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Abstract

Acute mental stressors have been implicated as variables that may deleteriously affect neuropsychological test performance by increasing distractibility and decreasing working memory function. This study examined 25 subjects with no known neurological or psychiatric impairment on a brief battery of neuropsychological measures on alternate days following either rest or induced mental stress in a counterbalanced design. The test battery consisted of the Rey Auditory-Verbal Learning Test, the Rey Complex Figure, and three Wechsler Memory Scale-III subtests (Logical Memory, Digit Span, and Visual Memory Span). The Ss average age was 24.8 years (S.D. = 10.1) and average education was 15.0 years (S.D. = 1.6). The mental stressor employed was a videotaped public-speaking exercise that has been shown in previous work to induce negative mood, cardiovascular reactivity, and perceived mental stress. Ss demonstrated statistically significant (P < .05) increases in negative mood, heart rate, diastolic blood pressure, and systolic blood pressure as well as elevated cortisol concentration following induced stress, suggesting substantially increased adrenocortical reactivity and cardiovascular stress response. There were, however, no statistically significant differences in any of the neuropsychological measures when stress versus rest days were compared. The results suggest that acute mental stressors may have no measurable effect on subsequent performance on selected neuropsychological tests in a normal population. Further work is suggested to determine whether pre-existing anxiety-related psychopathology or pre-existing neurological compromise might interact with induced mental stress to cause decrements in neuropsychological test performance.

Keywords: Neuropsychology; Cortisol; Memory; Attention; Cardiovascular

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Understanding the impact of acute stressors on test performance is critical to the clinical assessment of neuropsychological function. Acute anxiety and mental stress have been implicated as subject variables thought to deleteriously affect neuropsychological test performance by increasing distractibility and decreasing working memory function. The available evidence suggests that stressful experiences produce short-term and reversible deficits in episodic and spatial memory in both animal models and humans (McEwen, 2000, 2002). The immune system responds to acute stress via enhanced immune responses, which are mediated by adrenal steroids and catecholamines, as well as by locally produced cytokines and cell adhesion molecules (McEwen, 2000). Acute stress is dose dependent in its ability to activate the delayed-type immune system hypersensitivity response (McEwen & Sapolsky, 1995), and this is related to the magnitude of glucocorticoid secretion, specifically cortisol secretion. Psychological stressors cause the nearly immediate secretion of the catecholamines epinephrine and norepinephrine by the sympathetic nervous system, which typically increases heart rate and blood pressure. The second component of this stress response is the increased secretion of glucocorticoids by the adrenal gland (McEwen & Sapolsky, 1995). Bohnen, Houx, Nicolson, & Jolles (1990) reported that increased cortisol reactivity during mental stress was negatively related to attentional performance, and Bohnen, Nicolson, Sulon, & Jolles (1991) found a relationship between salivary cortisol secretion and individual coping ability during mental stress. The central role of the stress hormone cortisol has also been implicated in tasks involving continuous mental effort, such as the study of Bohnen et al. (1990) which demonstrated a negative relationship between increased cortisol reactivity and attentional performance. Bohnen, Jolles, Twijnstra, Mellink, and Sulon (1992) presented similar evidence that performance on a continuous performance vigilance task decreased with increased cortisol reactivity.

There have been equivocal results in previous work comparing self-reported anxiety and neuropsychological test performance. High levels of reported trait anxiety have been related to reduced neuropsychological performance in women (King, Hannay, Masek, & Burns, 1978) and diminished memory test performance in elderly subjects (Cockburn & Smith, 1994). Buckelew and Hannay (1986) have reported a direct relationship between reported state anxiety and performance on Block Design and Word Fluency tests, with no reported effect on Digit Symbol or Finger Tapping. In contrast, King et al. (1978) reported decrements in Finger Tapping and increased time to complete the Form Board Test in women who report increased trait anxiety. Chavez, Trautt, Brandon, and Steyaert (1983) reported no effect of test anxiety on subjects performance on Digit Span, Digit Symbol, Finger Tapping, or the Trail Making Test. Waldstein, Ryan, Jennings, Muldoon, and Manuck (1997) reported no effect of anxiety on multiple neuropsychological measures of attention, learning, memory, mental flexibility, and eye–hand coordination in a sample of healthy young and middle-aged men with elevated State and Trait Anxiety Inventory scores.

