Real Science Review: Stress

"I'm not doing well in school," Jason said to his buddy Arthur. "It stresses me out."

"You know what?" Arthur replied. "I heard that there is research showing that stress interferes with learning and memory. If so, you may be caught in a vicious cycle: low grades stress you, and the stress just makes your grades worse.

"Hmmm. I wonder what else the research shows," Jason thought.

There are many research reports showing that continuing stress impairs academic ability. Here, you are going to simulate a peer review of a report on the role of time between a stressful even and the time of learning. Also studied was the emotional aspect of items being memorized.

Vocabulary Used in the Original Report

Beta adrenergic receptor activity: Receptors are large molecules anchored in cell membrane. Receptors bind with specific chemicals that have compatible 3-dimensional shape and electrical charge. Think of it like a hand in glove. This report deals with a receptor that binds adrenalin. That binding changes the neuron's functions. Stress releases both adrenalin and cortisol.

Consolidation of memory: conversion of short-term temporary memory into longer-lasting form. This process takes time, because protein synthesis and even gene expression has to occur to create physical and chemical changes in synapses that enable memory storage. Think of the process like wet cement: it needs some undisturbed time to "set up."

Double blind: the design is double blind if neither the subject nor the experimenter knows who got the test treatment until after the results were recorded.

Hippocampus: brain area that converts temporary memory into more permanent form.

Hormone: a chemical secreted into the bloodstream by gland or nerve cells. The blood distributes the hormone into various tissues where it may bind to receptors on cell membranes. This changes the function of the target cells. If such a chemical secretion is

dumped from a nerve cell on another nerve cell, it is called a **neurotransmitter**. If it is dumped into blood vessels, it is called a **neurohormone**.

Placebo: test condition that should not produce the effect under study. In a drug study, for example, one group of subjects would get the drug being tested, while another received a sugar pill as a placebo.

Recognition Memory: memory that you can recall if you receive some kind of prompt, as in multiple choice answers where one of the choices is the one you were trying to memorize. This is a less demanding task than free-recall, where you must generate the correct answer without any prompts.

Statistically Significant: Differences in group data that are unlikely to have occurred just by chance. The decision is made based on mathematical tests that consider the variation of data in each test or control group and measure how much the group data differ when variation is considered. A rough estimate can be seen in data graphs and charts by looking at the overlap of group means and their error bars.

Temporal proximity: the nearness of events in time.

Working memory: memory that is held only temporarily for a few seconds or minutes, as in retaining a phone number that has just been identified from a telephone book.

Original Report: Zoladz, P. R. et al. (2011). Pre-learning stress differentially affects long-term memory for emotional words, depending on temporal proximity to the learning experience. Physiol. Behav. 103, 467–476.

Adapting Author: W. R. Klemm

Think About It!

In your notebook:

- **List things that stress you.**
- **Write down definitions of the vocabulary words in your own words.**
- **Summarize the two variables being tested in this study.**

The Timing of Stress Before Learning New Words Affects How Well They Are Remembered

Abstract

In this study, subjects were stressed at two different times before learning a list of words. Either immediately or 30 minutes later, subjects were asked to memorize a list of 30 words with either positive or negative emotional impact. A day later, memory was tested in a free recall test and in a recognition test for the words.

Stress was imposed by having subjects immerse their dominant hand into ice-cold water for three minutes, while non-stressed control subjects put their hand in a bath of warm water.

Stressed subjects reported pain and exhibited higher blood pressure and elevated salivary cortisol levels. Stress applied immediately before learning caused better ability to recognize emotionally positive words, while stress applied 30 minutes prior to learning impaired free recall of negative words. Thus, we conclude that stress effects on memory depend on when the stress occurs prior to learning and on the emotional content of words being learned.

Introduction

Stress has profound yet complex effects on learning and memory. Published research over the past few decades reveals that stress effects range from no effect to enhancement to impairment of learning and memory, depending on the nature of the stressor and the information being learned (references 1-3). A major factor seems to be the time relation of the stress to the particular stages of learning and memory and to the emotional nature of the information that is being learned (45). In general, stress impairs memory retrieval (6-12). However, stress can enhance memory consolidation if it occurs after learning (11,14,15). If the learning material is emotionally arousing, both impairment and enhancement effects are magnified (8,9,11,12,14).

