Stress and Hormones: How These Factors Contribute to Diabetes Mellitus Type II

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Objectives
- Describe hormones activated during acute and chronic stress
- Identify hormonal changes that lead to or worsen diabetes mellitus
- Describe the impact of lifestyle and hormonal balance on diabetes measurements

Functional Approach to Health
- The missing link
- Normal versus optimal
- Definition of a hormone

Hormones Affected by Stress
- Cortisol
- Adrenocorticotropic hormone (ACTH)
- Corticotropin Releasing Hormone (CRH)
- Catecholamine
- Vasopressin
- Thyroid
- Growth Hormone
- Prolactin
- Insulin
- Grehlin
- Leptin
- Gonadotropin
- Resistin

And many others
1. **Hypothalamic-Pituitary-Adrenal Axis**
   - Stress activates the Hypothalamic-Pituitary-Adrenal axis (H-P-A).
   - Acute stress causes CRH to be released from the hypothalamus.
   - CRH activates ACTH.
   - ACTH activates cortisol production.

2. **Cortisol**
   - Cortisol in acute stress stimulates the sympathetic nervous system, or fight or flight system.
   - Blood sugar production is upregulated to maintain a higher level, and sodium and water retention are also increased for perfusion to muscles and brain.
   - In healthy people, high levels of cortisol stimulate the negative feedback mechanism which down regulates these effects.
   - Homeostasis is maintained.

3. **Chronic Stress**
   - High levels of cortisol are sustained, leading to a desensitization, or resistance of receptors.
   - Hippocampal neurons are damaged, affecting memory.
   - Redistribution of body fat.
   - Insulin resistance, secondary to increased blood glucose and insulin.
   - Protein breakdown occurs.
   - Immune system is suppressed, with decreased WBCs and associated antibody and immunoglobulin decrease.

4. **CRH**
   - GI effects:
     - Increases parasympathetic nervous system receptors leading to decreased motility, causing bloating, excess gas.
     - Increases sympathetic nervous system in the colon causing increased motility, diarrhea, inflammation.

5. **ACTH**
   - Increases cortisol which in turn increases ghrelin.
   - Stimulates appetite.
   - Increases insulin.

6. **Leptin**
   - Stress increases leptin which decreases appetite.
   - Chronic stress can lead to leptin resistance.
   - Made in adipose tissue and many other sites.
   - Opposes ghrelin.
   - Decreases appetite.

**Sources:**
- Besedovsky et al
- Chiodini et al, 2007
- Smith et al, 2006
- Azzam et al, 2010
- Gagliardino et al, 1995
- Enriori et al, 2007
**Ghrelin**
- Appetite stimulant, upregulated with stress
- Affects GH, glucose, insulin, BP, adipogenesis and inflammatory processes, in experimental conditions
- Elevated cortisol can decrease sleep, which increases ghrelin and decreases leptin

*Mol Cell, 2011*

**Resistin**
- Made by adipose tissue
- The more adipose tissue present, the higher resistin levels are
- Affects LDL metabolism with a result of increased LDL
- Increases inflammatory processes
- Linked to insulin resistance

**Thyroid**
- Stress decreases production of T4 and T3, hypothyroidism
- TSH is decreased by stress as well
- May be linked to hyperthyroid, or thyroiditis. Seen in 65% of Nazi prisoners, but no recent research to support theory

**Insulin**
- Insulin production normally increases in response to higher blood sugar and decreases and blood sugar drops
- Acute stress causes a decrease in insulin to maintain higher blood sugars to supply instant energy to muscles for the "fight or flight" response.
- Cortisol levels remain high in early chronic stress with sustained higher blood sugars possibly leading to high levels of insulin, which in turn can cause insulin resistance.

How do we go about improving health in a pre diabetic or diabetic patient?

- **Lifestyle:** Diet, exercise, sleep, stress management, weight loss
- Balance hormones
- Medications
- Supplements

**Diet**
- Healthy, balanced diet, low in processed sugars and fats will reduce blood sugars, which will reduce insulin.
- Over time, insulin resistance may improve.
Inflammation in the Gut

- Foods can cause an inflammatory response in the gut
- Inflammation causes disruption of the gut lining
- Gut lining becomes more porous
- Cytokines are stimulated
- This process can contribute to the general stress response in the body.

Foods that can cause Gut Inflammation

- Foods containing high amounts of sugars
- Foods with trans fats
- Processed foods and foods high in sodium
- Artificial sweeteners
- MSG
- Gluten
- Dairy
- Personal food sensitivities

Exercise

- Burns calories
- Normalizes metabolism
- Weight loss
- Decreases blood glucose by expenditure, independent of insulin
- Increase in insulin sensitivity
- Positively stimulates the H-P-A axis, decreasing the effects of stress

Sleep

- 7-8 hours of quality sleep improve circadian rhythm with more normal melatonin, ghrelin production at night, cortisol production during the day.
- Sleep hygiene:
  - Try to maintain regular hours of going to bed and waking
  - No screen time for 1-2 hours before bed
  - No caffeine for at least 6 hours before bed
  - Sleep is improved in a dark, quiet and cool room

Stress Management

- Stress management is crucial in preventing and/or treating diabetes mellitus type II
- Stress leads to hormone activation that causes increased appetite, cravings for fast energy (simple carbs), interrupts sleep patterns
- Stress often interferes with healthy decision making
Cortisol levels

- Recognize there are **unavoidable stressors**, and stresses that can be modified by lifestyle decisions.
- **Identify** stressors, modifiable and unmodifiable
- **Reducing** modifiable stresses
  - “There isn’t time to go shopping for healthy foods, to prepare good meals, to eat regularly”.
  - “There isn’t time to exercise”.
  - “I can’t sleep, or I don’t have enough time to sleep”.

Weight Loss

- Improving diet, exercise, sleep and stress may very likely cause weight loss in an overweight or obese person.
- Weight loss improves T2DM by **decreasing adipose tissue** which decreases resistin.

Medications

- Metformin: restores enzyme activity and improves inflammation, decreases oxidative stress in T2DM.
- Insulin: long acting insulin may cause less weight gain than short acting.
- GLP-1 agonists like exanatide and sitagliptin can promote weight loss by increasing glucose dependent insulin secretion and suppresses inappropriate elevated glucagon secretion, which lowers ghrelin, the appetite hormone.
- Thyroid medications may improve diabetes by improving glucose metabolism.

Supplements

- Berberine: 500 mg 3 times a day, increases GLP-1 and decreases T2DM.
- Omega 3: antioxidant, preserves beta cells.
- Multivitamin: provides necessary vitamin and minerals for hormone conversion and use.
- Adaptogens: herbs and compounds that promote normal adrenal function, Ginseng, Ashwaganda, licorice root, rhodiola, and rhodiola.
- Chromium: decreases carbohydrate craving.
- Magnesium: increased insulin sensitivity.
- ALA (alpha-lipoic acid): antioxidant.
- Cinnamon: increased glucose uptake and improved insulin sensitivity.

Website references for supplements

- [https://ods.od.nih.gov](https://ods.od.nih.gov) Office of Dietary Supplements
- [https://nccih.nih.gov](https://nccih.nih.gov) National Center for Complementary and Integrative Health
Take Home Messages

- Be aware of the importance of lifestyle management in your practice with pre-diabetic and diabetic patients.
- Assist patients in lifestyle modifications for stress reduction.
- Consider the fact that many patients are gathering a great deal of information online, whether factual or from sources not trustworthy.
- Many patients are looking for alternative treatments instead of or complementary to traditional medicine.
- My goal is to learn everyday, and often it’s my patients that are the teachers.

References, cont.

References