The present study compares neuropsychological test performance following an induced stress response in a laboratory setting, while concurrently monitoring cardiovascular responses related to activation of the autonomic nervous system and neuroendocrine measures related to the hypothalamic–pituitary–adrenal (HPA) axis.
1. Method

1.1. Subjects and procedure

This study examined 25 volunteer college student subjects (10 males and 15 females) with no known neurological or psychiatric impairment by medical history on a brief battery of memory recall and working memory measures. Subjects were examined on alternate days following either rest or induced mental stress in a counterbalanced design. The subjects’ average age was 24.8 years (S.D. = 10.1) and average education was 15.0 years (S.D. = 1.6). The test battery consisted of the Rey Auditory-Verbal Learning Test (RAVLT), the Rey–Osterrieth Complex Figure Test (CFT), and three Wechsler Memory Scale—Third Edition (WMS-III) subtests (Logical Memory, Digit Span, and Visual Memory Span). These particular measures were selected because they are not only quite commonly administered tests, but they are also tests that can be administered in their entirety in a very brief span of time. More lengthy tests of distractibility and divided attention, such as continuous performance tests, were not selected because there was a concern that some of the effect of stress upon test performance might run its course during a more lengthy administration time. The Paced Auditory Serial Addition Task (PASAT) was initially considered for inclusion as a measure of attention that is sensitive to psychological stressors (Gronwall, 1977; Gronwall & Wrightson, 1981). There is some evidence to suggest that the PASAT may induce negative mood (Holdwick & Wingenfeld, 1999), however. The PASAT was not included in the battery of test administered out of a concern that the PASAT itself might be a stressor for some subjects, which could introduce a confounding factor in this type of experimental design.

To control for systematic learning effects, separate neuropsychological testing batteries were constructed and used in a counterbalanced manner. Test battery I consisted of the RAVLT developed by Lezak (1976, 1983), the CFT developed by Osterrieth (1944) and Meyers and Meyers (1995), Story A of the Logical Memory I subtest of the WMS-III, and the Digit Span and Visual Memory Span subtests of the WMS-III. Test Battery II consisted of the Majdan alternative form of the RAVLT (Form 2), the Taylor alternate form B of the CFT (Taylor, 1969, 1979), Story B of the Logical Memory I subtest of the WMS-III, and the Digit Span and Visual Memory Span subtests of the WMS-III. The mental stress employed was a videotaped public-speaking exercise that has been shown in previous work to induce negative mood, cardiovascular reactivity, and perceived mental stress (al’Absi et al., 1997).

Prior to each session, participants had abstained from alcohol for 24 h, from nicotine and caffeine for 12 h, and had eaten a light lunch at least 2 h prior to arrival. Testing was initiated at approximately 1.00 p.m. Upon arrival at the laboratory, each participant completed a questionnaire to confirm current good health and compliance with dietary instructions. The participant was then instrumented for cardiovascular measurements.

The protocol consisted of: initial rest (60 min, with the last 30 min being a physiological data collection period), continued rest or task (30 min), and recovery (30 min). They then completed the neuropsychological testing. During the baseline, rest and recovery periods, participants had a choice of reading general interest magazines or watching nature videos selected for their emotionally neutral content. The task consisted of three repeated public-speaking challenges. Participants were asked to deliver a 4-min presentation after a 4-min silent preparation period,
as detailed in a previous report (al’Absi et al., 1997). The public-speaking task has been shown to be a potent laboratory stressor, inducing significant cardiovascular, endocrine, and mood changes (al’Absi et al., 1997).

