HOW STRESS AFFECTS CONCURRENT LEARNING AND MEMORY INTEGRATION DURING DECISION-MAKING

A Thesis Proposal

by

Elizabeth Beveridge

Approved by:

DocuSigned by:
Thackery Brown
203DEDB2857046A...

Dr. Thackery Brown, Advisor — Date Approved 4/28/2022 | 4:00 PM EDT
School of Psychology
Georgia Institute of Technology

DocuSigned by:
Scott Moffat
7FBE50C84B4843C...

Dr. Scott Moffat, 2nd Reader — Date Approved 4/28/2022 | 4:15 PM EDT
School of Psychology
Georgia Institute of Technology

DocuSigned by:
Mary Holder
BEDD6D9BD9094B4...

Dr. Mary Holder, Research Option Coordinator — Date Approved 4/29/2022 | 9:09 AM EDT
School of Psychology
Georgia Institute of Technology

INTRODUCTION

We make decisions everyday with varying amounts of risk and different payouts. Often, we make these decisions under stress. Imagine you are a freshman and you are running late for your next class, Chemistry. You usually have Math before, and so you always go to Chemistry from the Math building, but today you accidentally overslept so you are starting from your dorm. You can either leave from your dorm to the Chemistry building, a route you are unfamiliar with although you have started to grasp the campus, or you could go to your Math building and then go to the Chemistry building, a route you are familiar with although it is longer. This scenario is an example of value-based decision-making or choosing between a safe, lower payout choice like going to the Math building first or a riskier, higher payout choice like leaving from your dorm. While you are making this stressful decision and future decisions on how to navigate the campus, you are simultaneously learning the environment, recalling past experiences, integrating those past experiences together, and weighing the potential benefits of each choice. This study investigates how acute stress such as being late to class on a new campus affects concurrent learning and subsequent decision-making.

Our recent model on decision-making has demonstrated a computational approach for measuring the degree of memory integration, which is the extent to which past experiences are recruited to aid the current decision (He et al., 2022). In the example presented earlier about walking from Math to Chemistry, you may give more weight to your last experience walking from Math to Chemistry than on the very first day of class. The current literature on how stress affects learning has focused on when the stress occurs during learning (Vogel and Schwabe, 2016). Specifically, studies have looked at the effect on learning when stress is introduced during encoding versus retrieval (Vogel and Schwabe, 2016). However, to the best of our knowledge,

there is no study that has investigated how stress affects concurrent learning and decision-making.

To fill this critical gap in the literature, this study used a decision-making task in a spatial navigation paradigm to measure learning and memory integration during decision-making. 82 participants will be divided equally between genders and will navigate a virtual environment searching for three goal objects. Half of these participants will be exposed to stress via an electrical shock. For each trial, the participant will be prompted to decide between a familiar route with a lower payout or an unfamiliar route with a higher payout. For each participant, we will use computational modeling to measure the degree of memory integration. In other words, we will measure how they weigh past experiences from previous trials to aid their current decision. For example, will they weigh all past experiences equally or place more weight on more recent experiences? We will compare the degrees of memory integration between stress and control groups and observe if there are any individual differences (i.e. memory capacity, risk-taking preference, and gender) that may modulate the effect of stress on memory integration.

Overall, this study will give a better understanding of how stress affects concurrent learning and memory integration in value-based decision-making. These findings have real world implications as many scenarios require simultaneous learning and application. For example, various important occupations like a physician, soldier, stock trader and fireman must learn to adapt to new scenarios and make important time sensitive decisions. In addition, this study will add to scant literature on how stress affects learning and decision-making differently in females compared to males as many previous stress studies have only included male subjects.

LITERATURE REVIEW

Value-based decision-making is a type of decision-making when an individual chooses between two options, in which neither is objectively correct (Busemeyer et al., 2019). In this way, an individual's decision represents their preference (Busemeyer et al., 2019). An example of this type of value-based decision-making is decision-making under risk and uncertainty. This form of decision-making occurs when an individual chooses between a safer but lower payout option or a riskier but higher payout option. An example of this is choosing to invest life-time savings in a company producing smaller but constant dividends or choosing to invest in a start-up business. Often in the real world, these types of decisions are made under stress. This project hopes to fill the critical gap in how stress affects learning and the concurrent and subsequent memory integration during decision-making. The current literature on this topic can be divided into the following two subgroups: how stress affects learning and how stress affects decision-making during spatial navigation. This literature review will examine the current literature on both of these along with general nuances of stress studies and benefits of this particular study.

2.1 How Stress Affects Learning

The basic and current model on memory and learning suggests that forming memories is a process that occurs over time. Information must be encoded, consolidated, and then retrieved (Vogel & Schwabe, 2016). This process of forming a memory is considered learning and is measured by successful retrieval. The information can later be updated as further encoding, and consolidating occur (Vogel & Schwabe, 2016). In this way, memory and learning are not mutually exclusive and occur simultaneously.

Much of the research on how stress affects learning has focused around when the stressor occurs during this memory process. Stress can enhance memory and learning when the stressor occurs right before or after encoding, but impair memory and learning when the stressor occurs before retrieval or before updating the memory (Vogel & Schwabe, 2016).

Furthermore, research has shown that stress can cause a shift in the type of learning. Specifically, the current literature on learning divides learning into two different types: rigid learning, which is based on the repetition of past behaviors and flexible learning, and flexible learning, which is learning a structure of the task or environment that facilitates switching between behaviors in the task and understanding of the task (Schwabe et al., 2007, 2010; Schwabe & Wolf, 2009; Dias-Ferreira, 2009). Studies on how stress affects memory and learning has shown that stress may encourage rigid learning over flexible learning (Schwabe et al., 2007, 2010; Schwabe & Wolf, 2009; Dias-Ferreira, 2009).

Some research has suggested that stress's impact on learning may differ between genders (Andreano & Larry, 2006; Guenzel et al, 2014). Specifically, Guenzel et al. (2014) applied acute stress before encoding and tested recall one week later. They found that spatial memory that relied on landmarks was in impaired in males but not females and spatial memory that relied on repeating a route was impaired in females but not males. To be more explicit, this suggests that acute stress before encoding impaired flexible learning in males but rigid learning in females when those memories were recalled one week later (Guenzel et al., 2014).

These studies on memory and learning have designed tasks such that encoding and retrieval are distinct events. There is currently no study that investigates how stress impacts rigid and flexible learning when encoding and retrieval are inseparable and how these effects may differ between genders.

2.2 How stress affects memory integration during decision-making

During decision-making, recall of learned memories is critical. Beyond just memory retrieval, He et al. (2022) provides an alternative theory that individuals not only use memory retrieval but memory integration, the integration of past experiences, during decision-making. In this study, participants navigated a virtual environment in search of three goal objects, and they were prompted to choose between an unfamiliar route, representing a riskier but higher payout option and a familiar pathway, representing a safer but lower payout option (He et al., 2022). During this decision-making, individuals had to both recall these previous experiences, but also integrate these experiences together (He et al., 2022). In other words, participants had to recall previous trials, a process known as memory retrieval, and decide how much weight to place on recent trials compared to those further in the past, a process known as memory integration. He et al. (2022) provides a model that uses a parameter ("sigma") to represent the extent of memory integration. A large sigma represents an averaging of all experiences while a lower sigma represents less memory integration such that more recent experiences are given a larger weight in our current decision (He et al., 2022). This study is a follow-up study to our work published in He et. al. (2022) such that it uses the same procedure but introduces stress.

