

Relations Among Indexes of Memory Disturbance and Depression in Patients With Lyme Borreliosis

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This study examined the relation between complaints of memory disturbance and measures of mood and memory functioning in 55 patients with serological evidence of late-stage Lyme Borreliosis (LB). Patients completed the Self-Ratings of Memory Questionnaire (SRMQ) and the Beck Depression Inventory. Memory functioning was assessed with the California Verbal Learning Test. Depressed patients exhibited more frequent complaints of memory disturbance on the SRMQ, although their pattern of responses did not differ from nondepressed patients. There was a significant correlation between subjective memory ratings and self-reported depression (Spearman $\rho = -.57$, $p < .001$). No relation was observed between subjective memory ratings and objective memory performance. The results indicate subjective complaints of more severe memory disturbance in patients with LB and depression. Particular attention should be paid to the assessment of depression and subjective symptoms of memory disturbance when administering neuropsychological tests of memory functioning in patients with LB.

Key words: Lyme disease, depression, memory, self-report, awareness

Memory disturbance is known to be a frequent complaint in patients with Lyme Borreliosis (LB). In an unselected sample of 56 patients diagnosed with LB,

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Hilton et al. (1994) found that cognitive impairment was the fourth most commonly reported symptom following joint pain, fatigue, and headache. Complaints of memory disturbance are found even more frequently in patients presenting with neurologic features. In a sample studied by Logigian, Kaplan, and Steere (1990), symptoms such as difficulty remembering things, forgetting names, missing appointments, and misplacing objects were reported in 81% of their patients with encephalopathic symptoms. Memory disturbance remains a prominent feature of patients with symptoms persisting following treatment. It has been reported in

over 90% of patients with features of post-Lyme syndrome (Bujak, Weinstein, & Dornbush, 1996; Gaudino, Coyle, & Krupp, 1997).

Complaints of memory disturbance in LB have been supported by the results of a growing number of neuropsychological studies. Patients with LB have been found to exhibit lower scores on memory tests than control groups using healthy participants and patients with chronic medical conditions such as fibromyalgia or osteomyelitis (Kaplan, Meadows, Vincent, Logigian, & Steere, 1992; Krupp et al., 1991; Ravdin et al., 1996). Other studies using neuropsychological testing have found evidence of chronic memory impairment in patients with persisting features of LB (Bujak et al., 1996; Gaudino et al., 1997; Shadick et al., 1994). In many of these cases, the neurologic symptoms of LB have been accompanied by abnormalities on other neurodiagnostic measures such as cerebrospinal fluid analysis, electromyography, and magnetic resonance imaging (Halperin, Krupp, Golightly, & Volkman, 1990; Logigian et al., 1990).

Although features of memory disturbance are commonly seen in patients with LB, it is clear that these features are not specific to the disorder. Symptoms of memory disturbance are frequently reported features of fibromyalgia, chronic fatigue syndrome, and a number of other conditions with symptoms that often mimic those seen in LB (Tiersky et al., 1997). Memory disturbance is also a common feature of depression that has been estimated to occur in 26% to 66% of patients diagnosed with LB (Fallon & Niels, 1994). The presence of depression may often complicate the presentation of memory because it is known that depressed patients often overemphasize the nature of their memory disturbance (Larrabee & Levin, 1986). Although the majority of neuropsychological studies on LB have found little relation between memory and depression, there have been some discrepancies (Kaplan et al., 1992; Krupp et al., 1991; Ravdin et al., 1996).

Understanding the nature of memory complaints becomes a critical issue when making a diagnosis of LB. It is important for the clinician to be able to determine whether a patient's complaints of memory disturbance are likely to be the result of the neurological consequences of LB or the result of an oversensitivity to cognitive symptoms secondary to depression. Little attention has focused on the nature of memory complaints in this population. The purpose of this study is to provide a systematic examination of these complaints and compare these to measures of mood and memory dysfunction.

Method

Participants

A total of 55 patients were examined during the initial course of treatment in an outpatient LB specialty clinic. The sample consisted of 27 men and 28 women. The mean age of the sample was 39.5 years (range = 19–66 years). The sample had an estimated verbal IQ of 108.7 ($SD = 9.31$), as determined by their performance on the North American Adult Reading Test (Blair & Spreen, 1989). All patients were assessed at the time of their initial diagnosis.

