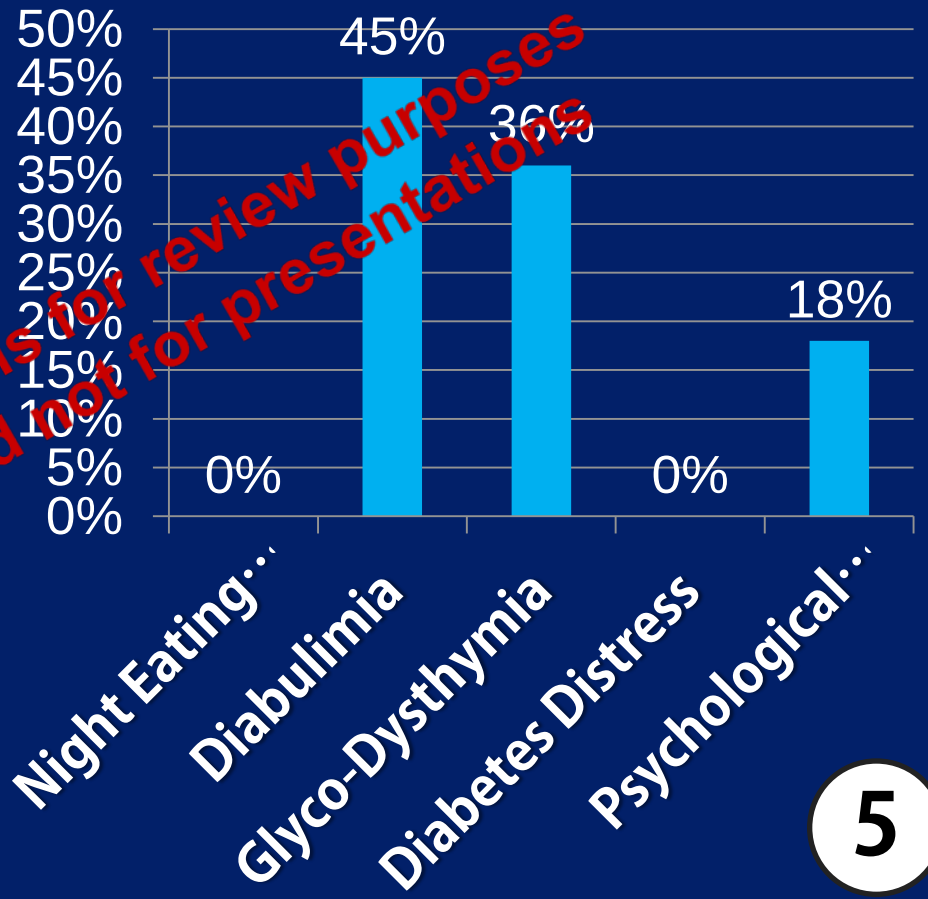


Question 3: Pre-Test

Which is <u>not</u> an entity described in the medical literature?

1. Night Eating Syndrome
2. Diabulimia
3. Glyco-Dysthymia
4. Diabetes Distress
5. Psychological Insulin Resistance



Night Eating Syndrome (NES)

- 10% of patients with T2DM
- 25% of calories after usual supper-time meal
- 2X rate of depressive symptoms...eat for emotional reasons
- 2X rate of obesity, poor glycemic control, higher rate of complications

Diabulimia

- Also known as *insulin omission*
- Restrict insulin to facilitate weight loss
- Up to 50% adolescent ♀ with AN/BN & T1DM
- High degree of body dissatisfaction in young patients with T1DM
- Adults with T2DM frequently have Food Addiction (Yale Food Addiction Scale)

Diabetes Distress/Burnout

- Concerns specifically related to managing diabetes, obtaining supports, coping with the emotional burden, and accessing needed care
- Best predictor of prognosis!
- P.A.I.D. scale is a 2-item diabetes distress screening instrument asking about:
  - ✓ Feeling overwhelmed
  - ✓ Feeling that one is failing to manage the treatment regimen

Problem Areas In Diabetes Scale
G.W. Welch et al. Diabetes Care, 1997 20(5): 760-766.

Diabetes Distress/Burnout

PAID Scale Version 2	
Overall Emotional Distress	Regimen-Related Distress
Interpersonal Distress	Prescriber-Related Distress

Problem Areas In Diabetes Scale
G.W. Welch et al. Diabetes Care, 1997 20(5): 760-766.

