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Beau Andrew Alward
University of California, Davis

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Beau Andrew Alward
University of California, Davis

Abstract

The glucocorticoid (GC) known as cortisol is secreted from the adrenal gland when someone is exposed to stress from their internal or external environment. Cortisol modulates various physiological functions during stress to help one adapt; however, it also has an effect on cognitive functions. One cognitive function affected by cortisol, with an increasing interest among scientists, is memory. Various experiments conducted with the goal in mind of finding cortisol's effect on memory, yield contradictory results. Some of the experiments show that cortisol weakens a person's ability to retrieve emotional memory, and enhances their ability to retrieve neutral (Kuhlmann et al., (2005); Tollenaar et al., (2008). Others show cortisol enhances a person's ability to retrieve emotional memory, and impairs their ability to retrieve neutral (M. Jelicic et al., (2004); P. Putman et al., (2004). This review paper focuses on analyzing these experiments and their results, to help expose methodological flaws and, as a consequence, give insight on how to improve future experiments to achieve more valid results. This collective analysis further corroborates the complex functioning of cortisol and how it affects one's ability to recall information of varying emotional valence while undergoing different levels of stress.

Introduction

When a person is exposed to stress from their internal or external environment, glucocorticoids (GC) known as cortisol are secreted into the bloodstream from the adrenal gland. When cortisol binds to glucocorticoid receptors (GR), it helps the person adapt to stress (De Kloet et al., 1998). While cortisol modulates the physiological changes associated with adapting to stress, e.g., accelerated carbohydrate metabolism, blood pressure, and heart rate, it also affects cognitive functions (De Kloet et al., 1999; Rozendaal, 2002). Scientists are conducting experiments to find the relationship between increased cortisol and cognitive functions, and yielding variable results. Memory, for example, seems to be the most controversial. Most of the studies on cortisol's influence on memory focus on how stress and cortisol affect emotional memory versus neutral memory. Some of the experiments show that cortisol impairs a person's ability to retrieve emotional memory, and enhances their ability to retrieve neutral memory (Kuhlmann et al., (2005); Tollenaar et al., (2008). Others show cortisol enhances a person's ability to retrieve emotional memory, and impairs their ability to retrieve neutral memory (M. Jelicic et al., (2004); P. Putman et al., (2004).

The experiments testing for the correlation between cortisol and memory show contradictory results, and the validity of each of these experiments is open for interpretation. These experiment's validity need to be addressed because of the possible implications they have on causes of diseases like Alzheimer's Disease, and Parkinson's Disease--diseases which are suggested to be associated with hyper-cortisolism (Hartmann et al., 1996). Future, valid experiments are needed to eliminate the confusion regarding cortisol's effect on memory. This review paper's main focus is to compare the current experiments and their results that test for cortisol's influence on memory and underscore the complex functioning of cortisol as it affects memory. Analyzing these experiments and their results will help to expose their flaws and, as result, give more insight on how to conduct future experiments that have valid results.

Discussion

Emotional Valence

In an experiment by M. Jelicic et al. (2004), stressed individuals showed an increased ability to recall words of high emotional valence compared to neutral words. For the experiment, 40 healthy undergraduate students, 31 women and 9 men (mean age=20.1 years (y)), participated. Participants were given an Auditory Verbal Learning Test (AVLT), which consisted of 15 emotional words and 15 neutral words that they attempted to remember. After the AVLT, 20 participants were exposed to a Trier Social Stress Test (TSST) followed by a difficult arithmetic task that lasted for 5 minutes. A TSST requires the test subject to give a 5-minute speech in front of a committee. The TSST is shown to stimulate a sense of fear and uncontrollability in the subject, as well as the cardiovascular and endocrine changes associated with stress (Dickerson and Kemeny, 2004; Kirschbaum et al., 1996). Moreover, B. Kudielka et al. (2002) demonstrated that the resulting cortisol concentrations per subject induced by a TSST, do not differ as a function of gender among younger (mean age= 23.5±0.5 y) men and women. The 20 participants not exposed to the TSST were in the control group. After the stressful tasks, participants were asked to retrieve as many words as possible from the AVLT. The control group, which had significantly lower stress scores and cortisol levels relative to the stress group, showed an increased ability to recall neutral words compared to emotional words (M. Jelicic, 2004). Conversely, the stress group showed an increased ability to recall words of high emotional valence, and a decreased ability to recall neutral words.

