RESEARCH

Changes in Working Memory Performance Over an Academic Semester in Student Pharmacists

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Submitted August 10, 2018; accepted April 22, 2019; published December 2019.

Objective. To preliminarily assess changes in Doctor of Pharmacy students’ working memory performance over the course of an academic semester and to determine whether any observed changes were associated with fluctuations in stress and fatigue.

Methods. Twenty-three PharmD students were recruited for this pilot study. At baseline, data were collected on students’ personality, stress, fatigue, and working memory performance using two measures, the operation span and the symmetry span. Approximately every four weeks throughout the semester students’ fatigue and stress levels were reassessed and they completed the two measures of working memory. A repeated measures analysis of variance was used to assess trends over time, and correlation analysis was used to assess potential relationships between working memory and other variables.

Results. The operation span, a measure of general working memory resources, showed a significant quadratic trend over time. Irrespective of time, some associations between working memory performance and fatigue were seen. Significant correlations between fatigue and the extraversion personality trait were identified. The symmetry span, a measure of visuospatial resources, did not show trends over time nor did it correlate with fatigue, stress, or personality factors.

Conclusion. Pharmacy students’ working memory performance may fluctuate over the course of a semester, but more research is needed to identify factors that may influence this fluctuation.

Keywords: working memory, fatigue, stress, personality

INTRODUCTION

Michael is sitting in his pharmacotherapy class listening to the instructor and simultaneously taking notes. This requires Michael to hold information in his memory of what the instructor is saying while trying to record what the instructor said just seconds prior. A similar situation may arise when Michael is receiving instructions or studying for an examination, ie, he needs to hold information in his short-term memory while attempting to do something else. The ability to hold information in short-term memory temporarily is a function of working memory performance. For this study, we focused on working memory performance over the course of a semester because working memory performance is one of the primary cognitive factors that underpin thinking and learning and is a significant predictor of academic success.1,2 The primary question of interest in this study was whether working memory performance changes over the course of the semester, and if so, do those changes correlate to changes in stress and fatigue.

Working memory (or short-term memory) is the component of human memory that allows for temporary storage and executive manipulation of information.3 It is the mind’s workbench, a place where information can be used and manipulated. Working memory can be separated into two distinct processes that vary from person to person: controlled attention allows a person to focus on relevant information, while controlled search allows a person to find information needed that is stored in long-term memory.4,5 The capability to use working memory, ie, working memory capacity, has been well-established as a strong predictor of higher order cognition, general fluid intelligence (the ability to reason in an abstract way), and academic success.6,7 Working memory capacity is considered an individual-difference variable, meaning that individuals with higher capacity are better at maintaining information in working memory, integrating information with long-term memory, and retrieving
information from long-term memory.\textsuperscript{5,8} That is, they have a larger “workbench.” As such, an individual’s working memory capacity can be a bottleneck for learning because information must pass through working memory before it can be integrated into long-term memory. Given the essential role of working memory capacity in cognition and learning, extensive research has focused on factors that impair working memory capacity, as well as elements that might influence individual differences in performance.\textsuperscript{19,10} As such, we sought to explore how working memory capacity changes throughout a semester in pharmacy school as it may impact student learning.

In the general population, stress and fatigue have been identified as two factors that can lower working memory performance.\textsuperscript{9,11-15} We use the term working memory performance instead of working memory capacity because working memory capacity may change over a person’s lifespan,\textsuperscript{16} while performance may fluctuate throughout the day or between days depending on contextual factors. That is, an individual’s capacity may be stationary over a relatively short time period (eg, an academic semester) but his/her ability to utilize the full working memory capacity may vary daily based on factors such as stress, fatigue, lack of sleep, anxiety, and medication use.\textsuperscript{9} However, while the literature has demonstrated that various factors can impact performance, research on the potential change in working memory performance over the course of a semester is lacking in the academic literature. These changes might be very salient in healthcare professional students who experience fluctuating levels of stress and fatigue. If performance does change as a function of the environment, it may impact student learning, study strategies, and academic performance.