2.3 How Stress affects Decision-Making during Spatial Navigation

While there are many ways to measure decision-making, spatial navigation presents as a realistic model for decision-making specifically under risk and uncertainty. In a recent literature review, Maxim & Brown (2021) uniquely discuss spatial navigation through the lens of a "Schema theory," which is a theoretical framework that suggests that new experiences become integrated into a network that we can use in future similar situations. This framework would support that both memory retrieval, recalling past experiences, and memory integration, the

degree of past experiences recruited, play a key role in the generalization behind decision-making during spatial navigation. Specifically, the use of a shortcut, which requires an individual to properly integrate and weigh those routes within the environment can represent a realistic measurement of memory integration.

The current literature on how stress affects learning and spatial navigation is consistent with one another. Similarly to how stress can encourage rigid learning over flexible learning, research has shown that stress can encourage the use of familiar paths over new shortcuts (Brown et al., 2020). Since the use of shortcuts represent a form of memory integration in the context of spatial navigation, this would suggest that stress can decrease memory integration in decision-making during spatial navigation. This study, however, did not include female participants partly because of the nuances of measuring and analyzing stress which will be described later.

Studies that have used both genders have shown differing results on the effect of stress on spatial navigation between genders. As mentioned earlier, when stress was applied before encoding, females had difficulty in repeating a route a week later while males had more difficulty in flexibly navigating using landmarks a week later. Gender differences exist more broadly in the context of risk-taking, which is an important consideration for value-based decision-making. Specifically, stress has been shown to make females more risk averse and males more risk taking (van den Bos et al., 2009; Lighthall et al., 2009, 2011, Byrne et al. (2020)).

2.4 Nuances of Stress Studies

The current literature on stress studies is partially convoluted because of the nuances in the stressor, paradigm differences, and individual differences of the participants. First, the

stressor can differ based on type, duration, and timing during the experiment. Specifically, there have been conflicting results on the effect of stress when the stress is a social stressor or physiological stressor or both (Dickerson & Kemeny, 2004). Pabst et al. (2013) investigated the effect of the length of the stress exposure on decision-making. They found that performance was better for groups that performed the task five or 18 minutes after stress than either the control or 28-minute stress group (Pabst et al 2013). Paradigm differences may affect stress's impact on behavior as well. Starcke & Brand (2016) found that stress decreased decision-making performance when risk-taking was disadvantageous (i.e. penalties); however, there was no effect when risk-taking was advantageous (i.e. reward). This suggests that even subtle differences in paradigms may make it difficult to compare results between studies.

One popular theory on the effect of stress suggests that there is an inverted U-shaped relationship between cortisol and task performance (Schilling et al. 2013). Specifically, Schilling et al. (2013) administered various doses of cortisol, a hormone involved in the stress response, prior to a declarative memory task, finding that individuals with the best performance had a moderate level of cortisol whereas poor performance was from individuals with either extreme level of cortisol. Although these findings are from a memory task, they would lead us to predict an inverted U-shaped relationship for decision-making task performance as well – perhaps at least to the extent the decision-making draws on memory integration and retrieval. This also may support the discrepancies across the literature, suggesting that acute levels of stress can increase task performance and decision-making preference, while extreme levels of stress or lack of stress entirely can decrease task performance and decision-making preference (Schilling et al. 2013).

Another additional factor in the nuances of stress is how stress is measured. Specifically, whether the results of the SAM axis (i.e. heart rate, sweat conductance, and systolic blood

pressure) or HPA axis (i.e. corticosteroid such as cortisol) are measured (Porcelli & Delgado, 2017). Dickerson & Kemeny (2004)'s meta-analysis investigated the most effective practices for measuring the effect of stress, considering the differences of stressor type and duration as discussed above. They determined that cortisol is a reliable method to measure stress and that peak cortisol secretion occurs 21-40 minutes after the stressor (Dickerson & Kemeny, 2004). They also determined that it is best to collect cortisol in the afternoon, as cortisol has a diurnal cycle and begins to steadily decrease after noon (Dickerson & Kemeny, 2004).

This presents an additional caveat, however, to measuring stress as it pertains to exposure to chronic stress and gender. Specifically, those exposed to chronic stress may have decreased sensitivity and therefore release of cortisol after exposure to acute stress. Likewise, since cortisol is tightly regulated by sex hormones, gender diffrences exist. Specifically, Kudielka & Kirschbaum (2005) found that female salivary cortisol levels fluctuate throughout their menstrual cycle with cortisol levels being the highest in luteal phase then follicular then oral contraceptives. This is partially why some stress studies have only included male subjects and why we record a female's point in the menstrual phase at the time of the study.

2.5 Benefits of this study

Unlike previous decision-making spatial navigation studies, we will present an explicit choice for participants to choose between a fixed route that encourages rigid learning or a random route that encourages flexible learning. In this way, this study will have a novel and explicit measurement over the effect of stress on memory integration during decision-making. It will also fill a critical gap in the literature on how stress affects memory and learning when encoding and retrieval are inseparable. This is in direct contrast to previous studies that have

separated encoding and retrieval. This finding will be more realistic and applicable to everyday behavior. Finally, this study will also shed light on how these effects may differ between genders.

3. METHODS and MATERIALS

3.1 Participants

For this study, 82 Georgia Tech undergraduates were divided such that males and females in the stress and control group were in a roughly 1:1 ratio. All recruited participants (age 18- 23) were healthy with good vision and without previous neurological disorders. All participants were compensated with credit and a bonus payment of up to $20 depending on task performance in the decision-making phase of our task. Participants gave informed consent using procedures approved by the Georgia Tech Institutional Review Board.

3.2 Procedure

After giving consent, participants were reminded that this experiment is a stress study and were briefly explained the stress set up should they be assigned to that group. They confirmed verbally that they were willing to participate if assigned to the stress group. Participants were not told their group assignment at this time to maintain a constant level of stress across both the control and stress groups during the working memory and numeracy tasks. Throughout this study, salivary cortisol samples were collected (an average of 3-4 per participant). After providing consent, the first salivary cortisol measurement was collected. The participants then completed various questionnaires on their demographic information, stress and anxiety tendencies, sense of direction (SOD) (Hegarty et al., 2002), risk-taking preference (Blais & Webter, 2006), initial affective rating, and ability to calculate probability (Cokely et al., 2012;

Schwartz et al., 1997). The participants then completed an operation span working memory task (Unsworth et al, 2005). At this point, an additional salivary cortisol measurement was collected, and participants were assigned to either the stress or control group and asked if they were comfortable continuing the task. These two initial cortisol samples act as a baseline during analysis as treatment between conditions has not differed.

3.3 Adding Stress

In participants assigned to the stress group, two electrodes were taped to the back of the participant's left ankle, which had been exfoliated to remove any oil that could affect the flow of current. The participant was told to choose a level of stimulus that corresponded to a 7 out of 10 pain level with a 10 being the highest level of pain and 1 being the lowest level of pain.

3.4 Virtual Navigation Task and Experimental Design

3.4.1 Practice Phase

All participants then completed a practice phase in which they navigated a 4 X 4 grid of virtual rooms to learn the control scheme of the experiment. Specifically, the participant used arrow keys to navigate.

3.4.2 Fixed Phase

At this point in the task, the stress group began to experience a randomized shock. The shock was "random" to the participant but determined using a cell array in Matlab that divided time into 5-minute intervals over a 300-minute time interval. There was no pattern to the shock delivery, so the participant was not aware of when a shock would be delivered, and no more than

a total of 6 shocks would be delivered over the course of the experiment. This shock continues throughout the Fixed phase, Random phase, and Decision-Making phase. Every 30 minutes from the onset of shock, cortisol samples are collected. The time to complete all three tasks varies individually, but on average 3-4 samples including the 2 baseline are collected.