An experiment by P. Putman et al. (2004) shows results that are consistent with the ones obtained by M. Jelicic et al (2004). The study consisted of 40 women (mean age= 20.8±2.8 y, range= 18-39 y) who participated in a Facial Relocation Task (FRT). The FRT exposes participants to facial expressions showing fear, happiness, or neutrality located in different areas on a 4x4 grid. Before the FRT, salivary cortisol levels were measured. Following the FRT, participants were asked to relocate the faces immediately, and then asked to relocate them at a moment 20 minutes later. When participants were cued to relocate the faces immediately after the FRT, they were able to relocate happy faces better than neutral and fearful faces. Whereas a 20-minute delay increases participant's ability to relocate both happy and fearful faces, a correlation between high levels of cortisol and increased memory for location of emotional faces was only present in the long-term group. Lastly, it is important to note that no protocol was used to invoke a stress response in the participants.

Kuhlmann et al. (2005) conducted an experiment that shows increased levels of stress and cortisol are associated with decreased ability to retrieve words of emotional valence from memory, and an increased ability to retrieve neutral words from memory. Nineteen male university students (mean age=24.58±1.26 y, range= 19-40 y) were given a list of 30 words, which was composed of 10 positive, 10 negative, and 10 neutral words. The test subjects were given 2 minutes to learn the list. Twenty-four hours after learning the list, participants either took part in a TSST or a control condition. The treatment group, which experienced a significant increase in stress and cortisol, showed impaired memory retrieval overall. However, words of emotional valence were affected most significantly. Interestingly, moderate increases in cortisol were also associated with retrieval deficit.

In an experiment by Tollenaar et al. (2008), 70 male university students (mean age= 21.34±2.9 y) performed a memory task consisting of learning a list of 40 words--20 neutral and 20 negative. The participants were then exposed to a TSST followed by a difficult arithmetic task, at a time one day later, as well as five weeks later. During and after the stressful task, memory retrieval was tested. When given a one-day gap, the stress and control group retrieved significantly less negative words than neutral ones during and after the TSST. After a five-week gap, retrieval of negative words was impaired compared to retrieval of neutral words during and after stress. However, when participants who experienced low sympathetic activation--a heart beat less than 10 bpm and an increase in blood pressure less than 10 mm Hg--were removed from the data calculations, the correlations between cortisol increase and impaired memory retrieval were even stronger. From this data Tollenaar et al. concluded that only during times of sympathetic arousal is cortisol increase associated with impaired memory retrieval.

The experiments described above focus solely on how emotional valence of a memory affects an individual's ability to retrieve it. There are experiments, however, that give participants a synthetic form of cortisol to see how their memory retrieval is affected. In addition, some experiments also use a synthetic form of cortisol while accessing its effect on retrieving memory of varying emotional valence.

Hydrocortisone and Memory Impairment

Ingesting 10 mg of hydrocortisone, a synthetic form of cortisol, impaired memory in an experiment by C.Buss et al., 2004. In the experiment, 22 male university students (mean age= 26.27±0.89) were given 10 mg of hydrocortisone, or a placebo. One hour later, they were given a autobiographic memory cueing test (AMT). The AMT consists of two positive adjectives, two negative adjectives, and two neutral adjectives. Immediately after being exposed to the AMT, participants were told to write about a specific event that was stimulated after reading the adjective. C. Buss et al. found that subjects treated with 10 mg of hydrocortisone show significantly impaired ability to recall events.