Psychological Insulin Resistance

- Refusal to begin using insulin
- Affects about 25% of people with T2DM (vs. half that for pills)
- Fear the complexity of administration
- Often feel as if they have failed
- May develop into a GAD-like picture

Question 3: Post-Test

Which is <u>not</u> an entity described in the medical literature?

1. Night Eating Syndrome
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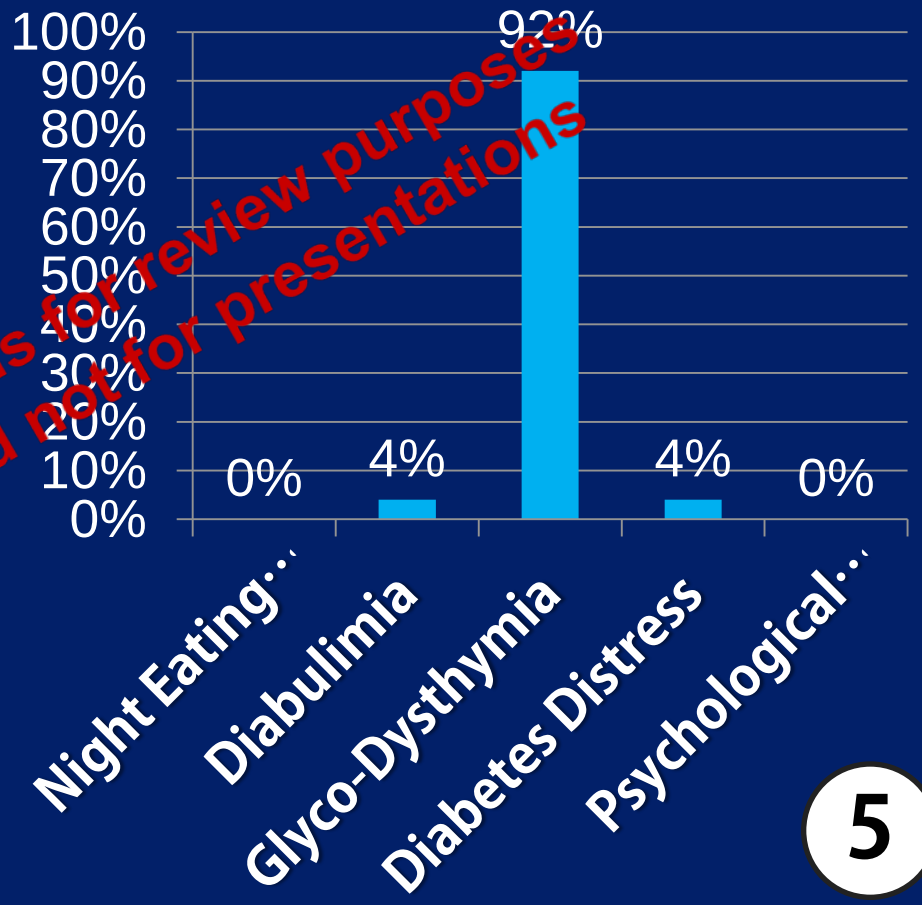
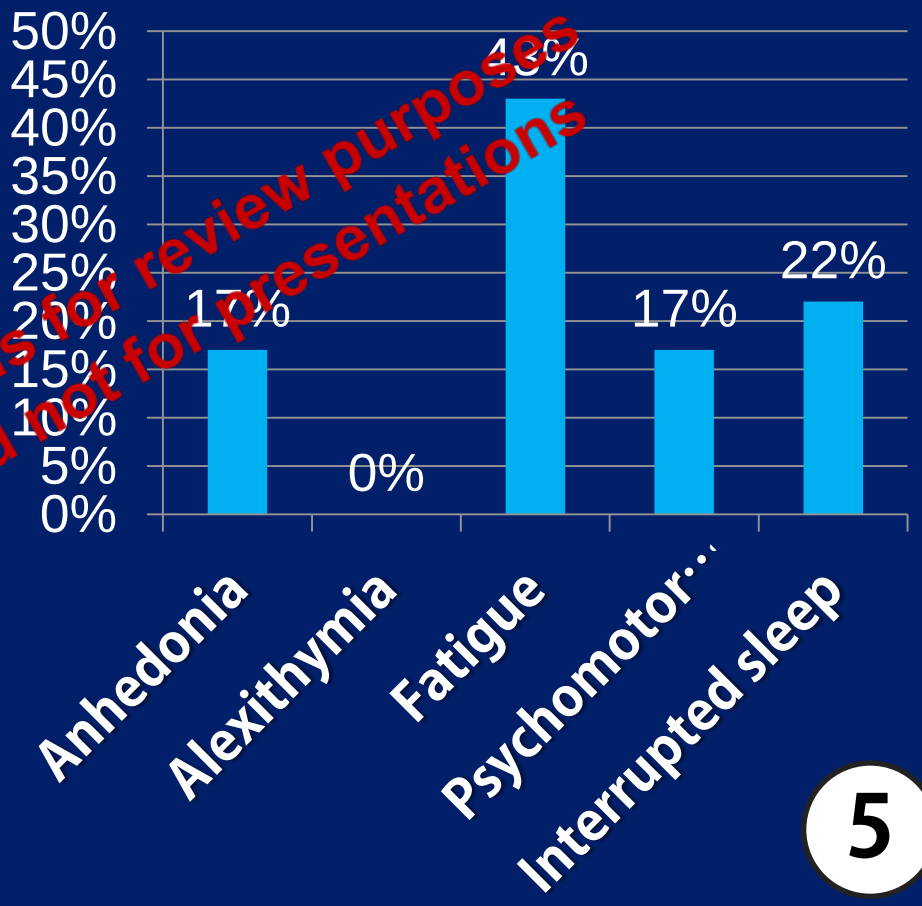
3. Glyco-Dysthymia
4. Diabetes Distress
5. Psychological Insulin Resistance