Using arrow keys, the same control scheme as the practice phase, all participants then completed the Fixed Phase of the experiment. The participants navigated a 6 X 6 grid of virtual rooms starting from the same position after each trial (Figure 1A). In each room, there was an object such as a toy, furniture or car that was unique to only that room. Two global landmarks (cactus and tower) were located on the North and West sides of the environment (Figure 1A). The Fixed Phase had a total of 6 trials with 2 trials for each goal object. The participants were told that they would be looking for three goal objects (apple, banana, watermelon) labeled T1-T3 in Figure 1A. The participants were told that the goal object position would not change, and the goal object would only appear in its room when they were searching for it (to avoid them experiencing both goals in the same navigational memory as they learned). After finding the goal object, the participants were automatically brought back to their original starting position, which is labeled “S” in Figure 1A and asked to find the next goal object. The goal object order was the same for all participants. On average, this phase took about 10 to 15 minutes.

3.4.3 Random Phase

All participants then completed the Random Phase of the experiment. The participants were told that the phases only differed in that they would start in a random room rather than the original starting place labeled “S” in Figure 1A. This phase also had six trials with two for each goal object. The goal object order was pseudorandomized so that it could not be predicted which

goal object the participant would be instructed to find next. On average, this phase took about 10 to 15 minutes.

3.4.4 Decision-Making Phase

After completing the random phase, all participants then completed the Decision-Making Phase. This phase is in the same virtual environment with the same three goal objects. Participants were instructed that they would start with $20 and over the course of thirty trials, they would be given the choice to choose between the "fixed" option or the "random" option (Figure 1B). The participant is told they would lose 1 cent per second in the fixed option and a lesser amount per second in the random option, which is calculated on an individual basis from their performance during the fixed and random phases such that the random option is always a more enticing yet riskier option. The participant is told that at the end of the thirty trials, the participant would receive both the remaining money and the course credit. The participant is only penalized during the time searching for the goal object and not in the feedback during decision-making (Figure 1B).

Once completing the Decision-Making Phase, participants then completed a final affective response questionnaire in which they reported their current ratings of safety and anxiety levels.

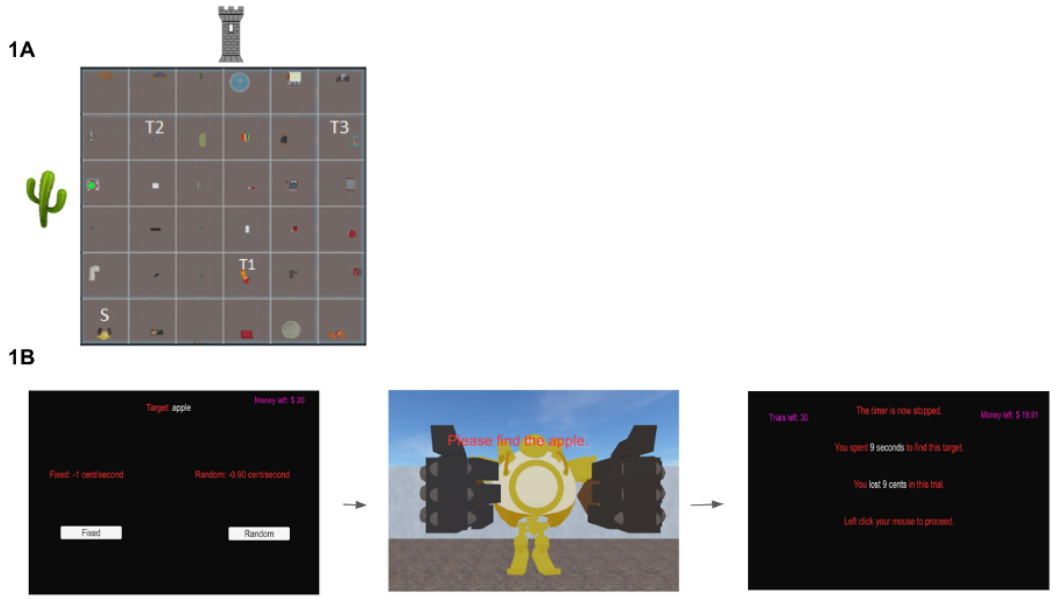


Figure 1. Image of Navigational Task and Prompts in the Decision-Making Phase

1A: *This is a bird's eye view of the 6 by 6 environment. "S" represents the starting point where the participants begin in the fixed phase. "T1", "T2", and "T3" represent the rooms in which goal object 1, 2, and 3, respectively, can be found.*
1B: *This is the sequence of screens a participant views in the Decision-Making Phase of the experiment. The participant will be prompted to choose from either "fixed" or "random". The participant can also observe the target object and the corresponding penalty for the fixed and random option. The participant is then placed in the environment as seen in the second image. The third image represents the screen visible once the participant finds the object. It displays the amount of time it took them to find the object and the amount of money they lost.*

4. RESULTS

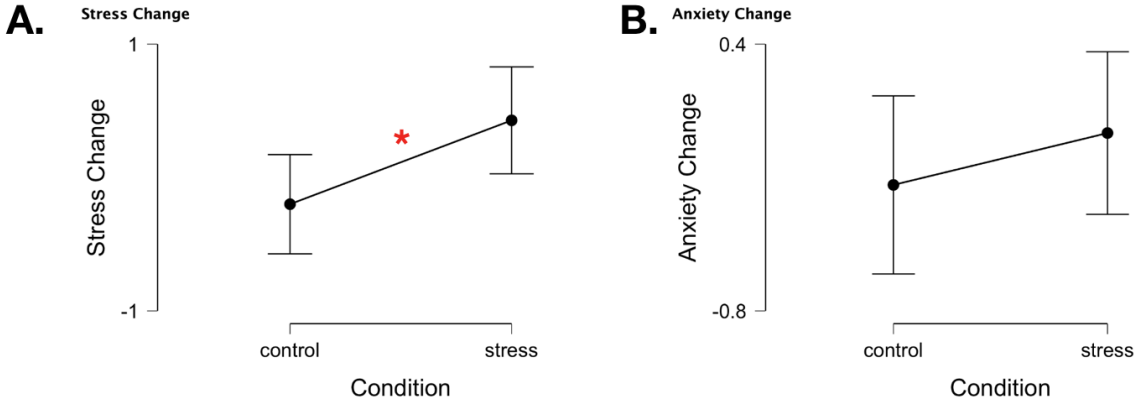
We used JASP (JASP Team, 2020) for statistical analyses.

4.1 Measuring and Validating Stress

We completed two types of analyses to validate the presence of stress. First, an affective valence measurement represented the perceived psychological effects of the stressor. Second, cortisol measurements before and throughout the task measured the physiological effects.