Introduction: Questions to Answer

1. If there was a hypothesis, either stated or implied, what was it?

2. How well did the authors justify doing this study?

3. What are some other related ideas that they did not test?

Stress presented before learning has more variable effects. For example, studies in both rodents and humans reveal that pre-learning stress can enhance, impair, or have no effect on memory (6, 16-24). Commonly, but not always, emotionally arousing information has been learned better under stress, while memory of emotionally neutral information is impaired. The effect on long-term memory of pre-learning stress depends on the stress duration and the time relationship of stress to the learning experience (25). At least for hippocampal-dependent stress, long-term memory is enhanced by a brief stress that occurs just before the learning (20, 21, 23-25) However, that same stress has no effect if it occurs more than 30 minutes before learning (25). If the duration of stress lasts as long as 30 minutes, long-term memory is impaired (6. 16, 18, 19).

One researcher has speculated that stress has different timing of effects in the hippocampus, the brain area that starts memory formation (25). This idea is supported by studies showing that adrenal cortex stress hormones produce an immediate excitation but a delayed inhibitory effect on neural activity in the hippocampus (26-31). Thus, we might expect that stress applied just before learning might benefit learning, but delaying learning relative to time of stress would not benefit learning. This had actually been demonstrated in an earlier study of maze learning in rats (25).

Not much has been reported on studies of pre-learning stress in humans. Based on the animal studies, we hypothesized that stress applied immediately before learning would enhance long-term memory, while learning would be impaired if the stress occurred 30 minutes before learning. We also suspected that emotional aspect of the learning material could affect results.

Material and methods

Participants

Methods: Questions to Answer

1. What acts as a control group by receiving no treatment? What is the purpose for having this group and how well does it serve that purpose?

2. What factors (variables) that might affect the results are not taken into account?

3. What are the advantages and disadvantages of the procedures and equipment used?

Seventy-two college students at our university were tested (20 men, 52, women; average age 19.7 years). None of those accepted in the study had a history that might affect memory, such as head injury, receiving any current treatment with psychoactive drugs, narcotics, beta-blockers, steroids or other medications. None had experienced any illness within the past three weeks. The test group did include three smokers, but their results did not differ from their group norms. Participants were asked to avoid intake of any substances that affect brain function for three days prior to the study and to avoid eating for 2 hours before the study.

Experimental Procedures

All testing was carried out in the afternoons. (Cortisol blood levels are greatest in early morning.)

Subjects were required to submerge their entire dominant hand up to and including the wrist in a bath of water for 3 minutes before encountering the learning task. Subjects were randomly assigned to a stress condition in which they placed their hand in ice-cold water (0-2^{o} C) or warm water (35-37^{o} C). Based on previous work (32), we also misleadingly told subjects in the ice-water group that they were being videotaped to monitor their facial expressions. Also, a member of the opposite sex stared at the subject during the ice-water bath.

Experimental Groups

Experiment 1: Immediately Before Learning	**Experiment 2: 30 Minutes Before Learning**

Ice-water stress (n=15)	Ice-water stress (n =21)
Warm water (n = 16)	Warm water (n = 20)

All subjects were asked to rate pain of the water bath on a scale ranging from 0 to 10 at 1-minute intervals. The few subjects who had to remove their hand from the ice water were automatically scored as 10.

After the water bath, we asked subjects were to memorize a 30-word list. We selected words from a published list that classified English words as emotionally neutral, positive, or negative (33). Ten words of each category were chosen. Subjects were asked to read each word aloud and rate it on a scale of -3 (very negative) to +3 (very positive). This took about 5 minutes. The timing of conditions was as follows:

1. For both Experimental groups 1 and 2: Within 5 minutes before the water bath exposure, we took a saliva sample for later cortisol analysis. We also measured heart rate and blood pressure and rechecked midway into the water bath exposure. We took saliva samples, heart rate and blood pressure for a third time approximately 10 minutes after the end of the water bath.

2. For Experiment 2: word list was presented 30 minutes after start of the water bath. Saliva samples were taken immediately before presenting the word list.

Testing for recall of the words occurred the next day and involved two series of tests. In the first memory test, subjects were given 5 minutes to write down as many words as they could remember (a "free recall" test). Then for the next 15 minutes, students sat quietly and completed unrelated school work they had brought to the lab.

At this point, they were given a word recognition test in which they were presented with a list of 60 words, half of which were present in the initial learning task and half which were new. Old and new words were matched in terms of emotional nature. Subjects were scored for the number of words on the initial list that they correctly recognized. An index was calculated for "hits" minus "false alarms" for each emotional category of word.

Data were analyzed for variation between subjects in each group with regard to stress and within subjects with regard to the negative-positive emotional category. No tests for gender were made because the distribution of males and females was uneven.