Stress among college students, both acute and chronic, has been shown to negatively impact working memory performance.\textsuperscript{13,15} In a randomly controlled study that evaluated the effect of stress, students assigned to the stress-induced group experienced a pronounced deficit in working memory.\textsuperscript{13} Another study found that participants with reported higher levels of stress following a long period of preparation for a major examination demonstrated changes in working memory dynamics; such neural changes correlated with reduced performance on working memory performance tasks.\textsuperscript{15} This potentially negative correlation between stress and working memory performance is concerning as healthcare professional students report relatively higher and more harmful levels of stress.\textsuperscript{17} Stress in student pharmacists, in particular, has been well-documented in several studies.\textsuperscript{18,19}

Fatigue is another relevant factor that is associated with working memory impairment. Chronic fatigue syndrome (CFS) patients who report higher mental fatigue exhibit significant impairment in spatial working memory tasks compared to CFS patients with low reported mental fatigue and non-fatigued patients.\textsuperscript{11} In healthcare, working memory performance is decreased in sleep-deprived medical residents.\textsuperscript{20} Additionally, fatigue induced by sustained work on cognitive tasks was found to be associated with impairment in executive function, which is higher-level cognitive skills used to control and coordinate other cognitive abilities and behaviors.\textsuperscript{8,9,12} As an example, a study in undergraduate students examined the impact of mental fatigue on executive function by using both complex and simple working memory tasks. The students in the induced fatigue group performed worse on tasks that were related to executive control (complex tasks) in that they made significantly more errors and had slower reaction times; importantly, there was no observed difference between the groups on a simple memory span task.\textsuperscript{14} These findings highlight the importance of using the appropriate working memory measurement for optimal assessment of any potential correlation.

Another aspect of our study was to examine the role gender and personality may have in any observed changes in performance. Any findings could help identify potential students who may be at greater risk of fatigue and stress-induced impairment. For gender, one study showed that men significantly outperformed women in working memory visuospatial tasks,\textsuperscript{21} but others have found minimal differences in working memory capacity between genders.\textsuperscript{22} Moreover, cognitive changes in response to stress may vary between men and women. For example, in an experiment among university students, induced stress was shown to produce a relatively greater impairment effect on the working memory of female participants compared to male participants.\textsuperscript{23} Regarding personality, there is some evidence introverts have higher dopamine levels in the prefrontal cortex,\textsuperscript{24} and dopaminergic drugs alter working memory performance with the extraversion/introversion continuum being an important factor in the drug effects.\textsuperscript{25} This was demonstrated in a study that found that introverts had a statistically significant slower reaction time on a paradigm that taps into the executive function of working memory.\textsuperscript{26} Other studies have found a negative relationship of neuroticism (a five-factor personality trait) with both general fluid intelligence and mind-wandering (an indication of executive attention)\textsuperscript{9,10,27,28} and a relationship of extraversion with vigilance/attention.\textsuperscript{27} Because stress, fatigue, gender, and personality may influence working memory performance, we included them as initial exploratory variables in our study. However, using the right tests to detect variation is important.

A variety of tasks have been developed to assess working memory capacity (eg, simple span, N-back).
Complex span tasks are the most commonly used, as they provide a more accurate assessment and correlation with measures of fluid intelligence (capacity to reason and solve novel problems independent of any knowledge from the past) and reasoning ability.\textsuperscript{29,30} This may be because of the potential of complex span tasks to tap into the executive functioning aspect of working memory (storage and processing) rather than just storage (short-term memory) as simple span tasks do.\textsuperscript{30} For example, complex span tasks may have broader predictive utility. As such, Engle and colleagues proposed that performance on operation, symmetry, and reading span primarily reflect individual differences in executive attention.\textsuperscript{8,22} Executive attention includes both memory and attention abilities, and reflects the ability to temporarily maintain goal-relevant information in primary memory and to retrieve information (e.g., using our earlier scenario, the lecture content Michael wanted to hold in memory and write down as notes)\textsuperscript{31} During a complex span task, participants engage in an unrelated processing activity called distractor that is interleaved between presentation of the items to be recalled; the processing component could be reading sentences (i.e., reading span task), assessing the symmetry of objects (i.e., symmetry span task), or solving math problems (i.e., operation span task).\textsuperscript{31} One limitation of using the traditional complex span tasks to measure working memory capacity in students is the length of time these tasks take.\textsuperscript{29} Consequently, several shortened versions of complex span tests have been developed and have been shown to substantially reduce measurement time without substantially decreasing the ability to predict fluid intelligence.\textsuperscript{29,30} Foster and colleagues suggested that the ideal combination of shortened complex span tasks deemed to best balance practicality with reliability, is one block of the Operation Span and three blocks of the Symmetry Span.\textsuperscript{32} This model is estimated to take about 35 minutes to complete in 95% of participants, accounts for about 85% of the fluid intelligence variance from the full model, and thus seems to be an ideal option. As such we employed the abridged measures of the operation span and symmetry span in this study.