The diagnosis of LB was based on (a) known exposure to an endemic area; (b) signs and symptoms of LB, including arthritis or neurological findings such as Bell's Palsy, meningitis, or polyradiculitis; (c) serological confirmation including positive enzyme-linked immunosorbent assay (ELISA) for antibodies to *Borrelia burgdorferi* and corroboration with Western blot (any five of the following bands: 18, 21, 28, 30, 39, 41, 45, 66, 93 kDa). All patients also had the Venereal Disease Research Laboratory (VDRL) or Rapid Plasma Reagent, Rheumatoid factor, Anti Nucleic Antibody, and Sedimentation rate. A full physical evaluation was performed with detailed focus on the signs of LB. Arthritic investigation included oentgenograms and aspirations of joint fluid, if present. If neurological symptoms or signs were present, a lumbar puncture was performed. Spinal fluid was analyzed for protein, glucose, cells, VDRL, oligoclonal antibody production, ELISA with corresponding serum ELISA, a ratio of antiborrelial specific antibody, and a ratio of cerebrospinal fluid with serum. If radiculopathy was suspected, electromyography and nerve conduction velocity studies were performed.

Procedure

All participants completed a series of self-report inventories and underwent neuropsychological testing at the time of their initial visit. The measures used in this study included the following.

Self-Ratings of Memory Questionnaire (SRMQ; Squire & Zouounis, 1988). The SRMQ is a measure of subjective symptoms of memory disturbance. This questionnaire was initially designed to show that self-rating instruments can be used to distinguish be-

tween complaints reported by patients with depression in comparison to those with symptoms of amnesia or dementia. Squire and Zouzounis (1988) cited the scale as having useful application to other populations where questions arise about the nature of memory complaints or about the relation between self-assessment and test performance. The instrument consists of 18 questions covering different aspects of memory functioning. These include: short-term recall, word naming, facial memory, general attention, and alertness. Patients are asked to compare their current memory functions to their past memory abilities, rating themselves on a 9-point scale ranging from 4 (*better than ever before*) to -4 (*worse than ever before*). Total scores in the negative direction thus indicate that participants are rating their memory as worse than before. These questionnaires were completed by patients in each of the three groups.

Beck Depression Inventory (BDI; Beck, 1987).

The BDI is a commonly used self-report index of symptoms associated with depression. The instrument consists of 21 items reflecting subjective and vegetative symptoms of depression. Each item is graded on a 4-point scale ranging from 0 (*I do not feel sad*) to 3 (*I feel so sad or unhappy that I can't stand it*).

California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1987). This objective measure of verbal learning and memory consists of 16 words presented over five trials followed by a series of short- and long-delay recall trials. The test was administered according to standardized instructions. Indexes included in this study included: Total Learning (5 trials: $x/90$) and Long-Delay Free Recall ($x/16$).

Results

A listing of test items with mean ratings from the SRMQ are provided in Table 1. The lowest mean ratings were obtained for Items 1, 3, 7, and 11. These items, endorsed by 43% to 53% of the total sample, include complaints of an inability to recall names, hold things in memory, know things will stick in memory, and remember what one was doing. Relatively lower ratings were obtained for Items 10, 14, 15, and 18. These items were endorsed by less than 40% of the sample and included complaints of an inability to make sense of things, recall things from a long time ago, reach back for things from a few minutes ago, and recall things from childhood. Patients with depression (as defined by BDI scores greater than 10) endorsed rela-

Table 1. Mean Ratings and Percentage of Respondents Endorsing Individual Items on the Self-Ratings of Memory Questionnaire

Item Number and Description	Rating: Total Sample ^a		% Endorsed		
	<i>M</i>	<i>SD</i>	Total Sample	Nondepressed	Depressed
1. Search through my mind ...	-1.00	1.83	52.7	31.4	70.0
2. Relatives judge memory ...	-0.66	1.43	34.5	17.1	55.0
3. Hold things in memory ...	-0.96	1.98	50.9	31.4	65.0
4. Recall things when I try ...	-0.77	1.81	50.9	28.6	70.0
5. Past memory on "tip of tongue" ...	-0.87	1.74	40.0	20.0	60.0
6. Remember names and faces of people ...	-0.88	1.57	45.4	22.9	70.0
7. Know things will stick in memory ...	-0.96	1.60	45.4	25.7	65.0
8. Remember things from year ago ...	-0.62	1.61	29.0	11.4	50.0
9. Remember what I read and watch on TV ...	-0.79	1.68	43.6	20.0	70.0
10. Understand what people explain to me ...	-0.50	1.40	32.7	14.3	55.0
11. Remember what I was doing ...	-0.98	1.54	43.6	25.7	60.0
12. Pay attention to what goes on ...	-0.73	1.51	43.6	25.7	60.0
13. Remember facts about this form ...	-0.61	1.51	34.5	20.0	50.0
14. Recall things from a long time ago ...	-0.54	1.40	27.2	11.4	45.0
15. Recall things from a few minutes ago ...	-0.55	1.32	34.5	20.0	50.0
16. Follow what people are saying to me ...	-0.66	1.29	41.8	20.0	65.0
17. Alertness to things around me ...	-0.68	1.56	47.2	25.7	70.0
18. Recall things from my childhood ...	-0.41	1.17	25.4	5.7	50.0

^aScores range from 4 (*better than ever before*) to -4 (*worse than ever before*).

