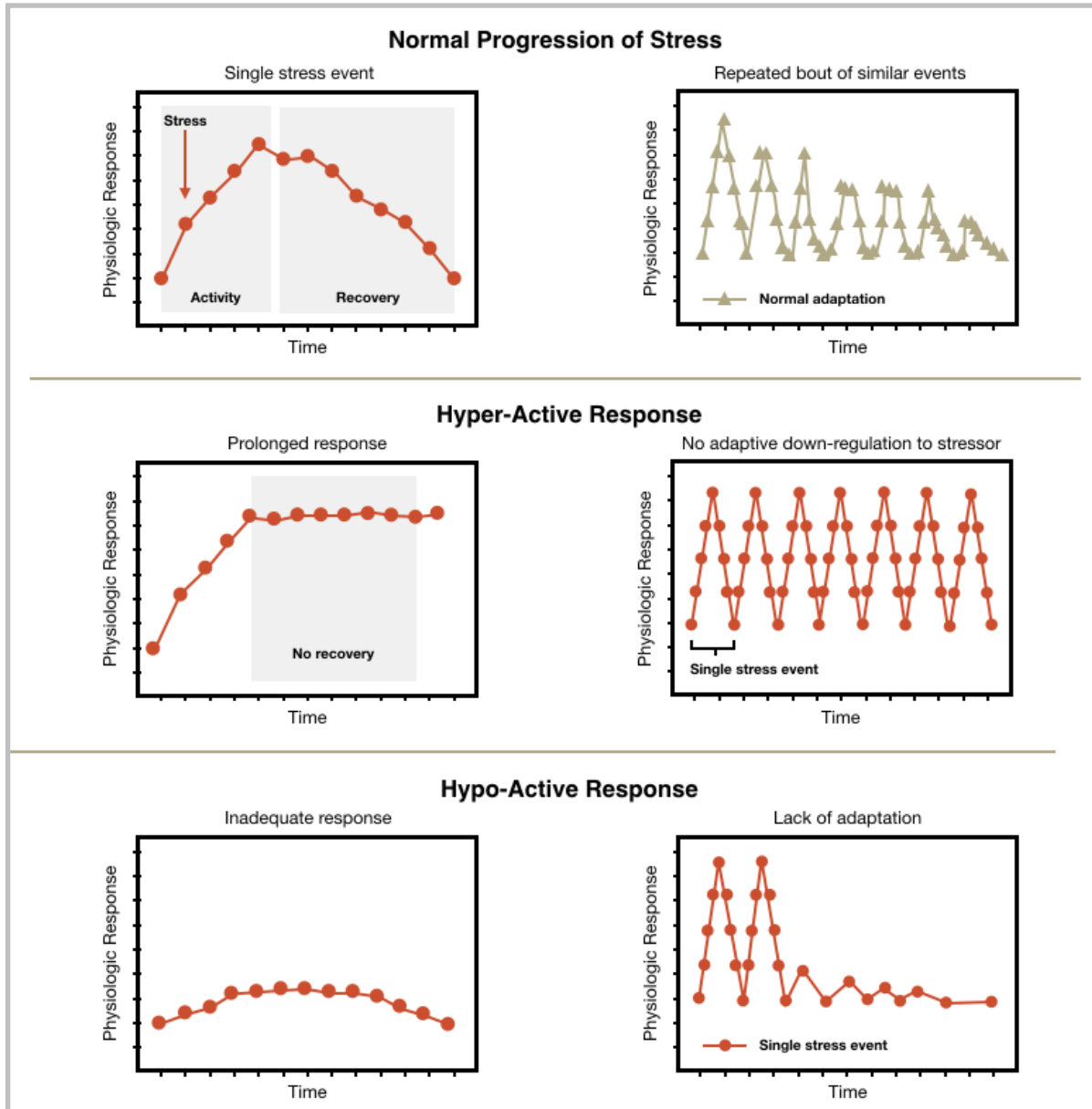


# HPA-D Pathology Review

General categories of dysfunction caused by allostatic load.



## 1. Normal progression of stress

- a. The stress response increases during the event, and then it declines over time after the stressful event has passed.
- b. Repeated bout of similar events.

- i. At first, the stress response is higher, but repeated bouts of the same event result in the stress caused by that event to be lower.

