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The Relationship Between Processing Speed and Working Memory Demand in Systemic Lupus Erythematosus: Evidence from a Visual N-Back Task

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Abstract

Objective—Working memory (WM) deficits have been reported previously in systemic lupus erythematosus (SLE), but the relationship between information processing speed (PS) and WM deficits in SLE is unknown. This study examined whether or not PS slowing could account for the WM deficits observed in SLE.

Method—A visual n-back task was used to measure simple and complex PS and WM in 40 SLE patients and 36 healthy controls. Simple PS was defined as reaction time (RT) to correct responses under a very low WM load condition (0-back), while complex PS was defined as RT to correct responses under moderate and high WM load conditions (1 and 2-back).

Results—The results showed that SLE patients performed as well as the controls at the lower WM load conditions but had fewer correct responses than controls under the highest WM load condition (2-back). SLE patients had slower RTs than controls under all conditions, but they had relatively greater RT slowing than controls under the higher WM load conditions. Further, when RT for simple PS was subtracted from complex PS, SLE patients still showed slower complex PS for the 1 and 2-back compared to controls. Both simple and complex PS slowing were related to poorer accuracy scores on the 2-back condition, only for the SLE group.

Conclusions—The n-back task provides a sensitive measure of PS and WM. The results suggest that PS deficits alone could not account for the WM deficits in SLE. Disease duration, disease activity, and depression did not appear to account for the observed PS and WM deficits.

Keywords

Systemic Lupus Erythematosus; autoimmune disease; working memory; information processing speed; n-back task

Systemic lupus erythematosus (SLE) is a chronic, autoimmune disease characterized by multisystem microvascular inflammation that can affect almost any organ systems of the body including the central and peripheral nervous systems. An ad hoc task force of the

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American College of Rheumatology has identified and defined nineteen neuropsychiatric syndromes of SLE (NPSLE) thought to have nervous system involvement (ACR Ad Hoc Task Force, 1999). These neurological and psychiatric syndromes encompass diffuse and focal manifestations ranging from headache, mood disorder, and cognitive dysfunction, to seizure disorders and cerebrovascular disease (Ainiala et al., 2001; Carbotte et al., 1986; Kozora et al., 1996; West et al., 1995). It has been reported that as many as 81% of SLE patients have cognitive dysfunction, making it the most common of the syndromes (Ad Hoc Committee on Lupus Response Criteria: Cognition Sub-committee, 2007; Ainiala et al., 2001; Brey et al., 2002; Denburg et al., 1997; Hanly et al., 1997; Kozora et al., 2008). Although a single pattern of cognitive deficits in SLE has not emerged (Kozora et al., 2008), studies suggest that the deficits are often seen on tests that place demands on attention, information processing speed (PS), and short term or working memory (WM) (Kozora et al., 1996; Ad Hoc Committee on Lupus Response Criteria: Cognition Sub-committee, 2007; Denburg et al., 1997; Kozora et al., 2008; Kozora et al., 2001; Shucard et al., 2004). These cognitive deficits are similar to those seen in other frontal-subcortical dementias (Kozora et al., 2008), and in multiple sclerosis (MS) (Benedict et al., 2008; Parmenter et al., 2006; Parmenter et al., 2007).

As suggested by Kozora et al. (2008), "...damage to white matter tracts may be relevant to cognitive dysfunction in NP-SLE." We and others have also suggested that damage to myelin and axons may be the primary CNS disturbance associated with disruption of cognitive processes such as WM and PS in SLE (Benedict et al., 2008; Leritz et al., 2000). Evidence of cortical involvement has also been reported. For example, functional imaging studies have shown abnormal metabolism and hypoperfusion throughout multiple cortical structures in SLE (Weiner et al., 2000; Kao et al., 1999). More recently, using magnetization transfer imaging, gray matter abnormalities were found in patients with NP SLE (Steens et al., 2004). Other neurochemical evidence supports increased neuronal degradation in patients with CNS involvement (Trysberg et al., 2003). A study from our laboratory reported a relationship between C-Reactive Protein, a marker of chronic inflammation, and WM deficits in SLE (Shucard et al., 2007), suggesting inflammatory involvement of brain parenchyma. Thus, data point to both subcortical and cortical involvement in SLE, with implications for detrimental effects on PS and WM.