Question 4: MCQ Round

Which MDD symptom is <u>most</u> indicative of worsening glycemic control?

1. Anhedonia
2. Alexithymia
3. Fatigue
4. Psychomotor retardation
5. Interrupted sleep



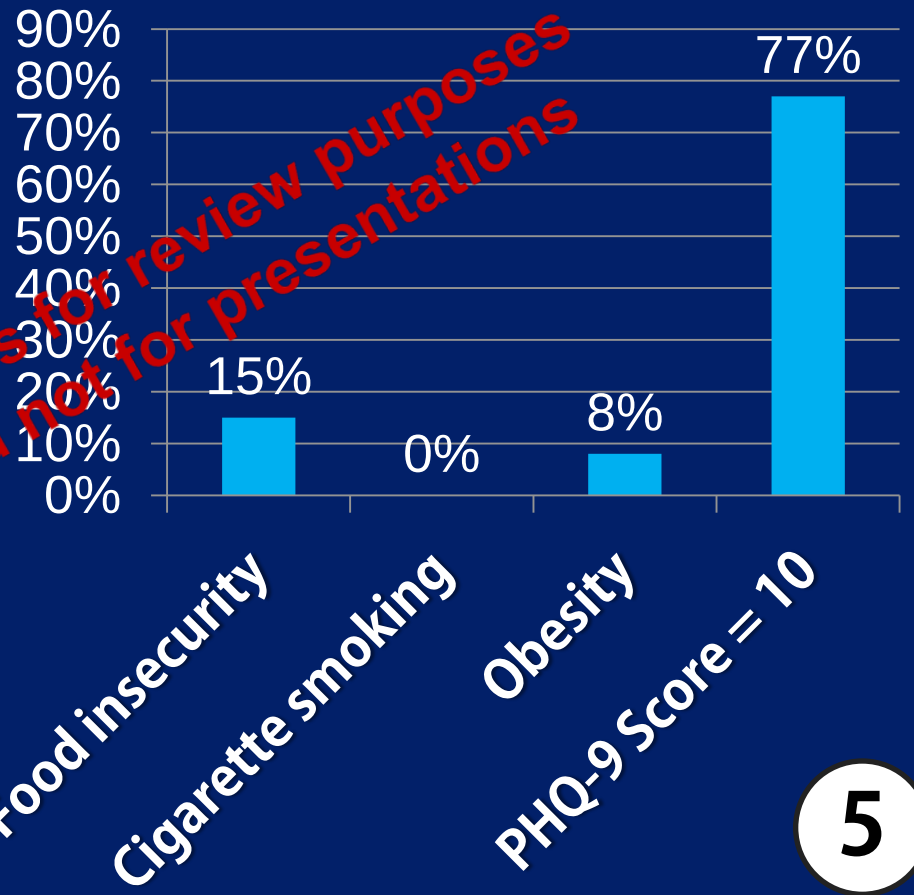
Alexithymia

- Difficulty finding the right words
- More likely to *analyze* than *describe* feelings
- Not introspective
- Not forthcoming about emotions
- Toronto Alexithymia Scale (20 items)

Question 5: MCQ Round

All of following are correlated with worse control of T2DM, <u>except</u>?