## **2. Hyperactive stress response**

- a. Prolonged response to a single stressor. An example would be PTSD.
- b. No adaptive downregulation to the stressor
  - i. Single stress event and then a repeated bout of similar events, but instead of seeing the healthy normal adaptation, we see repeated activation that's similar to the first time that we experienced the event.

## **3. Hypoactive response**

- a. Inadequate response to a single stressor
  - i. This often happens when the HPA axis has become downregulated, and then the patient is unable to mount an effective response to future stressors.
- b. Lack of adaptation to a repeated bout of similar events,
  - i. The whole HPA axis gets downregulated, and the patient is not able to mount a successful stress response to these repeated events.

There are two additional key concepts related to allostatic load:

### **RESILIENCE**

- The immediate capacity of cells, tissues, and organ systems to respond to changes in physiological need, which would be induced by stress.

### **METABOLIC RESERVE**

- Long-term capacity of tissues and organ systems to withstand repeated changes to physiological needs.
- Put in more simple terms, metabolic reserve is the stored-up reserve that's available for each metabolic and organ system to maintain and rebuild its physiological resilience.
- Metabolic reserve can be depleted, and it can also be replenished and strengthened.

The goal of the stress response is to keep us alive through physiological challenges and threats.

### **FIGHT-OR-FLIGHT RESPONSE**

- Heart rate and blood pressure increase
- Pupils dilate to take in as much light as possible
- Veins in skin constrict

- Blood glucose level increases
- Muscles tense up
- Smooth muscle relaxes
- Nonessential systems shut down
- Trouble focusing on small tasks

Once the threat has passed, the parasympathetic nervous system is activated, and the body starts using resources for activities that promote long-term survival again.

### **REST-AND-DIGEST RESPONSE**

- Heart rate and blood pressure decrease
- Saliva and digestive enzymes increase
- Bronchial tubes in the lungs constrict
- Muscles relax
- Pupils in the eyes constrict
- Blood flow to the GI tract and endocrine organs increases
- Immune function restored

Most of our patients are in a nearly continual fight-or-flight response. The body was never designed for that, and all of these things that happen in the fight-or-flight response will directly contribute to chronic inflammatory disease and all the symptoms that our patients experience.

Only one of these systems can be activated at a time: parasympathetic or sympathetic system. It's not just constant stressors such as traffic, circadian disruption, poor diet, sleep deprivation, shift work, jet lag, financial stress, or relationship stress that's an issue. It is mental or emotional stressors that have increased in the modern world.

The three other categories that we've discussed, glycemic dysregulation, circadian disruption, and inflammation, are also far bigger players today than they were for our ancestors.

Constant activation of the HPA axis increases allostatic load and then stretches physiological resilience and depletes the metabolic reserve in nearly every tissue in the body.

The repeated activation of the HPA axis eventually leads to downregulated response to new stressors. This is the body's attempt to protect itself from chronically elevated cortisol levels. This leads to an ongoing semipermanent catabolic state where breakdown and wear and tear are happening faster than the body can rebuild itself.

Most of the stress-induced changes in physiological function are mediated by alterations in gene regulation triggered by glucocorticoids. These are influenced by genetics but much more strongly modified by environmental factors that affect cellular changes influenced by cortisol. The two primary forms of epigenetic modification are DNA methylation and histone modification. These changes manifest as alteration in metabolism, circadian control, and brain function in particular.

**CONDITIONS RELATED TO HPA AXIS HYPERFUNCTION**

|                               |                  |
|-------------------------------|------------------|
| Depression                    | Alcoholism       |
| Anorexia nervosa              | Diabetes         |
| Obsessive-compulsive disorder | Central obesity  |
| Panic disorder                | PTSD in children |
| Excessive exercise            | Hyperthyroidism  |

**CONDITIONS RELATED TO HPA AXIS HYPOFUNCTION**

|                               |                      |
|-------------------------------|----------------------|
| Atypical/seasonal depression  | Nicotine withdrawal  |
| Postpartum depression         | Rheumatoid arthritis |
| Chronic fatigue syndrome      | Asthma               |
| Fibromyalgia                  | Eczema               |
| Premenstrual tension syndrome | Hypothyroidism       |