Working memory is defined as the temporary encoding, maintenance and manipulation of information in short term registers (Baddeley, 2000), and it is critical for virtually all cognitive functions and activities of daily living, such as planning, conversation, and problem solving. The rate at which the brain processes cognitive information is intricately related to WM (Nebes et al., 2000). Information processing efficiency depends, in part, on a balance between the rate at which the incoming information can be processed and the rate at which the information decays or is displaced. The Paced Auditory Serial Addition Task (PASAT) (Gronwall, 1977) is a speed-dependent task that is frequently used in clinical settings to assess WM, sustained attention, and PS (Fisk & Archibald, 2001; Rao et al., 1991). A study in our laboratory found that SLE patients, compared to controls, had poorer WM performance at the fastest presentation rate of the PASAT as indicated by a greater tendency to "chunk" responses in order to reduce the WM load of the task (Shucard et al., 2004). The degree to which PS deficits contributed to the observed WM deficits was not clear, however, from this investigation.

In the MS literature, two models of the effects of PS on WM have been proposed. The *Relative Consequence Model*, purports that impaired PS accounts for deficits in cognitive domains such as WM, particularly in patients with the less severe disease course of MS (DeLuca et al., 2004; Archibald & Fisk, 2000; Lengenfelder et al., 2006). Therefore, given adequate time, patients with PS deficits should perform within normal limits on tasks in

cognitive domains such as WM. Thus, what would appear to be a deficit in WM is, in actuality, an indirect effect of a PS deficit. The *Independent Consequence Model* suggests that impairments in separate cognitive domains such as PS and WM are independent, although not mutually exclusive, of each other (DeLuca et al., 2004). Accordingly, WM could be impaired independently of PS in SLE, even though PS is an important component of many cognitive domains including WM (Salthouse, 1996).

N-back tasks have been used often in experimental studies of WM (Carlson et al., 1998; Gevins et al., 1987). They provide behavioral indices of simple and complex PS and WM and allow for the parsing of PS and WM (Parmenter et al., 2006; Parmenter et al., 2007). During the n-back task, participants decide whether each currently presented stimulus matches the stimulus previously presented “*n*” trials back. As *n* increases, the task difficulty increases, placing greater demand on WM. Contrary to the PASAT, the *n*-back task provides measures of simple and complex PS, as measured by reaction time (RT). Simple PS reflects the mental speed required to perform undemanding attentional tasks such as target detection (i.e., 0-back), while complex PS reflects the additive time required to perform the increasingly more demanding executive aspects of WM (i.e., the 1-back and 2-back).

Using a visual n-back task, we reported previously that for MS patients, the contribution of PS on WM function did not support the *Relative Consequence Model* (Parmenter et al., 2007). Rather, impairments in both PS and WM were present in the early relapsing remitting course of MS. In support of the *Independent Consequence Model*, MS patients had slower complex PS, even when simple PS was removed, and poorer performance scores than controls on the most difficult WM task (2-back). The *Relative Consequence Model* would have predicted that with adequate time to perform a task, WM would not have been impaired. However, according to our results, deficient PS could not account fully for the WM impairments seen in MS (Parmenter et al., 2007).

In the present study, our goal was to determine whether or not the WM deficits observed in SLE are due to a true deficit in WM or are a secondary effect of a PS deficit. To accomplish this goal, a visual n-back task was used to parse PS and WM. It was hypothesized that compared to the healthy controls, SLE patients would exhibit deficits in both WM and PS, in support of the *Independent Consequence Model* and the presence of both cortical and subcortical involvement. It was anticipated that SLE patients would show longer RTs and poorer performance during the condition with the greatest demand on WM (2-back). Further, complex, but not simple, PS was predicted to relate to WM performance, with slower RT being associated with poorer accuracy scores on the 2-back condition.

Methods

Participants

The final sample included 40 SLE patients (38 females, 2 males) who met the American Rheumatism Association revised criteria for SLE (Tan et al., 1982) and 36 healthy controls (32 females, 4 males). Three SLE patients were not included: one exceeded the study criteria for depression and two exceeded criteria for level of alertness during the task. The SLE patients were recruited from our Systemic Autoimmune Disease center at Buffalo General Hospital and from local rheumatologists. Controls were recruited from advertisement in local newspapers. Medical records were obtained from the rheumatologists of SLE patient recruited outside of our center. The diagnosis of SLE was independently confirmed by a rheumatology specialist at our center. The Systemic Lupus Activity Measure (SLAM; Liang et al., 1989) was used to evaluate current disease activity.