Mood state ratings were administered during the two laboratory sessions. Participants completed these ratings after baseline, after the public-speaking task or rest, and after 30-min recovery. Ratings covered two factors, Activation and Distress, adopted from scales that were previously used in similar studies and found to be sensitive to laboratory stress protocols (al’Absi, Lovallo, McKey, & Pincomb, 1994; al’Absi et al., 1998). Each item references a seven-point scale anchored by the end points, “Not at All” and “Very Strong.” Subjects mark the scale at the point that best describes how they felt during the previous 30 min. Items that cover Activation include ratings of how cheerful, content, calm/relaxed, happy, in control, and interested the participant felt during the previous 30-min period. Distress items include ratings on how irritable, anxious/tense, sad/depressed, angry, confused, and impatient the participant felt during the previous 30 min.

Blood pressure (BP) and heart rate (HR) measurements were obtained at 3-min intervals during the baseline 30-min period, during rest or public speaking, and during the 30-min recovery period. All BPs and HRs were measured using a Dinamap oscillometric monitor (Critikon, Tampa, FL) with the cuff placed on the left arm.

Cortisol sampling was accomplished non-invasively. The subject produced 1–2 ml of saliva and collected it into a plastic tube (Salivette tubes, Sarstedt, Rommelsdorf, Germany). Salivary cortisol samples were collected every 30 min during baseline, once immediately after public speaking (or rest during the control session), and once after a 30-min recovery period. All samples were stored at −70 °C until assay. Cortisol assays were conducted using a time-resolved immunassay with fluorometric end point detection. All assay analyses were conducted at the Center for Psychobiological and Psychosomatic Research, University of Trier, Germany. The assay has a minimum sensitivity of 0.4 nmol/L (Dressendorfer, Kirschbaum, Rohde, Stahl, Strasburger, 1992).

2. Results

Subjects demonstrated statistically significant increases in heart rate, $F(1, 24) = 2.3, P < .01$, diastolic blood pressure, $F(1, 24) = 3.2, P < .01$, and systolic blood pressure, $F(1, 24) = 8.9, P < .01$, when compared to either within session baseline or control (see Fig. 1). These findings are consistent with a clearly defined cardiovascular stress response. Significantly elevated cortisol concentrations, $F(1, 24) = 6.0, P < .05$, were also seen following induced stress, suggesting substantially increased adrenocortical reactivity. Cortisol concentrations (see Fig. 2) were elevated both in reference to pre-stress levels (sampling periods 1 and 2 vs. sampling period 3) and in reference to baseline (rest vs. stress samples). This is consistent with changes in self-reported mood state ratings. Subjects reported statistically significant increases in anxiety following the induced stress, $F(1, 24) = 7.8, P < .05$, and increases in sweating, $F(1, 24) = 4.0, P < .05$, and significant decreases in feeling calm, $F(1, 24) = 4.4, P < .05$. There were, however, no statistically significant differences in any of the neuropsychological measures when stress and rest days were compared (see Table 1). There were no significant
Fig. 1. Mean salivary cortisol concentrations and standard error of mean (nmol/L) before (samples 1 and 2), following the public-speaking stressor or rest (samples 3 and 4) and immediately after the cognitive performance (sample 5). Solid line denotes session, dash line denotes rest session.
effects of age or gender either in physiological variables, self-reported mood state ratings, or neuropsychological measures.

3. Discussion

The observed results lend support to the notion that many neuropsychological measures typically used in office practice are very robust tests that are not likely to be invalidated by
the typical stresses of everyday life, particularly if administered following a brief rest period. From a practical standpoint, this suggests that the effects of demonstrable acute stress may be non-contributory to any variance seen in neuropsychological test performance if acutely stressed examinees are given a brief period of time to allow a return to pre-stress baseline levels of cardiovascular and adrenocortical activity. The results suggest that this return to baseline period may be as brief as 30 min.

Further work is suggested to determine whether pre-existing anxiety-related psychopathology might interact with induced mental stress to cause more enduring decrements in neuropsychological test performance. There is currently no clear consensus regarding the role that anxiety and mental stress might play in affecting the neuropsychological test performance of patients with anxiety disorders. There has been some reported evidence to suggest that anxiety may be related to the neuropsychological impairments seen in clinical samples of obsessive–compulsive disorder (OCD) patients. Zielinski, Taylor, and Juzwin (1991) reported higher levels of anxiety than controls and neuropsychological impairment of visual–spatial recall, recognition, and sequencing in OCD subjects. In contrast, significantly elevated emotional arousal had no reported relevant effect on neuropsychological test performance in a sample of adult cardiac patients (Vingerhoets, De Soete, & Jannes, 1995). This does not, however, preclude other long-term effects due to stress-related biological dysregulation, such as disrupted HPA regulation.