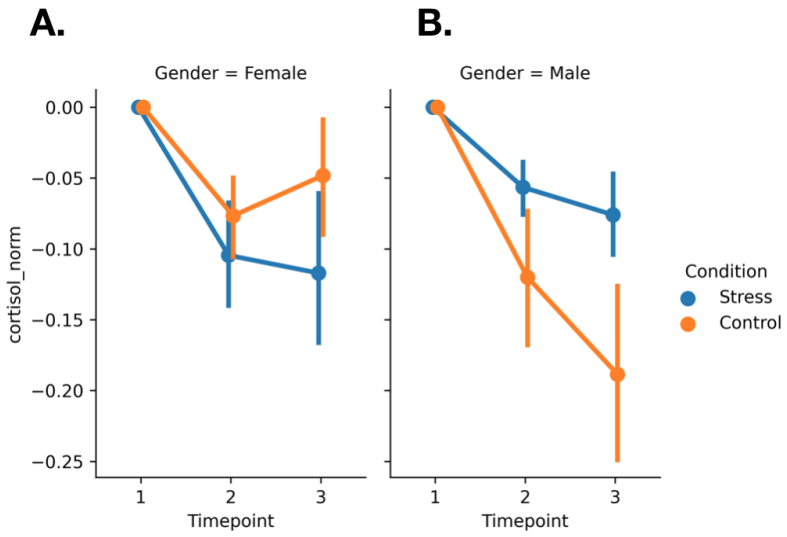
We used a t-test that compared the change in reported stress and anxiety between the stress and control conditions. Participants in the stress condition reported feeling both more stressed (t[56]= 2.357, p=0.022) and more anxious (t[56] = 0.877, p =0.384) after the experiment than before (Figure 2) (see Supplementary Table 1). Although only the change in reported stress was significant.

Figure 2. Change in Negative Affective Valence between Control and Stress Groups



This figure shows the difference in reported affective valence of stress and anxiety levels before and after the task.
2A: *The stress group had a significantly increased subjective change in stress (Supplementary Table 1).*
2B*: The stress group had a nonsignificant increase in anxiety levels compared to the control group (Supplementary Table 1). The error bars indicate the standard error of the mean, and * = $p < 0.05$, ** = $p < 0.01$, ***=$p < 0.001$.*

Figure 3. Salivary Cortisol: Physiological Measurement of Stress



Descriptive Statistics

	Cortisol_diff_2	
	control	stress
Valid	7	3
Missing	1	0
Mean	−0.064	−1.000e −3
Std. Deviation	0.058	0.044
Minimum	−0.163	−0.034
Maximum	0.012	0.049

3A: *This graph displays the cortisol levels in females for each timepoint 1, 2, and 3 in both the stress and control group. This shows that females in the control group had higher cortisol levels than females in the stress group. Timepoint 1 and 2 are both baseline measurements because they are prior to stress onset while timepoint 3 occurs during stress. Some participants reached timepoint 4, which was 30 minutes after timepoint 3 during stress, but this data was not included because too few participants reached this point, making the data noisy and unreliable.*
3B: *This graph displays the cortisol levels in males for each timepoint 1, 2, and 3 in the stress and control group. Note: There were no males that had a fourth cortisol collection in the stress group, so ut this data was not included because too few participants reached this point, making the data noisy and unreliable.*
3C: *This table is a subset of the females, who reported being in the Luteal phase of their menstrual cycle. This table shows the mean change in cortisol difference 2, which is the difference in cortisol values between timepoint 3 and timepoint 2. This shows that the control group had a larger decrease in cortisol than the control group.*

Salivary cortisol was used as the physiological measurement for stress. As described in the Methods section, there were four timepoints for cortisol with Timepoint 1 and 2 before stress onset and Timepoint 3 and 4 being 30 minutes or an hour after stress onset, respectively. Specifically, Timepoint 1 occurred after the participants signed the consent forms and Timepoint 2 occurred roughly 45 minutes later after the participant completed questionnaires and a memory

task, but prior to knowing their condition, so therefore both act as baseline. Not every participant had four time points if they finished the navigation task prior to timepoint 4, so this metric is noisy and not pictured in Figure 3. The salivary cortisol trends differed between genders. Females in the control group had higher cortisol levels than those in the stress group (Figure 3A) while males in the stress group had higher cortisol levels throughout the experiment than males in the control group (Figure 3B). There were seven females in the control group and three in the stress group who reported being in the luteal phase of their menstrual cycle. The second cortisol difference (Figure 3C) represents the difference in cortisol between timepoint 3 and 1, which would be the first difference that would show the effect of stress. This subset of females in the control group had a larger decrease in cortisol levels than those in the stress group, which is qualitatively consistent with the cortisol pattern seen in males (a diurnal drop in cortisol in controls that is counteracted in the stress group).

4.2 Effect of Stress on Rigid and Flexible Learning Between Genders

This navigational task has three different phases. The first phase, the Fixed Phase, measures rigid learning. The second phase, the Random Phase, measures flexible learning. The third phase, the Decision-Making Phase, measures decision-making. To measure learning, we used the dependent variable Excessive Distance. This variable is the number of extra rooms traveled when a participant goes from the starting position to the goal object. For example, if traveling to the apple from the starting position and the shortest possible path was 5 rooms and a participant traveled through 9 rooms, their excessive distance would be 4. We labeled males as 1 and females as 2. We split by both condition and gender to measure the excessive distance in both the Fixed Phase (Trials 1-6) to represent the effect of stress on rigid learning and in the Random Phase (Trials 7-12) to represent the effect of stress on flexible learning.

In an ANOVA, in both the Fixed phase and Random phase, we found a significant difference in excessive distance between genders. Females had a significantly larger excessive distance regardless of the presence of stress (Supplementary Table 2A). In the Fixed Phase, we found a significant interaction between gender and condition. Specifically, excessive distance significantly increased in females (Figure 2A, Supplementary Table 2A). This interaction between gender and condition was significant (p=0.40, Supplementary Table 2). However, we did not find a significant interaction between condition and gender in the Random Phase, representing flexible learning (Figure 2A, Supplementary Table 3A). In the Random Phase, we observed a downward trend in that stress seemed to decrease excessive distance in both males and females (Figure 4).

Figure 4. Effect of Stress on Excessive Distance between genders in Fixed and Random Phase

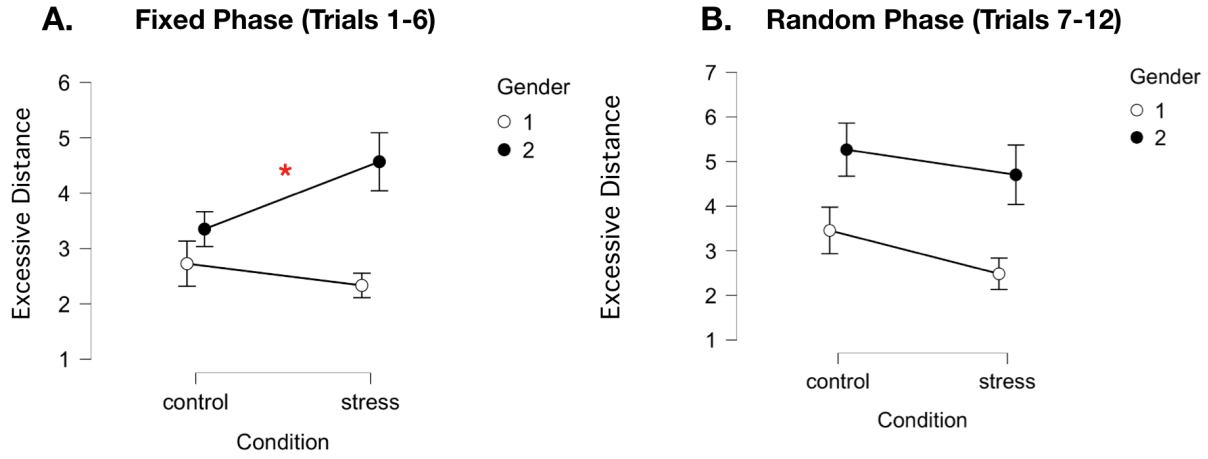


Figure 4. Excessive Distance in the Fixed Phase (Trials 1-6) and Random Phase (Trials 7-12). ***4A:*** *This figure displays the excessive distance in the Fixed Phase separated by gender and condition. The interaction between condition and gender was significant in the fixed phase. Specifically, there was a significant difference between females and males in the stress group, such that females had a significantly larger excessive distance than males (Supplementary Table 2).*
4B: *This figure displays the excessive distance in the Random Phase separated by gender and condition. The interaction between condition and gender was not significant in the random phase. However, there was a significant difference between genders in both the Fixed Phase and*

*Random Phase (Supplementary Table 2). The error bars indicate the standard error of the mean, and * = p < 0.05, ** = p < 0.01, ***=p < 0.001.*

Since the first three trials of the fixed phase are the first time the participant is navigating to each goal object, pure chance may play a role and as such their path and excessive distance are less representative of learning. Rather a more representative measure of learning may be the excessive distance in trials 3-6 of the Fixed Phase. Observationally, the trend became more distinct as can be observed when comparing Figure 5A and Figure 5B. Specifically, Figure 5B shows that females' excessive distance increases under stress while the opposite appears in males. However, this interaction between condition and gender is not significant (p=0.051, Supplementary Table 4B). There is a significant difference in the gender differences, however (p=0.010, Supplementary Table 4B).