This pilot study was the first of its kind to longitudinally examine potential changes in the working memory performance of student pharmacists related to stress and fatigue secondary to the demands of a rigorous pharmacy program. The findings could help identify students who may be more impacted by stress and fatigue, based on gender and personality. This study also provided important information to assess the need for strategies to minimize student cognitive impairment, whether through reevaluation of curricular design or the addition of more formal student success interventions.

**METHODS**

We used two complex working memory tasks to assess changes in working memory performance over the course of the semester. At each time point, student pharmacists were assessed on their level of fatigue and stress. By measuring working memory performance, stress, and fatigue over time, in addition to personality and gender information, we were able to assess whether stress, fatigue, and working memory performance change in tandem or if they were more independent of each other and if the effects were dependent on personality or gender.

Participants were recruited from the Eshelman School of Pharmacy and offered either a $15 gift card or extra credit in their pharmacokinetics course. Because this was a pilot study, no formal power analysis was conducted. Once enrolled, participants completed a baseline survey asking for their name, gender, and response to the five factor personality test (100 questions, HEXACO).\textsuperscript{33} The range of possible scores for openness to experience, conscientiousness, extraversion, agreeableness, and neuroticism was (16 – minimum possible score, 80 – maximum possible score).

Students reported for testing on four occasions throughout the semester. On each visit, participants completed an assessment of stress and fatigue. They subsequently completed two tests of working memory: the shortened version of the operation memory span (OSPAN) and the shortened version of the symmetry span (SYMSPAN, E-Prime, Psychology Software tools, Inc, Pittsburgh). Testing occurred throughout the day as students were available (mostly lunch time or early morning). Subjects were scheduled for testing ideally every four weeks but at a minimum of at least three weeks apart and at relatively consistent times.

To assess their level of fatigue, participants completed the Iowa Fatigue Scale (11 questions), and to assess stress, participants completed the Perceived Stress Scale (10 questions). Both assessments are retrospective, reflecting students’ experience during the prior month.\textsuperscript{34-36} The range of values for the Iowa Fatigue Scale were 11-55 and for the Perceived Stress Scale were 0-32.

Prior to each working memory task, there were three trials to familiarize the subject with the test. The first working memory test was the OSPAN. This test primarily measures verbal working memory, but also serves as a general measure of working memory performance. For this test, subjects went through an iterative process of solving a simple math problem while simultaneously being asked to remember a letter. After this iterative process, subjects were asked to recall the sequence of letters. For this final recall, subjects were prompted to
report the presented letters in order after completing three to seven of the equation-letter events (set-size; randomly determined on each trial). Students selected the letters by clicking with a mouse on their choices from a 4×3 grid presenting the complete set of 12 letters that could be shown. To maintain correct serial position in the response sequence for recalled letters, participants were instructed to click a “blank” option for any letters they could not recall. The ranges of possible scores were 0 to 75.

The second was the Symmetry Span task. This task assesses visuospatial working memory. Participants were presented with a pattern where they needed to assess symmetry, followed by red squares in a grid of potential locations, which were to be remembered. Subjects reported the square locations in order after completing two to five of these symmetry-square events by clicking on their choices in the cells of a 4×4 grid. To maintain correct serial position in the response sequence for recalled square locations, participants were instructed to click a “blank” option for any square locations they could not recall. The range of possible scores was (0 through 42).

For each test, partial credit scoring was used and data were included in the study analysis if the intervening task scored above 85%. Data from the two working memory tasks were analyzed independently. A repeated measures ANOVA was used to identify trends in data over time (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY). Correlation analysis was used to assess relationships between the working memory capacity and personality as measured at baseline, fatigue, and stress. Another correlation analysis was performed to account for an intrinsic relationship of symmetry (baseline, fatigue, stress) with working memory tasks and the relationship of stress, fatigue, and working memory performance. No personality trait was associated with working memory at baseline despite the association of extraversion with baseline stress and fatigue.