The present findings, of course, cannot be generalized either to all neuropsychological tests or to all tests of attention, concentration, and working memory. It is certainly possible that the induced stress employed in the present study, although meaningful in a physiological sense, may not have been sufficiently intense to disrupt cognitive processing in this sample as measured by these particular test instruments. The relatively small sample size used also did not allow a further partitioning of the sample into high and low cortisol responders. Preliminary work using mental arithmetic as an induced stress has suggested that individuals who secrete high levels of cortisol following induced stress have poorer subsequent performance on a mental arithmetic task than individuals who secrete lower levels of cortisol (al’Absi, Hugdahl, & Lovallo, 2002). The effect of induced stress on neuropsychological performance may therefore be highly variable from one individual to another, and the effect may be more pronounced on working memory tasks that require both short-term information storage and executive processes that include both task management and selective attention. Further work in this area is needed to clarify these relationships.

Further work is also suggested to determine how pre-existing neurological compromise might interact with induced mental stress to cause more enduring decrements in neuropsychological test performance. This may be especially useful in furthering our understanding of post-injury symptom presentation in mild TBI and concussion. Gouvier, Cubic, Jones, Brantley, and Cutlip (1992) noted that the number of post-concussion symptoms reported in their sample covaried with the level of subjective stress reported, consistent with the observation that increases in post-concussion symptoms (PCS) in mild head injury patients are more likely to be reported during stressful periods of their lives, such as returning to work or returning to other previous duties post-injury. Bohnen et al. (1992) noted that their PCS patient group sample performed a vigilance task significantly less well than non-concussed
control subjects, although not worse than the asymptomatic patient group; the observed decrements in the vigilance task were positively correlated with higher cortisol responses during the task.

More recent work by Hanna-Pladdy, Berry, Bennett, Phillips, and Gouvier (2001) suggests that individuals who have been concussed may be more sensitive to stress. Their subjects with TBI had the greatest changes in autonomic arousal when exposed to the experimental stress. Their symptomatic TBI group in the stress condition also had the highest heart rates and the greatest skin conductance responses during the PASAT and RAVLT, corresponding to lower rates of information processing and reduced memory performances.

This potential for an increased sensitivity to stress may be potentiated by chronic stress effects in some individuals. Cortisol production and the HPA axis may have a central role in a number of neuropsychiatric disorders, affecting memory functioning and adaptability to stress in general (Hanna-Pladdy et al., 2001). Repeated or prolonged stress impairs cognitive function in animal models, and repeated glucocorticoid elevation in humans has been shown to be accompanied by cognitive dysfunction (McEwen, 2000). Prolonged elevations of glucocorticoids after neurological insult or after chronic stress also may possibly play a role in neurodegeneration and brain dysfunction, including neuroendocrine responses in mild TBI (Cernak, Savic, Lazarov, Joksimovic, & Markovic, 1999; McEwen, 2000).

There are several limitations in the present study design that should be noted. There are inherent problems with some of the neuropsychological measures selected. In an attempt to create a very brief battery to capture potential autonomic nervous system and neuroendocrine effects, many more lengthy tests were omitted which are worthy of study. To control for systematic learning effects, alternative forms of some tests were used. It is not clear how equivalent the parallel forms are for the tests used, however. The Taylor Figure, for example, is likely easier than the original Rey Figure. The sample consisted of subjects with no known neurological or psychiatric impairment, which may be useful in terms of establishing normal baseline functioning, but such a sample certainly is not representative of the typical neuropsychological patient population and limits the generalizability of the findings. The sample size of 25 increases the likelihood of a Type II error, and the present study should be replicated with a larger sample size of non-neurological and non-psychiatric normal subjects. This study should also be replicated using prospective, consecutive samples of mild TBI patients as well as alternate non-neurological control groups such as highly anxious or depressed patients to increase the generalizability of the findings.

References