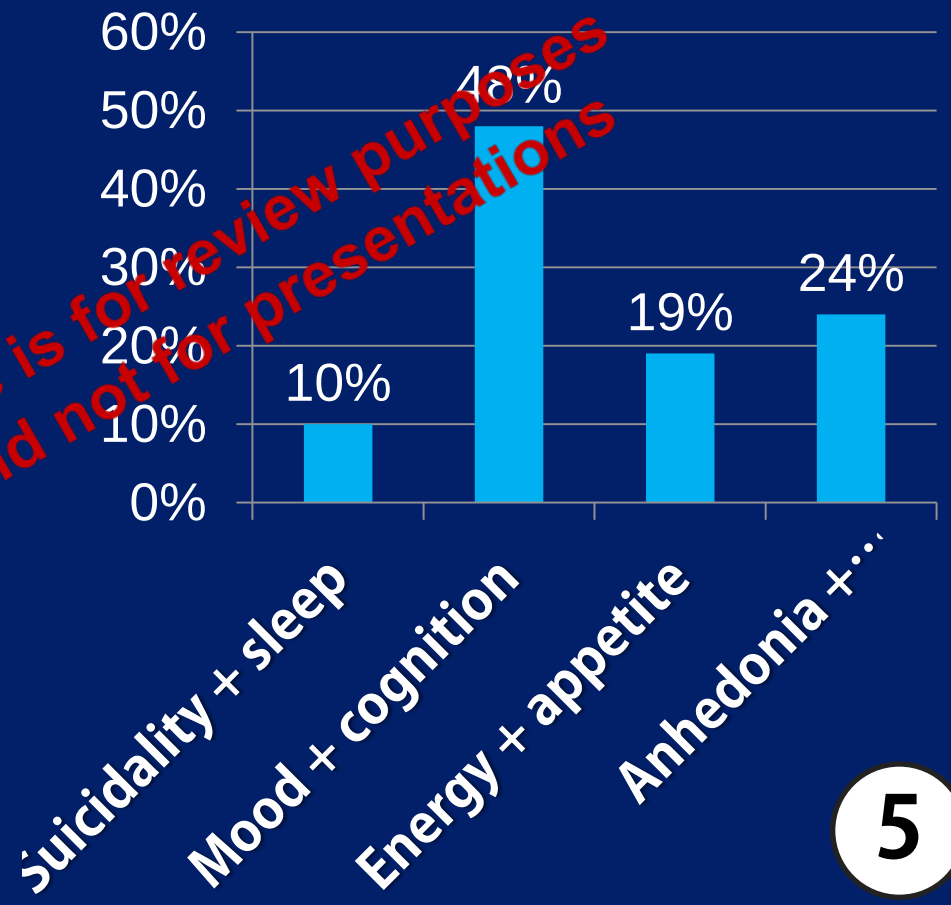
1. Food insecurity
2. Cigarette smoking
3. Obesity
4. PHQ-9 Score = 10



Question 6: MCQ Round

Metformin improves which symptoms in people with MDD and T2DM?