Beckwith et al. (1986) conducted an experiment that shows the effects of hydrocortisone on memory are dependent on dose, as well as duration of the memory retrieval test. Eighty male undergraduate students-whose mean age was not disclosed-from the University of

North Dakota participated and were given either 40, 20, 10, or 5 mg of hydrocortisone mixed with glucose or a capsule with just glucose. One hour following ingestion of the capsule, subjects participated in a memory retrieval test, which requires participants to read through a list of 12 neutral words. Immediately after reading through the list, subjects were cued to recall as many words as they could. Subjects were exposed to eight different lists, and thus were cued to recall from eight different lists. The 5, 10, 20, and 40 mg dosages of hydrocortisone facilitated recall of words during the first two lists. However, only the 40 mg dose enhanced recall as the experiment continued. The lowest dose, 5 mg, decreased memory retrieval as time of the experiment continued.

Conclusion

As expected, the experiments described above reveal indecision among researchers about the role cortisol has on memory. For example, the experiments that used TSST as a stressor show contradictory results. However, these same experiments allowed different amounts of time for consolidation, which could account for the different effects of cortisol. The experiment done by P. Putman et al (2004) yields results in line with M. Jelicic et al's (2004); however, the methods used during the experiments were drastically different. For instance, M. Jelicic et al (2004) used the TSST to induce a stress response and measured the correlating increase in cortisol, whereas P. Putman et al (2004) did not induce a stress response in participants, nor did they measure cortisol levels as they correlate with stress. However, P. Putman et al's (2004) experiment focused solely on individual's abilities to locate faces of variable emotional valence—not the magnitude at which stress impairs memory retrieval.

The experiments that used hydrocortisone to increase cortisol show some positive trends. The experiment by Beckwith et al. (1986) shows the effect cortisol has when its concentration in the blood is varied, along with increasing length of a memory retrieval test, while C. Buss et al. (2004) only gave 10 mg of hydrocortisone to participants, and their memory was impaired. The two studies that are compared above, however, were performed using different types of experiments, and also performed 18 years apart from each other. So, the disciplinary context of the experiments must be considered.

In addition to variable experimental conditions, the experiments on cortisol and memory use sample sizes that are too small. To decrease variability within an experiment, it is important to use a large enough sample size. Also, most of the experiments described above include only one gender, which intuitively means the results obtained from each experiment can only apply to the corresponding experiment. Lastly, the experiments analyzed used a similar age group, young men and women, and thus the results can only apply to that age group. However, as B.M. Kudielka et al (2002) show, stress responses for young men and women correlate with similar amounts of circulating cortisol—however, during the same experiment, boys and girls (mean age = 12.1±0.3 y) had similar circulating cortisol caused by the TSST. Interestingly, in the experiment by B.M. Kudielka, older men (mean age= 67.3±1 y) experienced circulating cortisol significantly higher than younger men and women and boys and girls. Thus, future experiments should use caution when analyzing data that contain results from older men.

Regarding the experiments described above, what can be concluded about cortisol and its influence on memory is that its effect is dependent on context--in some situations it is detrimental to emotional memory retrieval and enhances our neutral memory retrieval, and in other situations the opposite pattern is seen. Since each study shows results that only apply to its experimental situation, there is not one answer to the question of what cortisol does to memory. Nevertheless, current and past researchers have provided a platform of salient results that expose the complexities underlying cortisol functioning.

Priorities for Future Research

To eliminate the uncertainty about cortisol's effect on memory, future research is required. Sample sizes used in future experiments should be large enough--at the lowest, should include 100 participants. Also, the gender issue needs to be eliminated by either including both men and women in equal amounts in an experiment, or performing two identical experiments that include only men or women. Possible gender differences in the impairment effect of cortisol need to be established. Furthermore, the amount of corticosteroid binding globulin (CBG), which binds to cortisol in the blood making it inactive (Fernandez-Real et al.,1999), was not measured in any of the above experiments. However, when total cortisol is measured in the blood, the amount of CBG-bound cortisol is included, even though it cannot bind to glucocorticoid receptors. Thus, including the amount of active cortisol versus total cortisol will increase fidelity. Nevertheless, there remains promise that future experiments will establish a reproducible pattern between cortisol and human memory.

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