Participants were first phone screened for general selection criteria, and then further tested for other exclusionary criteria during a psychiatric interview. For all participants, exclusionary criteria included history of head trauma, visual problems not corrected by glasses, learning disability, or other medical conditions unrelated to SLE that could affect cognition. Control participants were not included if they had an Axis I psychiatric disorder or were on any psychotropic medications or other medications that could affect cognition. SLE Patients with and without neuropsychiatric involvement were included, other than those with a history of a stroke that produced focal cognitive damage (e.g., aphasia), or a history of psychosis. Table 1 lists the neuropsychiatric syndromes, with the exception of cognitive dysfunction, for each of the SLE patients included in the study. Most of the participants had not been tested for cognitive dysfunction prior to participation, and cognitive dysfunction was the measure of interest for this study. Six patients had a history of cerebrovascular disease (stroke) or seizure, as well as at least one other less focal or overt manifestation. Of the three patients with a history of a seizure, only one was taking anticonvulsant medication. Twenty-four patients had a history of one or more neuropsychiatric syndromes other than stroke or seizure, and ten patients had no history of NPSLE. Major Depression (current and lifetime) was assessed during the psychiatric interview (see measures below). Patients with current depression in the mild to moderate range were included. None of the patients met diagnostic criteria for any other mood disorders. None of the controls were taking prescription medications, and the medications for the SLE patients were carefully documented.

N-Back Task

Participants completed a visual n-back task (0-, 1-, 2-back) similar to that reported previously from our laboratory (Parmenter et al., 2006; Parmenter et al., 2007). The n-back task was administered during the electrophysiological component of a multifaceted study of cognitive function in SLE. The task consisted of the 0, 1, and 2-back conditions, presented in that order. See Figure 1 for a diagram of the task. A practice trial preceded each condition. In each of the conditions a total of 150 letters were presented one at a time on a computer screen. Letters of the alphabet were repeated in upper and lower case. Correct responses were not dependent on the case. Each condition was divided into two blocks of 75 letters. A brief break was taken between blocks (approx 1 minute), and a 5 minute break was taken between conditions.

For the 0-back condition, participants were instructed to identify the letter “X” (match) when it occurred within the sequence of letters (non-matches). For the 1-back condition, each letter was compared with the previously presented letter (the letter 1-back) to determine if it was the same letter (match) or not (non-match). Likewise, for the 2-back condition, each letter was compared with the letter presented 2 letters back. The participants were instructed to press two inner buttons on a response pad with their left and right thumbs to each letter that was a match, and two outer buttons to each letter that was a non-match. Fifty of the letters in each condition were match letters and 100, 98, and 96 were a non-match letters in the 0- 1- and 2- back conditions, respectively (the first letter of each block for the 1-back, and the first two letters of each block for the 2-back were not counted due to the task requirements).

The n-back task was created and stimuli were presented via computer using E-Prime software (E-Prime, 2002). Stimulus duration was 400 msec, with a 2000 msec ISI. Task Performance (RT, Correct Responses) was also recorded with E-Prime software. The stimuli for the task were presented to the participant in the center of a computer monitor located 70 cm from the bridge of the participant's nose. Participants were seated in a comfortable chair facing the computer monitor in a sound attenuated room.

Measures

N-Back accuracy and speed measures—Three accuracy measures were calculated for each n-back condition: the total number of correct matches, correct non-matches, and correct responses (the sum of correct matches and correct non-matches). Three RT measures were also obtained for each n-back condition: RT to correct matches, correct non-matches, and total correct responses (correct matches + correct non-matches). To examine further the independent contribution of complex PS, scores were derived for each participant by subtracting their mean RT on the 0-back condition (i.e. simple PS) from their mean RT on the 1-back and 2-back conditions, separately. These difference scores allowed us to remove simple PS so that the remaining PS would be reflective of the more demanding executive aspects of the WM task.

Demographic and health-related measures—The North American Adult Reading Test (NAART) was used to obtain an estimate of full scale IQ. The Beck Depression Inventory –II (BDI- II), which assesses current cognitive, and non-cognitive (affective and somatic) symptoms of depression, was used to obtain current total and subscale symptomatology. The cognitive subscale score of the BDI-II eliminates somatic items associated with medical illness, such as low energy and sleep disturbance, and, thus, is thought to be a more accurate measure of depression in individuals with chronic illness (Steer et al., 1999). The Structured Clinical Interview for the DSM-IV (SCID-IV) was administered by a clinical psychologist (JLS) to assess further for current and lifetime history of major depression as well as other Axis I disorders.