Table 2. Spearman Rank Correlations Among BDI Scores, Self-Ratings of Memory, and Objective Measures of Memory Performance

	Self-Ratings of Memory Questionnaire	CVLT Total Learning	CVLT Long Delay
BDI Scores	-.57*	-.13	-.06
Self-Ratings of Memory Questionnaire		.08	.04

Note: BDI = Beck Depression Inventory; CVLT = California Verbal Learning Test.

* $p < .001$.

Table 3. Mean CVLT Scores in Groups Classified According to BDI Scores

BDI Depression Level	Number		CVLT Total Learning		CVLT Long Delay	
	<i>N</i>	%	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Minimal (BDI Score 0–9)	35	63.6	52.8	10.2	11.0	2.8
Mild (BDI Score = 10–16)	14	25.5	56.7	6.9	12.1	2.4
Moderate and Above (BDI Score = 17 and Above)	6	10.9	54.2	17.3	11.0	4.5

Note: CVLT = California Verbal Learning Test; BDI = Beck Depression Inventory.

tively more items than other patients, but there was no distinguishable pattern to the items that were endorsed.

The ratings for the total 18 SRMQ items were combined into a total mean rating score for the entire questionnaire. The distribution of scores has a negative kurtosis ($k = -.095$, $SE = .634$) with the majority of the patients rating their overall memory functioning as worse than before. Variation from the normal distribution was confirmed by a significant Kolmogorov–Smirnov test with Lilliefors correction ($K-S$ Statistic = 0.130, $df = 55$, $p = .021$). The distribution of BDI scores also revealed a variance from the normal distribution with a negative kurtosis ($k = -.095$, $SE = .634$). In this case, the majority of scores are below the level associated with depression. Variation from the normal distribution was confirmed by performing a Kolmogorov–Smirnov test with Lilliefors significance correction ($K-S$ Statistic = 0.130, $df = 55$, $p = .021$).

BDI scores were not analyzed as continuous variables as a result of their distribution. For purposes of data analysis, patients were classified into three groups according to the level of symptoms endorsed on the BDI. The three groups included (a) minimal symptoms of depression (scores ranging from 0–9), (b) mild symptoms (scores ranging from 10–16), and (c) moderate to severe symptoms (scores ranging from 17–30). These levels were based on those outlined in the BDI manual (Beck, 1987). Nearly two thirds (63.6%) of the sample endorsed symptoms below the level associated with depression. Approximately 25% of the sample endorsed a mild range of symptoms and 10% endorsed moderate to severe symptoms of depression.

Memory test scores were distributed normally. As a group, the patients recalled a mean of 53.9 words over five learning trials ($SD = 10.4$). They recalled a mean of 11.3 from a total of 16 words following a half-hour delay ($SD = 2.9$). This level of performance is consistent with what was reported in other groups and in a previous sample of LB patients from this institution (Ravdin et al., 1996). Results of preliminary analyses revealed no significant age or sex differences on either of these scores. As a result of the violations of the assumptions of normal distributions, relations between memory scores and subjective rating scores were assessed with nonparametric tests. Spearman rank correlations are provided in Table 2. Significant relations were observed between SRMQ and BDI scores (Spearman $\rho = -.57$, $p < .001$). Patients with greater levels of self-reported depression also reported themselves as having increasing levels of memory impairment. There were no significant relations between BDI scores and either of the memory variables. No significant relations were observed between subjective ratings of memory and scores on objective memory tests, Total Learning, Trials 1–5: $F(2, 54) = 0.72$, $p = .49$; LD Free Recall: $F(2, 54) = 0.68$, $p = .51$. The findings indicate that patients with higher ratings of self-reported memory impairment did not have greater levels of disturbance as assessed by a more objective measure of memory functioning.

The means and standard deviations of CVLT scores for the three depression groups are provided in Table 3. The three groups did not differ in their objective memory scores for both total learning and delayed

free-recall indexes from the CVLT. The mean scores for all groups were within the average range according to normative standards. Patients with signs of objective memory disturbance, as defined by total recall *T* scores lower than 40, did not exhibit any tendency to underreport symptoms of memory disturbance.