Results

Stress Immediately Before Learning

Cardiovascular and Hormonal Activity. Ice-water stress manipulation did not affect heart rate but did increase systolic and diastolic blood pressure (Table 1. Data not shown here). In both Experiment 1 and 2 groups, the ice-water stressed group had elevated cortisol at both sampling times. No change occurred in the warm-water controls.

Subjective Ratings of Water Bath. The warm water bath group never reported pain, but the stressed group reported average pain scores ranging from 5.3 to 5.9 (out of 10) in both Experimental groups. These scores increased to 6.1 to 6.7 at the last report. Stress scores ranged from 4.2 to 4.4 initially and increased to 4.8 to 5.1 at the last report.

Word List Ratings and 24-hour Memory. Both positive and emotional words were remembered in all groups better than neutral words. Stress had no statistically significant effect on neutral words in either free recall or recognition tests. However, stress increased the number of emotionally positive words that were correctly recognized (data not shown here).

Stress 30 Minutes Before Learning

Word List Ratings and 24-hour Memory. All participants had better free recall memory for emotional words than neutral words (Fig. 1). In the stressed group, free recall was significantly lower for negative words (see asterisk over the bar). The apparent increase in recall of positive words was not statistically significant. Recognition memory was slightly better for positive words than negative or neutral words and stress had no significant effect on recognition of any type of word (Fig. 1).

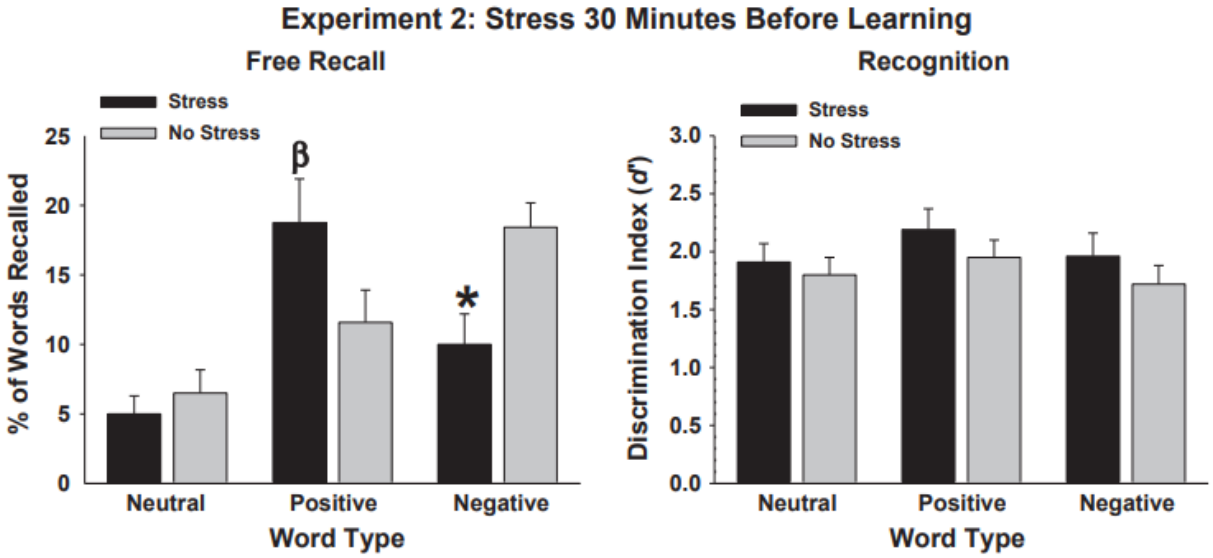

Fig. 1. Long-term memory for positive, negative, and neutral words in free recall and recognition tests. Stress at 30 min. prior to learning significantly reduced the number of emotionally negative words that subjects could freely recall. No statistically significant effect was seen in recognition testing.

Results: Questions to Answer

1. Do the results support the hypothesis or not? How convincing is that support?

2. Do you notice anything of possible importance in the data that authors failed to mention?

3. Is the variation in data large enough to suggest that some unknown variables interfere with reliable results? What might these be?

4. How big is the 'treatment' effect? Is it large enough to be of much practical importance?

Free recall of negative words correlated inversely with blood pressure during water-bath treatment and with cortisol levels after the water bath. That is, blood pressure and cortisol levels dropped as the percentage of negative words recalled increased. (Data not shown here).

Discussion

Our data generally supported the initial hypothesis. That is, stress applied immediately before learning could enhance long-term memory, but stress applied 30 minutes before learning could impair memory. However, the effect varied depending on the emotional nature of the words and whether the testing was by free recall or recognition testing.