Figure 5. Effect of Stress on Excessive Distance between genders in Beginning and End of Fixed Phase

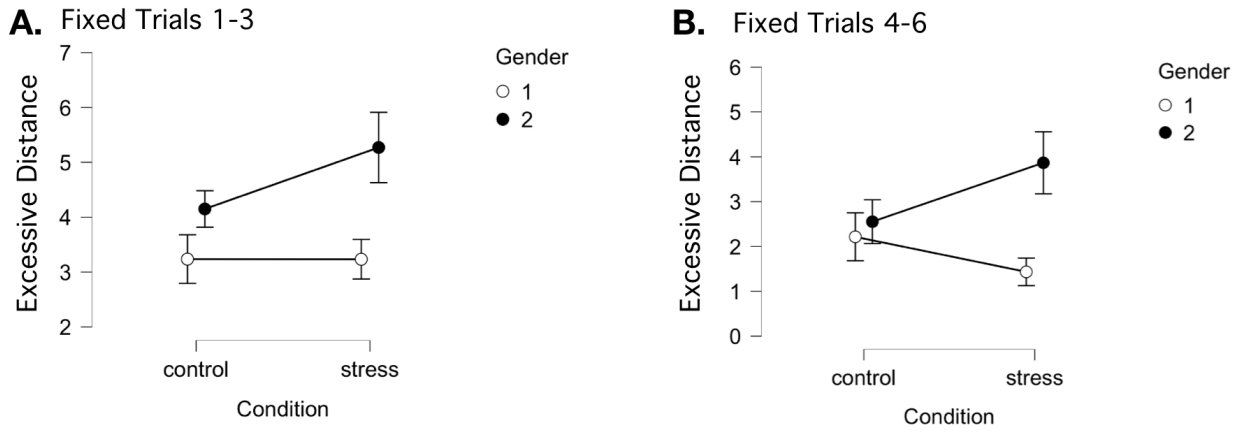


Figure 5. Excessive Distance Between Genders in the Beginning of Fixed Phase (Trials 1-3) and the End of Fixed Phase (Trials 4-6).

4A: *This shows the excessive distance in the first three trials of the Fixed Phase split by gender and condition. While there was a significant difference in the excessive distance between genders (p=0.002) (Supplementary Table 4), there was not a significant interaction between gender and condition.*

4B: This shows the excessive distance in the second three trials of the Fixed Phase split by gender and condition. While there was a significant difference in the excessive distance between

genders (p=0.010), there is not a significant difference between condition and gender (p=0.051) (Supplementary Table 4). The error bars indicate the standard error of the mean.

The second phase, the Random phase, measures flexible learning. Like in the Fixed Phase, the Random Phase was split into two halves to check for differences. While there were no significant findings, both had similar trends in that males had lower excessive distance than females and the stress group had lower excessive distance than the control group (Figure 5). The difference in excessive distance between genders in trials 10-12 was significantly different ($p<0.001$) (Supplementary Table 3).

Figure 6. Effect of Stress on Excessive Distance between genders in Beginning and End of Random Phase

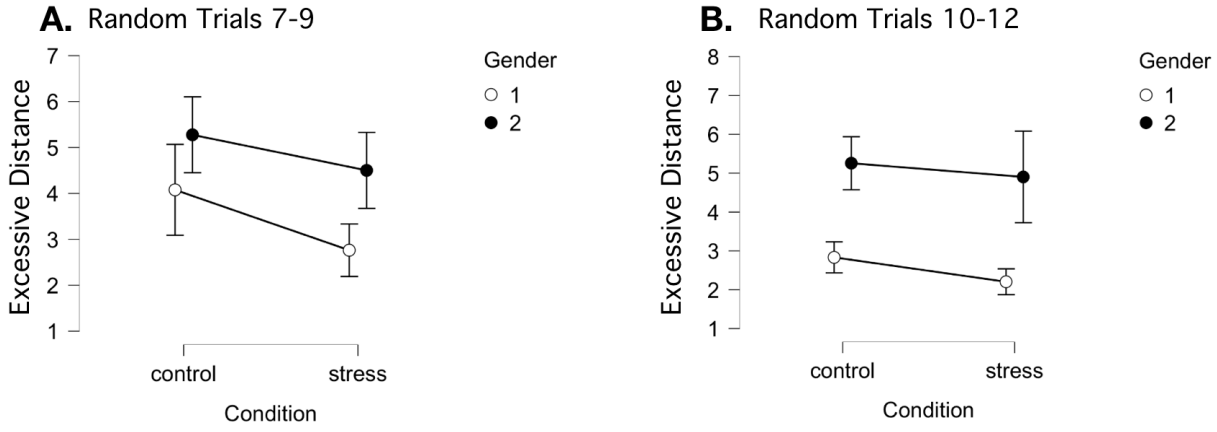


Figure 6. Excessive Distance Between Genders in the Beginning of Random Phase (Trials 7-9) and the End of Random Phase (Trials 10-12).
6A: This shows the excessive distance for the first half of the Random Phase split by gender and condition. There was not a significant interaction between gender and condition.
*6B: This shows the excessive distance for the second half of the Random Phase split by gender and condition. While there was not a significant interaction between gender and condition, there was a significant difference between genders ($p<0.001$). The error bars indicate the standard error of the mean, and * = $p < 0.05$, ** = $p < 0.01$, ***=$p < 0.001$.*

4.3 How stress affects memory integration during decision making

The third phase of the experiment was the Decision-Making Phase. Using a computational model, sigma, a parameter that represents the degree of past experiences

integrated, was calculated for each participant. In an ANOVA, we found that sigma was significantly lower for individuals in the stress group than individuals in the control group (p=0.002) (Figure 7 and Supplementary Table 5). We found males and females did not statistically differ in their sigma for each respective condition.