Overall, the reliability of the two working memory tests (OSPAN = 0.97; SYMSPAN = 0.84) and measures of stress (.94) and fatigue (.93) were high.

Next, we examined if any of the potential factors of interest were associated with baseline working memory performance or to each other. As such, we conducted a correlation analysis on the factors of interest (Table 2). There were strong correlations (r > .5) between the two working memory tasks and between each of the following: stress and fatigue, stress and extraversion, fatigue and extraversion, and agreeableness. These results suggest an association between stress, fatigue, and working memory performance. No personality trait was associated with working memory at baseline despite the association of extraversion with stress and fatigue.

Subsequently, we conducted an intra-individual correlation analysis to examine the relationship between working memory, stress, and fatigue within each subject over time. This analysis was performed to account for an individual’s ability to self-report stress and fatigue meaning, ie, two people may have the same amount of stress placed on them but perceive the stress differently. As seen in Figure 2, there was a wide range of correlations suggesting an unclear relationship between fatigue, stress, and the measures of working memory. We then collapsed all the data to examine mean stress, fatigue, and working memory to minimize the effects of time. Overall, there was a negative correlation between the OSPAN and stress (r = -.39, p = .07) and fatigue (r = -.43, p = .04). There were no correlations with SYMSPAN and stress or fatigue.

We further examined the relationship of working memory performance and sex and personality traits. There was no difference between men and women at any

### Table 1. Demographics of Pharmacy Students Who Participated in a Study to Identify Changes in Working Memory Performance Over a Semester

| Demographic                        | Measure     |
|------------------------------------|-------------|
| Professional year, No. (%)         | 21 (91)     |
| First                              | 0 (0)       |
| Second                             | 2 (9)       |
| Male, No. (%)                      | 7 (30)      |
| Age, y (mean, range)               | 23 (21-27)  |
| Personality (mean, range)          |             |
| Openness to experience             | 56 (34-74)  |
| Conscientiousness                  | 60 (39-76)  |
| Extraversion                       | 50 (35-69)  |
| Agreeableness                      | 50 (26-67)  |
| Neuroticism                        | 56 (41-72)  |
| Stress (mean, range)               | 17 (5-28)   |
| Fatigue (mean, range)              | 29 (18-45)  |

Twenty-three students completed the study. Demographic information can be found in Table 1. We first examined the changes in working memory performance over the course of the semester. We identified a significant quadratic trend in the operation span (OSPAN)(p = .02) (Figure 1A). We identified a near significant cubic trend in the symmetry span (SYMSPAN)(p = .07) (Figure 1A).

Over the semester, there was a significant linear trend (increase) in fatigue (p < .001) and a near significant linear trend (increase) for stress (p = .06 (Figure 1B).
timepoint for stress, fatigue, OSPAN, or SYMSPAN. For personality, there were no differences between the top and bottom of the median split for openness to experience, conscientiousness, agreeableness, or neuroticism. There were differences between the top and bottom of the median split for extraversion with respect to fatigue (d = .68 to 1.0) and stress (d = .95 to 1.4), but not with working memory performance.

**DISCUSSION**

This study examined how an essential part of student learning, working memory performance, may change throughout an academic semester and whether those changes are associated with fatigue and stress. There were some trends suggesting that working memory performance changes over the course of the semester. Furthermore, on average, stress and fatigue correlated with working memory performance but there was high inter-individual and/or temporal variability in this relationship. Of note, student pharmacists can still have high working memory performance despite increased levels of stress and fatigue. The response to semester induced stress and fatigue may be moderated by personality type. Given this was a preliminary investigation, more work is needed to assess how stress, fatigue, and personality may interact to modify working memory performance over the course of a semester. Thus, in our earlier example, Michael may be at risk of lower working memory performance and thus lower academic performance during parts of the semester, and these “dips” may be caused by stress or fatigue or may be dependent on personality type.

It is difficult to conclude from these preliminary findings the exact relationship between stress and changes in working memory performance. First, having students complete the working memory tasks over time may have increased their performance on the test as participants may have learned how to “play the game.” In other words, students’ scores may have been impacted by a sort of learning curve in taking the test. This is consistent with the literature on programs aimed at cognitive (or brain) training.