1. Suicidality + sleep
2. Mood + cognition
3. Energy + appetite
4. Anhedonia + psychomotor changes



Cognition

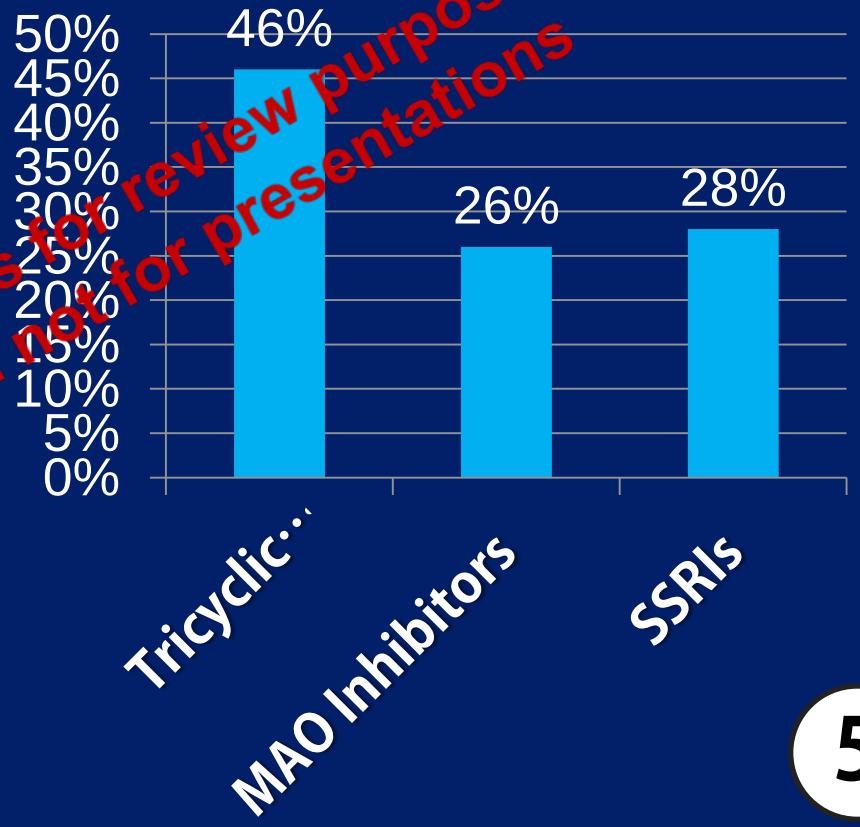
- Patients had MDD and T2DM
- Cognition assessed by the WAIS
- Mood assessed by MADRS and HAM-17
- Drop in A1C levels correlated strongly with improvement in cognitive testing
- Higher scores on depression rating scales strongly correlated with diabetic complications
- Metformin may promote neurogenesis

Guo et al, 2014

Question 7: MCQ Round

Which class of medication is metabolically the safest for treating depression in patients with diabetes?

1. Tricyclic Antidepressants
2. MAO Inhibitors
3. SSRIs



Antidepressants

TCAs and MAOIs

- High incidence of cardiovascular side effects
- Adrenergic stimulation is not beneficial
- Increase glucose levels
- Weight gain/stimulate appetite

SSRIs

- Reduction in appetite/weight loss is more likely
- Increase insulin sensitivity
- Decrease glucose levels

Many antidepressants appear to have anti-inflammatory effects

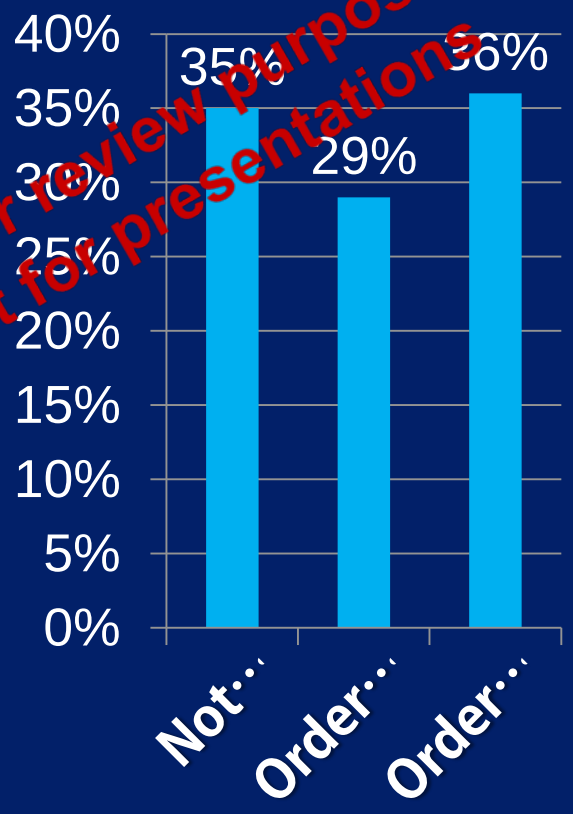
Antipsychotics

- Weight gain can be highly variable, especially with second/third generation medications
- Increased risk of diabetes and dyslipidemia
- The mechanism of untoward metabolic effects is presently unknown
- Regardless of the medication chosen, regular monitoring is critical
- Lower monthly doses with long-acting injections

Question 8: Opinion?

When it comes to monitoring metabolic indices in psychiatric patients, do you think psychiatrists should…

1. Not order tests
2. Order routine tests but not treat T2DM, ↑BP, dyslipidemia
3. Order tests and learn to treat T2DM, ↑BP, dyslipidemia



In Summary…

- Screen for DD/PIR/NES
- Only 50% of patients with co-morbid [DM+MDD] are accurately diagnosed, and only half of this group receives minimal treatment
- Antidepressant medications alone do not appear to help glycemic control
- CBT demonstrates better results for improving depressive symptoms and glycemic control
- Monitor patients on psychiatric medications for metabolic effects