Discussion

The purpose of this study was to provide a systematic examination of memory complaints in patients with LB. Responses to self-report inventories of memory functioning indicate that more than 50% of these patients experienced subjective symptoms of retrieval impairment (e.g., searching through my mind), working memory dysfunction (e.g., holding things in my mind), and impaired attention or encoding (e.g., alertness to things around me). The findings indicate that more than one third of our sample also reported mild or greater levels of depression. Patients with depression exhibited higher rates of memory complaints, although the pattern was not different in comparison to nondepressed patients. A significant correlation was obtained between subjective ratings of memory and the degree of self-reported depression. There was no relation between memory ratings and performance on more objective measures of memory functioning. No differences in memory scores were found in patients with mild or moderate depression as compared to nondepressed patients. The results indicate that patients with LB and increasing levels of depression report greater symptoms of memory disturbance than what is observed on formal indexes of memory functioning.

Inconsistencies between subjective complaints and memory test results have been observed in previous studies of LB. Although more than 80% of the sample studied by Logigian and colleagues reported symptoms of memory disturbance, only 48% of these patients had impairments identified on formal neuropsychological testing (Logigian et al., 1990). In another study, patients with no evidence of impairment on neuropsychological testing were found to have the highest levels of depression (Krupp et al., 1991). Kaplan et al. (1992) found little relation between depression and memory impairment in their sample. Patients with LB exhibited the lowest scores on memory indexes, whereas the highest rates of depression were found in control groups of patients with fibromyalgia and depression. Only one other study has used a formal questionnaire measure of subjective

memory functioning. In a previous sample from this center, there was no correlation between self-ratings of memory functioning and CVLT variables. Patients with LB had higher rates of self-reported depression than normal controls and patients with osteomyelitis (Ravdin et al., 1996). No relation between memory and depression has been found in two studies examining patients with post-Lyme syndrome (Bujak et al., 1996; Gaudino et al., 1997).

The ability to detect discrepancies between subjective and objective features of memory functioning is aided significantly by the use of self-report indexes of memory functioning. Although there has been a substantial literature examining the tendency for depressed elderly patients to exaggerate the degree of their memory disturbance (Gilewski & Zelinski, 1986; Larrabee & Levin, 1986), this topic has been examined less frequently in younger samples. One study has recently demonstrated that younger patients with depression exhibit mild levels of cognitive impairment and report more self-reported cognitive failures, although no relation was observed between the self-report ratings and scores on the CVLT (Otto, Bruder, Fava, & Delis, 1994). A similar pattern of findings has emerged in groups with a number of neurological and medical conditions including headache, closed head injury, and cancer (Branca, Giordani, Lutz, & Saper, 1996; Cull et al., 1996; Gass & Apple, 1997). In most of these disorders, complaints of memory dysfunction are viewed within the context of increasing somatization. However, it is important to note that inaccurate ratings of memory can also go in the other direction. Studies of patients with Alzheimer's disease, HIV-1 infection, and temporal lobe epilepsy have found that patients with the greatest degree of memory disturbance tend to underreport the level of their symptoms (Hinkin et al., 1996; McGlone, 1994; McGlynn & Kaszniak, 1991). In these cases, it is hypothesized that judgments of memory functioning are affected by a disturbance in cerebral mechanisms responsible for awareness and metacognition (Schacter, 1991).

In this study, scores from self-report indexes of memory and mood were not normally distributed. The majority of patients reported overall decreases in their memory functioning, with only a few reporting gains in their functioning since developing symptoms of LB. The majority of patients reported only minimal or mild symptoms of depression with only a few reporting a high level of mood disturbance. These variations from the normal distribution made it necessary for us to analyze these data with nonparametric methods. This is a

relatively common problem that is encountered when using self-report indexes in clinical populations and may lead to erroneous results if left unchecked. We caution other investigators to examine the distributions of brief self-report scales before analyzing them through parametric methods.

The results of this study have a number of practical implications for the diagnosis of LB. Previous research has demonstrated that a clinical history alone gives minimal information regarding diagnosis, particularly when patients come from endemic areas (Hilton et al., 1994). Appropriate serological and neurodiagnostic testing are needed to distinguish physical symptoms of LB from those associated with fibromyalgia, chronic fatigue syndrome, and depression (Steere, Taylor, McHugh, & Logigian, 1993). Symptoms of self-reported memory disturbance and other forms of cognitive dysfunction should be treated in a similar manner as these complaints as they are also seen frequently in these same conditions. We recommend the use of both subjective and objective indexes of memory functioning. Presenting complaints of memory disturbance in patients with suspected LB should be followed up routinely with formal questionnaires and objective neuropsychological tests of memory functioning.

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