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An Introduction to the Cortisol Awakening Response Test

The Cortisol Awakening Response (CAR) Test provides insight into the health of the Hypothalamic-Pituitary-Adrenal (HPA) axis. The CAR was first mentioned in the medical literature in 1997.[1] A healthy CAR increases alertness, initiates conscious awareness, improves memory, reduces inflammation, promotes immune tolerance (self-tolerance), mobilizes the motor system, and boosts energy levels upon waking.[2,3]

Research suggests a healthy CAR is characterized by an increase in the salivary cortisol level by at least 50% within 30 minutes of awakening.[4]

Research shows the magnitude of the CAR could be associated with prior-day experiences and anticipation of the stress level or workload for the day ahead; however, the exact neurobiological mechanisms that generate the CAR have not yet been fully elucidated.[5]

Some research suggests the hippocampus plays a role in the CAR since a blunted CAR is associated with lower hippocampal volume.[6,7,8] Other research indicates the CAR is modulated by the suprachiasmatic nucleus (SCN) in the hypothalamus, known as the body's central clock.[5,9] Some researchers suspect the CAR is activated when light stimulates the SCN, which then increases adrenal sensitivity to adrenocorticotropic hormone (ACTH) by way of the splanchnic nerve.[5]

While light can impact the amplitude of the CAR, a CAR will still occur in the absence of light, according to Bowles et al. Thus, CAR dynamics could be regulated by a complex interplay of internal circadian mechanisms, daily behaviors (awakening), and environmental cues (light).[5]

The available data also demonstrate that the CAR is physiologically different from a stress response.[10] A morning stressor could increase morning cortisol production, but the CAR is a unique, natural part of the circadian rhythm modulated via different pathways that will continue to be investigated.[11]

When Should I Order a Cortisol Awakening Response Test?

The results of the CAR test could be clinically helpful for all patients with a health condition that is associated with an abnormal CAR, including hypertension, depression, anxiety, PTSD, diabetes, obesity, and more.[12,13] Please review the "Health Concerns Associated with an Abnormal Cortisol Awakening Response (CAR)" document for more information.

Since the robust amount of cortisol released during the CAR reduces inflammation, those with a blunted CAR can awaken with inflammatory symptoms, such as acute pain, asthma symptoms, GI issues, profound fatigue, etc. Therefore, the CAR test should ideally be ordered for all patients who experience significant symptoms in the morning.[2]

Also, consider testing the CAR in patients with cancer or a family history of cancer. Research shows the CAR can predict cancer survival. Specifically, a flattened or abnormal diurnal cortisol rhythm is associated with earlier mortality. Thus, optimizing the CAR could be protective for patients with or concerned about cancer.[14,15]

Collection Considerations

The CAR naturally occurs just after awakening. Therefore, ensure all patients understand the importance of the optimal timing of saliva sample collection. The first saliva sample must be collected immediately upon waking. The second saliva sample is collected 30 minutes after the time of waking. The third saliva sample is collected 60 minutes after awakening. Patients should use a timer or alarm to prompt the 30- and 60-minute saliva collections.[16,17]

Patients should not eat, drink coffee or anything other than water, exercise, smoke, or engage in significant conversation until after the three precisely timed saliva samples are collected.[18,19]

Ideally, CAR testing will occur on an average, typical day. If the patient awakens exceptionally earlier or later than usual or with the flu, consider collection on a different day.[20] It could be clinically useful to assess the CAR during an unusual circumstance. In these cases, though, it is ideal to test the CAR on an average day and a symptomatic day for comparison.

Retest the CAR every 3-4 months until optimal, then monitor annually or more often if the patient is symptomatic.

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