In Experiment 1 based on stress immediately before learning, recognition of positive words correlated with heart rate. However, in Experiment 2, free recall of negative words had a negative correlation with blood pressure and cortisol levels. While the meaning of these effects is not clear, it does suggest that timing of the stress involves different mechanisms on cardiovascular and cortisol functions.

Previous work (17) had also shown that pre-learning stress effects on memory were associated with different beta-adrenergic receptor activity (which influences cardiovascular function). In one study from that lab, rats exposed to a cat stress for 2 minutes before maze training showed enhanced memory retrieval, while 30 minutes of being exposed to a cat impaired memory (25). Dosing the rats with propranolol, a drug that blocks beta-adrenergic receptors, blocked the memory effects of the 2 minutes of stress but not the effects of 30 minutes of stress. Perhaps some of this difference was attributed to delayed effects of stress-induced cortisol.

Discussion: Questions to Answer

1. Summarize how the authors discussed the results in terms of their original hypothesis.

2. Did the authors point out ideas that go beyond the hypothesis?

3. What ideas for future research did the authors generate?

4. What ideas for future research do you generate?

5. How would you state the "so what" take-home lesson?

This seems consistent with the results in Experiment 2 where the impairment of negative free recall only occurred in subjects who had a significant increase in cortisol. The failure to see such an effect in Experiment 1 suggests that cortisol might act differently on the mechanisms that impair memory than on those that promote memory. The

blood pressure effects seen in Experiment 2 could suggest that cortisol and sympathetic nervous system actions on cardiovascular functions combine to produce memory impairment.

Future studies would benefit from having more indicators of sympathetic nervous system activity by monitoring, for example, salivary alpha amylase (which is increased by stress).

Our study revealed greater memory for emotional words than neutral ones. Moreover, stress seemed to increase recognition of positive words in Experiment 1 but impaired recall of negative words in Experiment 2.

Multiple other studies have established that memory effects are greater for emotional words than neutral ones (35-40). Previous work has established that the amygdala part of the brain is necessary for enhanced memory of stressful emotional information and also for stress-related effects on hippocampal dependent learning (18, 19, 41-43). Perhaps our results reflect varying action of the stress conditions on amygdala function. This possibility is supported by prior electrical stimulation studies of the amygdala, where results differed depending on the timing of the stimulation (26, 27). In our Experiment 1, the immediate effect of stress might have come from activation of the amygdala, which in turn could have excited the hippocampus. The delay in Experiment 2 might have allowed the amygdala effect to "wear off."

Our results suggest that different mechanisms operate in free recall and in recognition memory. We saw that stress applied immediately before learning selectively affected recognition memory, while stress applied 30 minutes before learning affected free recall. Other investigators have suggested that free recall relies on the hippocampus, while recognition relies on the perirhinal cortex (66-60). Others disagree (70, 71).

We should be concerned about the poor recall performance in both of our experiments. In Experiment 2, for example, the average percentage of words recalled was below 20%. This may have created a floor or basement effect that makes it difficult for any manipulation to cause a further decrease in recall. Maybe we could have avoided this problem by telling the subjects that they would be tested for memory, in which case they might have made more of an effort to remember. It is also possible we could have strengthened the initial encoding by testing recall immediately after the presentation of the word list.

We had the additional problem of relatively small sample sizes, which could have reduced the statistical power to reveal stress effects. Even so, we still observed significant effects of pre-learning stress. There were also many more females in the study than males. Since the data were pooled across gender, we may have missed gender differences. It is well known that males and females do not respond the same to stress effects on learning. Females also present the variable of the menstrual cycle. (Other studies have indicated that memory ability is enhanced when estrogen levels are highest during the cycle.)

Our results should be interpreted cautiously because only a few variables were manipulated. Additionally, the emotional impact of presumed emotionally-charged words was not fully assessed. Subjects could respond differently to the same word.

Conclusions

Pre-learning stress effects on long-term memory (defined here as 24-hour memory) depend in part on when the stress was applied and on the emotional nature of the information. Specifically, when learning occurred right after the stress, recognition memory of emotionally positive words was enhanced. But when learning was delayed 30 minutes from the stress, free recall of negative words was impaired.

Participants recognition of positive words correlated with their heart rate during stress in Experiment 1, while their free recall of negative words in Experiment 2 correlated with blood pressure and cortisol levels.

These results are preliminary, but do tend to support the idea that timing of stress relative to learning is a key variable in how much of the learning is remembered.

References

Identification of the numbered references can be found in the original report and are not necessary for our purposes here.

You might want to watch our PEER video on "Stress and How to Overcome It" at:

https://www.youtube.com/watch?v=e1RvqwyT7Hk&t=741s.

The video explains ten ways to help youngsters cope with stress.