SLE disease duration was calculated as the number of years since diagnosis. SLE disease activity rating was based on standardized criteria specified in the SLAM (Liang et al., 1989). A disease activity score was calculated as the sum of positive responses on a 19 item checklist derived from the clinical manifestation categories of the SLAM.

The Stanford Sleepiness Scale (Hoddes et al., 1973) was administered to all participants before the first n-back condition, during the two breaks between conditions, and at the end of testing to evaluate level of alertness throughout the testing procedure. This scale is a brief subjective measure of arousal, ranging from 1 (high level of alertness) to 7 (extremely sleepy). Level of drowsiness was also determined by EEG recording and by observation via video monitoring of the participant during their task performance.

Statistical Analyses

Independent sample t-tests were used to determine if differences were present between the SLE and control groups for age, education level, estimated full scale IQ, and depression scores. Analyses of covariance (ANCOVA) were conducted, with depression as the covariate, to compare the two groups on RT and performance accuracy for each condition of the n-back. One-way ANOVAs (group) were conducted to determine if RT and accuracy differences were present between the SLE and control groups for each of the n-back conditions, separately. Significance was set at $p < .05$. Pearson product-moment correlations were used to compare RT and accuracy measures, with significance set at $p < .01$ to account for multiple comparisons.

Results

Demographic and patient health characteristics are presented in Table 2. Table 3 lists the number and percentage of patients taking each of the primary medications of interest in our SLE sample. Patients and controls did not differ on age [$t(74) = 1.05$, n.s.], education [$t(74) = -.42$, n.s.], or estimated full scale intelligence based on scores on the NAART [$t(74) = .$

368, n.s.]. A significant difference between groups was found for the BDI total score [$t(74) = 6.77, p < .001$] and cognitive subscore [$t(74) = 2.81, p < .01$], with SLE patients reporting significantly higher levels of depression than controls on both scores.

N-Back Reaction Time

Mean RTs for the SLE and control groups are presented in Table 4. To evaluate group differences in RT across n-back conditions, a Group (SLE, Control) $\times$ Response Type (correct match, correct non-match) $\times$ Condition (0-, 1-, 2-back) analysis of covariance (ANCOVA) was performed, with the BDI-II cognitive score as the covariate. The analysis yielded a significant Response Type $\times$ Condition interaction [$F(2, 146) = 43.76, p = 0.000$] and a significant Group $\times$ Condition interaction [$F(2, 146) = 6.42, p = 0.006$]. The Response Type $\times$ Condition interaction was produced by slower responses to match than non-match stimuli, particularly during the 2-back condition, regardless of group. In this study, group differences were of interest and, thus, only main effects and interactions that included group were probed further. The response type (correct matches or correct non-matches) did not interact with group, so correct responses were used for all remaining analyses.

Figure 2 illustrates the Group $\times$ Condition interaction for RT to correct responses. In order to probe the Group $\times$ Condition interaction, separate Group $\times$ Condition ANCOVAs were conducted to compare the 0 and 1-back, the 0 and 2-back, and the 1 and 2-back. For the 0 versus 1-back, and 0 versus 2-back ANCOVAs, significant Group $\times$ Condition interactions were present [$F(1, 73) = 4.93, p = 0.029$; and $F(1, 73) = 7.35, p = 0.008$, respectively], indicating that the SLE group had greater RT slowing from the 0 to 1-back and 0 to 2-back than controls. For the 1 versus 2-back, only main effects were present for group [$F(1, 73) = 11.70, p = 0.001$] and condition [$F(1, 73) = 105.44, p < 0.001$]. The depression score was not a significant covariate in any of these analyses.

Comparisons were also conducted to test for RT differences between the SLE and control groups for the 0, 1, and 2-back conditions separately. One-way ANOVAs revealed that RTs were significantly slower for the SLE group compared to controls for the 0-back [$F(1, 74) = 6.38, p = 0.014$], 1-back [$F(1, 74) = 9.85, p = 0.002$], and 2-back [$F(1, 74) = 11.33, p = .001$].