Figure 7. Effect of Stress on Memory Integration measured by Sigma

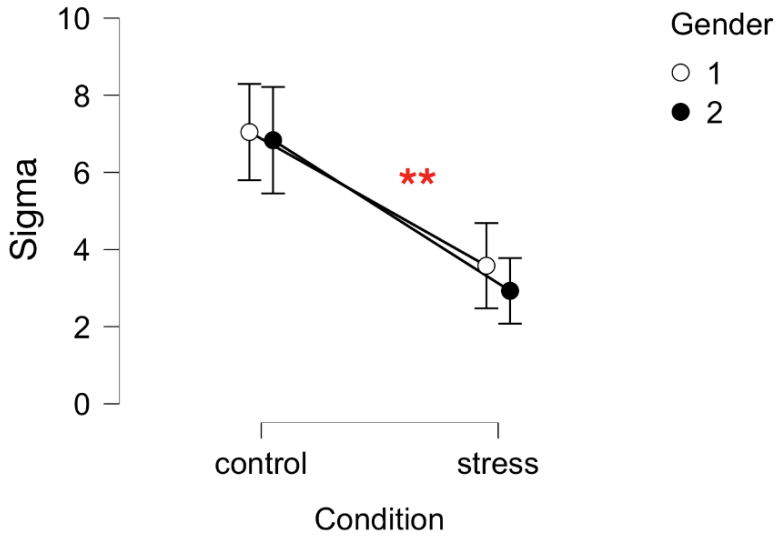


Figure 7. Effect of Stress on Memory Integration measured by Sigma. *The stress group had a statistically smaller sigma than the control group (p=0.002) (Supplementary Table 5).*

4.4 Stress decreases decision time

In an ANOVA, in the Decision-Making Phase, the stress group had a significantly lower decision time than the control group (p=0.010, Supplementary Table 6) (Figure 8). Decision time was measured by the time it took for the participant to choose either "Fixed" or "Random" in the Decision-Making Phase. There was also a significant difference between genders (p=0.019, Supplementary Table 6), in that males were significantly faster than females regardless of the condition (Figure 8).

Figure 8. Stress Decreases Decision-Time

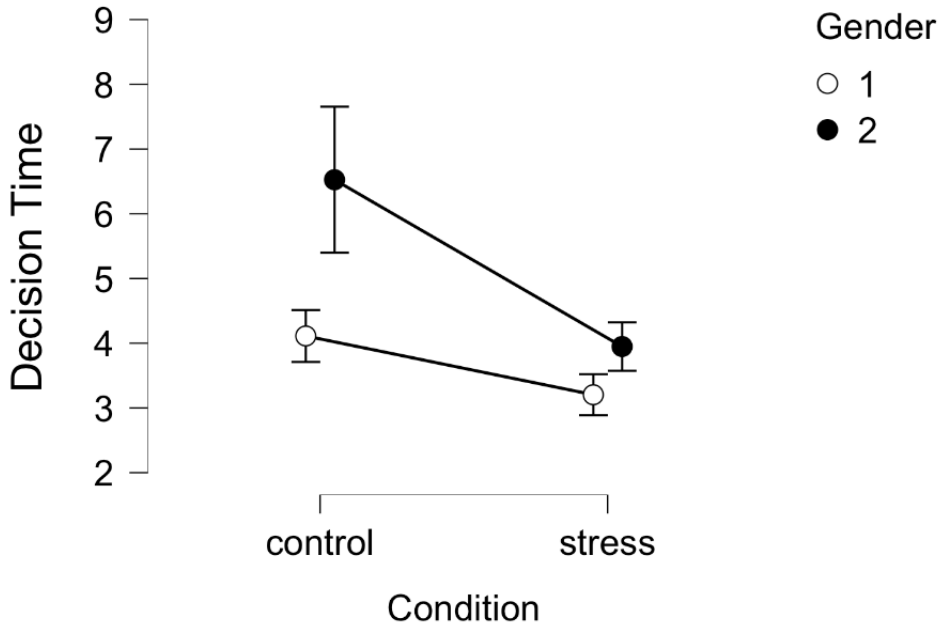


Figure 8. Stress Decreases Decision-Time. *The stress group had a significantly faster decision time than the control group (p=0.010, Supplementary Table 6). Males had significantly faster decision time regardless of condition than females (p=0.019, Supplementary Table 6).*

4.5 The relationship between decision time and memory integration

Decision time and sigma both decrease in the stress group with a significant correlation ($r=0.364$, $p<0.001$, Supplementary Table 7). To investigate the directional effect of stress on decision time and sigma, a mediation analysis was completed. The direct effect of the condition predicting sigma was significant ($p=0.013$). The indirect effect of decision time playing a mediator role in that condition predicts decision time which predicts sigma was almost significant ($p=0.054$). The final effect of condition predicting sigma was significant ($p=0.001$) (Supplementary Table 8).

4.6 Stress does not change risk taking

Risk-taking was operationally defined as the percent that the individual chose “random” in the Decision-Making Phase. In an ANOVA, there was not a statistical difference in the random percentage between conditions or gender (Figure 9).

Figure 9. Percent "Random" chosen in Decision-Making Phase between Gender in each Condition

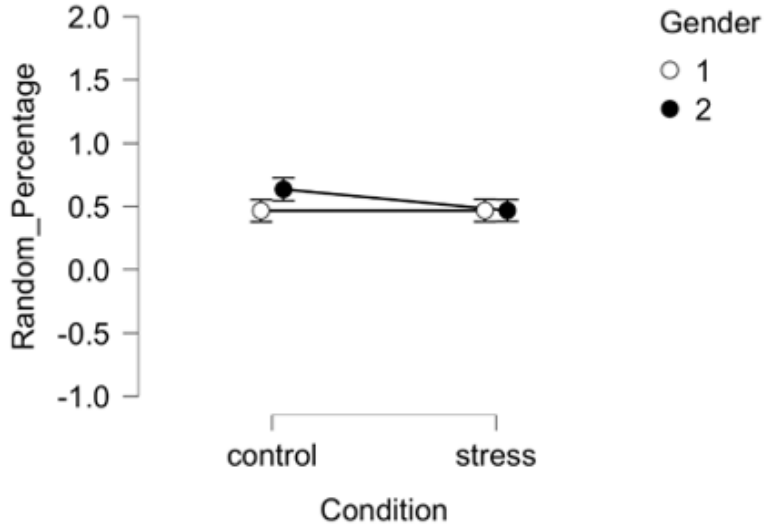


Figure 9. Percent Random chosen in Decision-Making Phase between Gender in each Condition. *Random percentage represents the percent the participant chose "Random" in the decision-making phase. Using an ANOVA, there was not a statistical difference between males and females or participants in the control and stress group. Males are coded as 1 and females are coded as 2, and the error bars indicate the standard error of the mean,*

5. DISCUSSION

This is the first study of our knowledge that investigates how concurrent acute stress affects learning and the subsequent memory integration during decision making. Rather much of the previous literature has focused on how stress affects learning either during encoding or retrieval. However, in everyday decisions, there is often not a distinction between encoding and retrieval, thus the findings of this study are more realistic. Likewise, research on decision-making has focused around memory retrieval rather than also measuring or controlling for the simultaneous process of memory integration.

There were four major findings of this study. As it pertains to learning, we found that (1) acute stress disrupted rigid learning in females but not in males while (2) acute stress improved flexible learning in both genders. During decision-making we found that (3) acute stress

decreased memory integration during decision-making in both genders and (4) acute stress did not affect risk taking in either gender.

5.1 Validation of stress

To validate the exposure of stress via an electrical shock, we measured both physiological and psychological levels of stress using affective valence responses and salivary cortisol respectively. Both of these measurements presented conflicting and unexpected results. First, the stress group had a significantly greater reported change in levels of stress ($p=0.022$, Supplementary Table 1) and while the reported change in anxiety levels for the stress group increased, it was not significant (Supplementary table 1).