Table 2. Correlation Analysis of Baseline Characteristics of Pharmacy Students Who Participated in a Study to Identify Changes in Working Memory Performance Over a Semester Including Performance on Working Memory Tasks, Fatigue, Stress and the Five-Factor Personality Scale

|            | 1   | 2          | 3          | 4          | 5          | 6          | 7          | 8          | 9          |
|------------|-----|------------|------------|------------|------------|------------|------------|------------|------------|
| OSPAN (1)  | 1   |            |            |            |            |            |            |            |            |
| SYMSPAN (2)| .61a| 1          |            |            |            |            |            |            |            |
| Fatigue (3)| -.44a| -.22      | 1          |            |            |            |            |            |            |
| Stress (4) | -.40| -.055      | .76a       | 1          |            |            |            |            |            |
| Openness to experience (5) | .058| -.13      | .079       | .07        | 1          |            |            |            |            |
| Conscientiousness (6) | .16 | .18        | -.45a      | -.35       | -.48a      | 1          |            |            |            |
| Extraversion (7) | .27 | -.22      | -.52a      | -.59a      | .17        | .23        | 1          |            |            |
| Agreeableness (8) | .13 | -.005    | -.38       | -.41a      | .17        | .24        | .52a       | 1          |            |
| Neuroticism (9) | .21 | .11        | -.32       | -.16       | -.15       | .099       | .063       | -.48a      | 1          |

Abbreviations: OSPAN = operation span, SYMSPAN = symmetry span  
*a p < .05
training (e.g., Luminosity). While these training tools are purported to increase the user’s working memory capacity, research shows that users get better at the game but do not actually improve their working memory capacity. Thus, the challenge is to separate gains in performance from practice from changes impacted by stress or fatigue. This could be resolved with more baseline trials to minimize the effects of a learning curve — that is, more practice trials until the baseline measures are stable. However, there may be other explanations for the rise in performance at the second time point, e.g., the subjects had a reduction in task-irrelevant thoughts. In other words, if subjects were less apprehensive about taking the working memory tests because they already completed similar tests in a previous session, they could have less intrusive thoughts and perform better. This phenomenon would be similar to what is seen with test anxiety where task-irrelevant thoughts may occupy a student’s working memory and lead to poorer performance.

Both of the working memory tests used represent an individual’s ability to temporarily maintain goal-related information and to retrieve information from memory. Both tests have high test-retest reliability (.83 and .77, respectively). The sample within this study showed scores similar to undergraduate populations. We found significant trends over time with the operation span but not the symmetry span. The operation span intermixes mathematical calculation with remembering a series of letters and reflects verbal material. The symmetry span intermixes visuospatial puzzles and thus represents visuospatial working memory performance. This may indicate that the visual-spatial aspects of working memory performance are less impacted throughout the semester compared to a more general assessment of executive attention.

There are potential implications for this study. The original interest was to answer the question of whether working memory performance changes over the course of the semester. This interest stems from changes in performance impacting study decisions, attention, and note taking. We did find a change in working memory performance over time, but it is difficult to conclude whether these changes are meaningful in terms of impact on learning. We did not find a clinically significant change in performance.
are seen when comparing laboratory models of stress or fatigue or in clinical populations such as patients with chronic fatigue syndrome or anxiety. However, most of these studies also used larger study populations. The current study was a pilot to identify potential future studies. The results did note some potential changes in working memory performance throughout the semester and these may be influenced by stress and fatigue. While further investigation is warranted, these initial findings may explain student learning behavior from midsemester to the end of the semester, either because of the levels of stress or fatigue either on, or independent of, working memory performance.

CONCLUSION
This is one of the first studies to examine changes in working memory performance in pharmacy students over the course of a semester. While measures may fluctuate over time, it is unclear how stress and fatigue may contribute to this fluctuation. More importantly, more research is needed on whether these changes in working memory performance impact academic decision making such as study decisions by the student.

ACKNOWLEDGMENTS
The authors would like to thank the Attention and Working Memory Laboratory (Robert Engle, Georgia Tech University) for access to their working memory tasks. The authors also would like to thank Michael Kane (University of North Carolina at Greensboro) and Chris Was (Kent State University) for their insights throughout this project.

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