Analyses were also conducted on the RT difference scores (0-back RT subtracted from 1-back and 0-back subtracted from 2-back conditions) to examine group differences after eliminating simple PS. A Group $\times$ Condition (1-back minus 0-back, 2-back minus 0-back) ANCOVA was performed. Main effects were present for condition [$F(1, 73) = 104.13, p < .001$] and group [$F(1, 73) = 8.75, p = .004$]. The Group $\times$ Condition interaction was not significant. The significant main effect for group indicated that when complex PS was compared between the groups after the effects of simple PS were eliminated, the SLE group showed significantly slower RTs than controls for both the 1-back and 2-back conditions. The complex PS difference scores for RT are presented in Table 4.

N-Back Accuracy

A Condition (0-, 1-, 2-back) $\times$ Group ANCOVA, with the BDI-II cognitive score as the covariate, was conducted for accuracy scores on the n-back (total correct responses). The mean accuracy scores for each group are presented in Table 4 and Figure 3. A significant Condition $\times$ Group interaction was present [$F(2, 146) = 3.64, p = .029$]. The BDI-II cognitive score was not a significant covariate. To examine the simple effects, comparisons were also conducted to test for accuracy differences between the SLE and control groups for the 0, 1, and 2-back conditions, separately. One-way ANOVAs revealed that accuracy (total correct responses) was significantly poorer for the SLE group compared to controls only for

the 2-back [$F(1, 74) = 5.23, p = .025$]. In sum, compared to healthy controls, SLE patients performed more poorly than controls only on the task with the greatest WM demand.

N-Back RT and Accuracy Comparisons

To examine the relationship between PS and performance accuracy, Pearson correlations were performed between the mean RT and accuracy scores on the 0, 1, and 2-back for the SLE and control groups, separately. No significant correlations were present between RT and accuracy scores in the control group. For the SLE group, RTs for the 0, 1, and 2-back were all related significantly to accuracy on the 2-back only ($r = -.50, -.57, \text{ and } -.48; p < .002$, respectively). Thus, for the SLE group, slower PS (both simple and complex) was related to poorer task performance on the most demanding WM condition (2-back). Figure 4 illustrates the correlation between 2-back RT and accuracy (total correct responses) for the SLE group.

Working Memory and Disease Measures

To identify patients with a history of neuropsychiatric syndromes, colors were used in Figure 4 to note SLE patients who had both focal and diffuse syndromes (red squares) and only diffuse syndromes (blue squares) as defined by the American College of Rheumatology (ACR Ad hoc committee, 1999). The remaining SLE patients (black squares) did not have a neuropsychiatric syndrome.

In order to determine if measures of disease duration and current disease activity influenced WM and PS, correlational analyses were conducted. Neither disease duration nor current disease activity was correlated with RT to correct responses for the 0, 1, and 2-back or with WM accuracy. However, the correlation between 0-back RT (simple PS) and current disease activity approached significance ($r = .30, p = .059$).

Discussion

The present study examined the relationship between WM deficits and PS in SLE patients using a visual n-back task, which provided measures of RT and accuracy at three levels of WM load. We found that for accuracy, SLE patients did not differ from controls in the number of correct responses for the 0 or 1-back conditions. However, as hypothesized, SLE patients had significantly fewer total correct responses for the 2-back, the condition that places the greatest demand on WM. Unlike previous studies of WM in SLE, RT measures on the n-back allowed us to parse processing speed and WM effects and examine the effect of PS on WM performance in SLE.

As expected, for all participants (including controls), longer RTs were associated with increased task complexity (load) from the 0 to the 1 to the 2-back (see Figure 2). When SLE patients were compared to controls, however, there was a significant Group $\times$ Condition interaction. Although the SLE patients had significantly slower RTs than controls for all three conditions, a greater difference was present between controls and SLE patients for the 1 and 2-back conditions than for the 0-back, with SLE patients showing increased slowing relative to controls as WM demand increased. When we controlled for simple PS differences between the groups by removing RT for the 0-back from the 1 and 2-back conditions, SLE patients still showed significantly longer RTs on both the 1 and 2-back conditions compared to controls.

Complex PS in this study reflects the combined effect of the cognitive burden of WM and the motor response to simple identification of stimuli. We hypothesized that group differences would be present only for complex PS during the 2-back condition, but we found PS differences for all three n-back conditions. Although simple PS was slower in SLE

patients compared to healthy controls, the complex processing demand of WM produced significantly greater response slowing in SLE compared to controls as indicated by the group $\times$ condition interaction. This interaction suggests that slowed simple PS alone cannot explain sufficiently the slower RTs seen in the SLE group compared to controls during the 1- and 2-back conditions. Thus, we conclude that the slowed complex PS reflects WM deficits for both WM load conditions.