Similar to affective valence, the salivary cortisol had unexpected and surprising findings. While the stress condition in males showed greater cortisol levels as would be expected (Figure 3A), females had the opposite trend in that those in the control group had higher cortisol levels (Figure 3B). This cortisol trend in males is similar to Brown et al. 2020. These conflicting findings in females may be due to hormonal fluctuations as levels of cortisol can vary throughout a female's menstrual cycle. Specifically, Kudielka & Kirschbaum (2005) found that unlike women in the follicular phase or those taking oral contraceptives, women in the luteal phase had similar salivary cortisol responses to males. To observe whether this was true in our study, we compared the change in cortisol from timepoint 3 and timepoint 4 from timepoint 1, the baseline. While the sample size is small (seven females in the control group and three in the stress group), we found similar trends to males looking at the first difference from timepoint 3 and conflicting trends looking at timepoint 4. While these indescrepencies may be due to hormonal fluctuations, the length of the study could also explain this. Individuals that require a timepoint 4 take longer to navigate the experiment, suggesting they may have impaired spatial navigation, which could

increase frustration and general stress regardless of condition assignment. Nonetheless, these cortisol findings question the effect of stress throughout the experiment, and also highlight the difficulty of stress studies specifically as it pertains to the analysis for females.

5.2 Stress may disrupt rigid learning in females but not males

Our first major finding showed that acute stress disrupted rigid learning in females but not in males. Specifically, females in the stress group had a significantly larger excessive distance than males in the stress group ($p_{tukey}<0.001$, Figure 4 & Supplementary Table 2). The Fixed Phase of our paradigm occurs over the first six trials of the navigational task, forcing participants to find each goal object twice (Figure 1). It starts the participants in the same starting position, so for this reason, it encourages repetitive routes and can serve as a model for rigid learning. Excessive distance measured the degree of learning with a lower excessive distance representing a greater understanding of the route and environment. Both males and females had a similar excessive distance in the control group (Figure 4); however, under stress females had a significantly higher excessive distance than males. Overall, this suggests that acute stress may impair rigid learning in females but not in males.

A study by Guenzel et al. (2014) found similar findings. In their study they applied stress to males and females before encoding in a navigational task and found that females performed significantly worse in repeating a learned route a week later. Our study confirms and expands on this finding to suggest that acute stress impairs rigid learning in females not only when the stress occurs before encoding and measured during retrieval but also when the stress is concurrently applied during both encoding and retrieval.

However, there is a limit to the conclusivity of these findings. Since the first three trials of the fixed phase were the first time the participant navigated this environment for these objects,

their path could be due to random chance rather than learning. When we controlled for this and only analyzed trials 4-6, our findings were less conclusive. We observed the same trend that females in the stress group had a larger excessive distance than males in the stress group (Figure 5B); however, this was not significant, although barely ($p=0.51$) (Supplementary Table 4). This could become significant if the number of participants and trials increased to control for individual variation.

5.3 Stress was not found to affect flexible learning in either gender.

Although acute stress impacted rigid learning in females, it did not seem to impact flexible learning differently between genders. We found a significant difference in excessive distance between males and females ($p<0.001$); however, we found this difference remained constant whether or not stress was applied (Figure 4B, Supplementary Table 2). Although not significant, the acute stress decreased the excessive distance in both genders (Figure 4B). While the results were not significant, individuals exposed to acute stress had a lower excessive distance, suggesting that acute stress may improve flexible learning in both genders.

A study by Guenzel et al. (2014) applied stress before encoding found that males exposed to acute stress had impaired spatial memory that relied on local landmarks a week later after stress exposure. Our finding suggests that the specificity of the timing in encoding rather than concurrently in both encoding and retrieval may explain the impact of flexible learning in males.

5.4 Stress was found to decrease memory integration in both genders.

The findings above have used the first two phases, the Fixed and Random Phases, to focus on the impact of acute stress on rigid and flexible learning and how these effects may differ between genders. The following phase, the Decision-Making Phase, allows us to uniquely

measure how the impact of stress on learning may impact decision-making during spatial navigation.

We found that sigma, the parameter that measures memory integration, was significantly lower for both males and females that were exposed to acute stress ($p=0.002$) (Figure 7, Supplementary Table 5). This suggests that stress may cause both males and females to use more recent experiences than those further in the past during their decision-making. We also found that sigma was significantly correlated with decision time ($p<0.001$, Supplementary Table 7). We measured decision-time as the time it took for a participant to choose either Fixed or Random during the Decision-Making Phase (Figure 1B). We also found that individuals in the stress group had a significantly lower decision-time than those in the control group ($p=0.010$, Figure 8, Supplementary Table 6).

Due to similar trends between sigma and decision time in the stress group compared to the control group, we ran a mediation analysis to determine the causal direction of these trends. We found that the direct effect of condition on sigma was significant ($p=0.013$, Supplementary Table 8) while the indirect effect of condition on decision time on sigma was not significant, although barely ($p=0.054$, Supplementary Table 8). These findings suggest that while acute stress also decreases decision-time, it is the stress exposure that is causing the decrease in memory integration during decision-making for both genders.

Many studies have found that stress impairs memory retrieval (Vogel & Schwabe, 2016) but have not measured its effect on memory integration. However, any decision-making requires both memory retrieval and memory integration. Therefore, this finding that stress decreases the extent of memory integration in both genders fills a clear gap in the literature.

These findings have major implications on how stress may disrupt decision-making. First, spatial navigation offers a realistic way to measure decision-making. In the spatial navigation literature in mouse models, there is evidence that planning does in fact occur. Specifically, place cells in the hippocampus and head direction cells may play a role in our egocentric framework (Knierim et al. 1995) and grid cells in the entorhinal cortex may play a role in a more allocentric framework like a cognitive map (Shine et al. 2019). Wikenheiser and Redish (2015) found that place cells fire sequentially and prospectively, giving evidence that there is a level of planning during spatial navigation that could aid decision-making. To replicate these findings in humans, Brown (2016) used machine-learning in a spatial navigation task that found that the posterior hippocampus and areas in the prefrontal cortex were involved in prospective planning. Gagnon et al. (2018) expanded on these findings to find that this hippocampal prefrontal network was disrupted under stress.

Even further, spatial navigation acts as a realistic way to measure memory integration during decision-making because the ability to navigate a shortcut can operationalize the degree of memory integration as an individual must adequately recall routes and place weight on which might give the greatest reward. Brown et al. (2020) found that healthy young adults successfully navigate these shortcuts; however under stress, these adults take the longer more familiar routes. From fMRI data, we know that the frontal precortex is involved in short cuts, and there is less frontopolar cortex (FPC) activity in the stress groups that use familiar routes (Brown et al., 2020). Our new findings of memory integration validate these findings that stress disrupts planning during decision-making. One possible explanation could be that participants in the stress group have less time to recall these memories, therefore they rely on their more recent experiences before making a decision.

5.5 Stress was not found to impact risk taking in either gender

We measured risk-taking by looking at the percentage that individuals choose "Random" in the decision-making task since this choice was of higher risk. We found no significant difference in the percentage that "Random" was chosen between gender or condition (Figure 9). This suggests that at least in our paradigm, acute stress did not seem to impact risk-taking. To expand on this further, it is not risk-taking that is explaining the decrease in memory integration during acute stress exposure.

This finding adds to the inconclusive nature of research on the effects of acute stress on risk-taking in both genders. Specifically, some studies have found that stress may cause females to become more risk-averse while it causes males to become more risk-taking (van den Bos et al., 2009; Lighthall et al., 2009, 2011).

Future studies could repeat this methodology and include imaging to further investigate the neural mechanisms behind memory integration. These studies would expand on the existing literature on how stress disrupts planning in the FPC and may add to whether memory integration occurs in the FPC. These imaging studies could also investigate how stress impacts the neural mechanism of fixed learning differently between genders. Future studies could also collect more participants, especially females to further investigate how different phases of the menstrual cycle and cortisol fluctuations impact these findings.