According to the *Relative Consequence Model*, poorer WM performance would be a secondary effect of a simple PS deficit and not a true WM deficit. If this model had been supported by the present study, SLE patients would have shown slower RT than controls, but the increase in RT from the 0 to 1 to 2-back conditions would have been parallel to that of controls. Rather than supporting this model, our findings of both PS and WM impairments in SLE support the *Independent Consequence Model* in that an interaction was present, and also that the SLE patients had WM deficits even after subtracting the effects of simple PS. These findings were present for SLE patients regardless of disease duration or disease severity.

In this study, we also found that PS (both simple and complex) negatively correlated with task performance only on the 2-back condition and only for SLE patients. Slower PS during the 0- 1- and 2-back conditions each was related to poorer performance during the highest WM load condition. As seen in Figure 4, this relationship between PS and WM was present in SLE patients with and without neuropsychiatric syndromes. The twenty-four patients with diffuse syndromes (blue squares) were distributed throughout the scatterplot. The six patients with focal syndromes (red squares) had a range of performance scores and they did not fall in the poorest range. Thus, the presence of one or more neuropsychiatric syndromes does not appear to explain the WM and PS deficits that were observed. Rather, as a group the SLE patients showed PS and WM deficits compared to controls, and within the SLE group, slower PS was related to poorer n-back performance for the 2-back condition.

Although as many as 75 to 81% of SLE patients have been identified as having NPSLE (Brey et al., 2002; Steens et al, 2004), the pathophysiology of CNS dysfunction for many of the neuropsychiatric syndromes is not well understood. In particular, some of the more common neuropsychiatric syndromes, such as mood disorders, anxiety disorders, headache/migraine, and mild cognitive dysfunction are not clearly linked to CNS involvement. Studies have found white matter involvement in SLE patients with and without neuropsychiatric syndromes, as revealed by white matter hyperintensities on MRI (Abreu et al., 2005; Kozora et al., 1998). One study, using magnetization transfer imaging (MTI) to detect microscopic CNS damage, found structural damage to gray matter but not white matter in a group of SLE patients with heterogeneous neuropsychiatric syndromes (Steens et al., 2004). Future studies using quantitative MRI measures of microscopic brain damage are needed to determine the interrelationships among gray and white matter damage and the type and specificity of neuropsychiatric manifestations, as well as the differential effects of white and gray matter damage on PS and WM deficits in SLE. For example, it may be predicted that the patients with the slowest RTs and poorest accuracy scores would show both gray and white matter involvement.

There were several potential limitations to this study. It could possibly be argued that patients achieved fewer total correct scores due to an inability to respond within the 2 sec interstimulus interval. However, this conclusion is unlikely because the mean response time for patients was 960.9 msec (SD 224.4 msec). It is also possible that fatigue may have had some effect on WM performance of the SLE patients, although the mean ratings on the Stanford Sleepiness Scale for both groups were in the alert range (scores 1 to 3). Other potentially confounding factors could include depression, medications, and disease severity

and duration. Most of these variables were considered in the statistical analyses and did not affect the results, but their effects on cognitive function cannot be ruled out. Several previous studies that examined the effects of corticosteroids on cognitive function in SLE reported no significant findings (see for example, Glanz et al., 1997; Kozora et al., 1996; Shucard et al., 2004), and one study reported that brief exposure to low dosage corticosteroids in SLE had a positive effect on cognition (Denburg et al., 1994). The mean dosage for the patients on steroids in our study was low at the time of testing. Thus, it is unlikely that steroids played a significant role in producing the observed WM and PS deficits. Interestingly, current disease activity did not relate to complex PS or WM performance, but did produce a positive correlation that approached significance with 0-back RT (simple PS). It is possible that current disease activity acted as a third variable in the significant correlation between simple PS and 2-back accuracy by exerting an adverse effect on simple PS.

In summary, this study was the first to use an n-back task to examine the cognitive functions of PS and WM in patients with SLE. The findings provide new information about the relationship between PS and WM functions in SLE. Both functions were impaired, and WM deficits were present even after removing the contribution of simple PS. These deficits were found in a group of SLE patients with and without neuropsychiatric syndromes. Further studies are needed to compare WM and PS deficits with quantitative MRI measures of microscopic brain damage in SLE to determine the extent to which white and gray matter involvement can be related to each of these cognitive deficits.

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Figure 1.

Diagram of n-back conditions. Each letters is presented one at a time on a computer screen. The arrows indicate the occurrence of a match. All other letters are non-matches. Participants respond to every letter (outer button press for non-matches and inner button press for matches). For the 0-back the letter X is a match. For the 1-back and 2-back a match occurs when the letter is the same as the one either 1 or 2 letters back, respectively.

Figure 2. Mean RTs (msec) for correct responses (correct matches + correct non-matches) in each condition of the n-back for SLE and control participants. Error bars reflect standard error of the mean.

Figure 3. Mean accuracy scores (number of correct responses) for each condition of the n-back for SLE and control participants. Error bars reflect standard error of the mean.

Figure 4.

Scatter plot of significant correlation between 2-back RT and accuracy scores for SLE patients only ($n = 40$). Blue indicates patients with a history of one or more diffuse neuropsychiatric symptoms, red indicates patients with a history of a focal manifestation (either stroke or seizure) as well as one or more diffuse manifestations, and black indicates patients with no history of a neuropsychiatric syndrome (with the exception of cognitive impairment).

Table 1

History of NPSLE Syndromes in SLE patients studied

Number of Pts.	
1	stroke, peripheral neuropathy, migraine, mood disorder
1	stroke, peripheral neuropathy, mood disorder
1	stroke, migraine, mood disorder
1	seizure, migraine, mood disorder
1	seizure, migraine
1	seizure, encephalitis
2	peripheral neuropathy, cranial neuropathy, migraine, mood disorder
2	peripheral neuropathy, migraine, mood disorder
1	cranial neuropathy, migraine, mood disorder
1	peripheral neuropathy, migraine
6	migraine, mood disorder
3	peripheral neuropathy
6	migraine
2	mood disorder
1	encephalitis
10	none

Table2

Demographic and health variables: Means, ranges, and standard deviations.

	SLE (N=40)		Control (N=36)	
	M (range)	SD	M (range)	SD
Demographics				
Age	46.9 (20-63)	12.5	44.1 (20-59)	10.7
Education Level	15.1 (12 – 21)	2.0	15.3 (12 – 18)	1.8
Estimated IQ (NAART)	108.9 (97 –122)	6.3	108.4 (98 – 120)	6.1
Health Characteristics				
Disease duration (yrs)	14.2 (1 – 34)	8.8	-	-
Disease activity checklist	5.6 (0 – 11)	2.9	-	-
BDI total score *	11.6 (0 – 34)	8.3	1.8 (0 – 11)	2.7
BDI cognitive subscale *	2.5 (0 – 14)	3.3	0.8 (0 – 7)	1.8
Steroid dose (mg/day) **	9.5 (1 – 30)	7.0	-	-

* significant difference between SLE group and controls, $p < .01$

** For 17 patients on steroids at time of testing

Table 3

Medication Summary for SLE patients (some patients were on more than one medication at the time of testing).

Medication	N (%)
NSAIDs ¹	21 (48)
Antimalarials	27 (68)
Corticosteroids ²	17 (42)
Immunosuppressives	7 (18)
SSRIs ³	16 (40)
Other Antidepressant ⁴	6 (15)
Narcotic pain med ⁵	2 (5)
Anticonvulsants	1 (2)

¹ NSAID = Nonsteroidal anti-inflammatory drugs

² The corticosteroid medication was Prednisone in all cases

³ SSRI = Selective Serotonin Reuptake Inhibitor

⁴ Other antidepressant = 3 on Wellbutrin, 3 on Amitriptyline or Trazadone

⁵ Six other patients took narcotic pain medication as needed, and did not take it within a minimum of 24 hrs of testing

Table 4

Accuracy and RT on the n-back task

	SLE		Healthy controls		p
	M	SD	M	SD	
Total correct responses					
0-back	147.45	2.34	147.33	2.14	n.s.
1-back	142.67	4.90	143.81	3.46	n.s.
2-back	126.03	13.17	132.11	9.52	.025
RT (ms) to correct responses					
0-back	580.2	107.9	526.7	71.7	.014
1-back	749.0	159.8	644.0	126.8	.002
2-back	960.9	224.4	812.4	137.8	.001
1-back minus 0-back	170.48	91.04	117.30	106.6	.022
2-back minus 0-back	380.67	185.53	285.35	121.7	.011