6. CONCLUSION

This study uses spatial navigation to investigate how acute stress impacts learning and decision-making. The results of this study suggest that while acute stress may disrupt fixed learning in females, acute stress may improve flexible learning and decrease the degree of memory integration in the subsequent decision-making in both genders. These findings seem to

validate literature that acute stress may disrupt fixed learning in females more so than males. These findings also validate a more conclusive finding amongst stress and spatial navigation that acute stress disrupts the degree of planning during decision-making. Future research could pair this task with fMRI imaging to determine the neural activity behind memory integration.

However, there are limitations to this study. While the psychological measurements validate the experience of stress and cortisol trends in males are consistent with previous literature, the female cortisol data is noisy and unexpected. More female participants in each phase of the menstrual cycle are needed to conclusively say whether females experienced the physiological effects of stress. Likewise, more participants are needed to investigate stress's effect on females during fixed learning.

7. SUPPLEMENTARY TABLES

Supplementary Table 1. T-test for Change in Stress and Anxiety Affective Valence Between Conditions

Independent Samples T-Test

	t	df	p
Stress Change	−2.357	56	0.022
Anxiety Change	−0.877	56	0.384

Note. Student's t-test.

Supplementary Table 1. Student's t-test between the change in mean post- affective stress valence and mean pre- affective stress valence for the stress group. *The change in stress levels for the stress group was significant; however, the change in anxiety levels was not, although anxiety levels did increase in the stress group.*

Supplementary Table 2. ANOVA: Excessive Distance in the Fixed Phase and Random Phase

A. ANOVA: Excessive Distance in Fixed Phase

Cases	Sum of Squares	df	Mean Square	F	p
Condition	3.486	1	3.486	1.141	0.289
Gender	41.912	1	41.912	13.713	< .001
Condition ∗ Gender	13.274	1	13.274	4.343	0.040
Residuals	238.408	78	3.057		

Note. Type III Sum of Squares

B. Post Hoc Comparison: Interaction of Condition and Gender

Post Hoc Comparisons – Condition ∗ Gender

		Mean Difference	SE	t	p_{tukey}
control, 1	stress, 1	0.392	0.553	0.710	0.893
	control, 2	−0.625	0.546	−1.145	0.663
	stress, 2	−1.843	0.546	−3.374	0.006**
stress, 1	control, 2	−1.018	0.546	−1.863	0.252
	stress, 2	−2.235	0.546	−4.092	< .001***
control, 2	stress, 2	−1.217	0.540	−2.256	0.117

Note. P-value adjusted for comparing a family of 4
* p < .05, ** p < .01, *** p < .001

2A: ANOVA for excessive distance in the Fixed Phase. *The difference in excessive distance between males and females is significant (p<0.001). The interaction between the condition and gender is significant (p=0.040).*
2B: Post Hoc Comparison for the interaction between condition and gender. *Females, labeled 2, under stress compared to males, under stress, were significantly different (p<0.001).*

Supplementary Table 3. ANOVA for Excessive Distance in Random Phase

ANOVA – Random_ED

Cases	Sum of Squares	df	Mean Square	F	p
Condition	12.080	1	12.080	1.937	0.168
Gender	83.185	1	83.185	13.340	< .001
Condition ∗ Gender	0.852	1	0.852	0.137	0.713
Residuals	486.388	78	6.236		

Note. Type III Sum of Squares

Table 3. ANOVA for excessive distance in the Random Phase. *There was a significant difference in excessive distance between males and females in the Random Phase (p<0.001). However, the interaction between condition and gender was not significant.*

Supplementary Table 4. ANOVA for Excessive Distance in the first half of Fixed Phase and the random half of the Fixed Phase

A. ANOVA: Excessive Distance in Trials 1-3 of Fixed Phase

Cases	Sum of Squares	df	Mean Square	F	p
Condition	6.404	1	6.404	1.457	0.231
Gender	44.585	1	44.585	10.141	0.002
Condition ∗ Gender	6.465	1	6.465	1.470	0.229
Residuals	342.934	78	4.397		

Note. Type III Sum of Squares

B. ANOVA: Excessive Distance in Trials 4-6 of Fixed Phase

Cases	Sum of Squares	df	Mean Square	F	p
Condition	1.449	1	1.449	0.254	0.616
Gender	39.323	1	39.323	6.886	0.010
Condition ∗ Gender	22.507	1	22.507	3.942	0.051
Residuals	445.398	78	5.710		

Note. Type III Sum of Squares

4A: ANOVA for excessive distance in the first half of the Fixed Phase. *There was a significant difference between genders (p=0.002). The interaction between condition and gender is not significant.*

4B: ANOVA for excessive distances in the second half of the Fixed Phase. *There was a significant difference between genders (p=0.010). The interaction between condition and gender is almost significant (p=0.051).*

Supplementary Table 5. ANOVA for Sigma between Gender and Condition during Decision-Making Phase

ANOVA: Sigma

Cases	Sum of Squares	df	Mean Square	F	p
Condition	278.191	1	278.191	10.064	0.002
Gender	3.816	1	3.816	0.138	0.711
Condition ∗ Gender	0.991	1	0.991	0.036	0.850
Residuals	2156.051	78	27.642		

Note. Type III Sum of Squares

Table 5. ANOVA for Sigma between Gender and Condition during Decision-Making Phase*. The stress group had a significantly smaller sigma than the control group (p=0.002). There was*

no statistical difference in sigma between genders (p=0.711) and there was not a significant interaction of condition and gender (p=0.850).

Supplementary Table 6. ANOVA for Decision Time between Gender and Condition during Decision-Making Phase

ANOVA - Decision_Time

Cases	Sum of Squares	df	Mean Square	F	p
Gender	51.087	1	51.087	5.751	0.019
Condition	62.195	1	62.195	7.001	0.010
Gender ✻ Condition	14.271	1	14.271	1.606	0.209
Residuals	692.908	78	8.883		

Note. Type III Sum of Squares

Table 6. ANOVA for Decision Time between Gender and Condition during Decision-Making Phase. *There was a significant difference in decision time for both gender (p=0.019) and condition (p=0.010). There was not a significant interaction of condition and gender (p=0.209).*

Supplementary Table 7. Correlation between Sigma and Decision Time

Pearson's Correlations

Variable		Sigma_best	Decision_Time
1. Sigma_best	Pearson's r	—	
	p-value	—	
2. Decision_Time	Pearson's r	0.364	—
	p-value	< .001	—

Table 7. Correlation between Sigma and Decision Time. *There was a significant positive correlation between sigma and decision time in that both decreased in the stress group compared to the control group.*

Supplementary Table 8. Mediation Analysis between Condition, Decision Time and Sigma

Direct effects

							95% Confidence Interval	
			Estimate	Std. Error	z-value	p	Lower	Upper
Condition	→	Sigma_best	−2.803	1.127	−2.488	0.013	−5.012	−0.595

Note. Delta method standard errors, normal theory confidence intervals, ML estimator.

Indirect effects

									95% Confidence Interval	
					Estimate	Std. Error	z-value	p	Lower	Upper
Condition	→	Decision_Time	→	Sigma_best	−0.887	0.461	−1.924	0.054	−1.791	0.017

Note. Delta method standard errors, normal theory confidence intervals, ML estimator.

Total effects

							95% Confidence Interval	
			Estimate	Std. Error	z-value	p	Lower	Upper
Condition	→	Sigma_best	−3.690	1.134	−3.255	0.001	−5.912	−1.468

Note. Delta method standard errors, normal theory confidence intervals, ML estimator.

Table 8. Mediation Analysis between Condition, Decision Time and Sigma. *The direct effect of the condition on sigma was significant (p=0.013). The indirect effect of decision time on sigma was almost significant (p=0.054). The total effect of the condition on sigma was significant (p=0.001).*

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