Neuropsychological assessment in systemic lupus erythematosus patients: clinical usefulness of first-choice diagnostic tests in detecting cognitive impairment and preliminary diagnosis of neuropsychiatric lupus

K. Nowicka-Sauer¹, Z. Czuszyńska², Ż. Smoleńska², J. Siebert¹

¹Department of Family Medicine, Medical University of Gdansk; ²Department of Internal Medicine, Connective Tissue Diseases and Geriatrics, Department of Rheumatology, Internal Medicine, and Connective Tissue Diseases Outpatient Clinic, Medical University of Gdansk, Gdansk, Poland.

Abstract Objective

To evaluate the usefulness of neuropsychological tests in order to distinguish the first-choice methods useful in quick detection of cognitive impairment in SLE and preliminary diagnosis of neuropsychiatric manifestation. Study aimed at assessment of the prevalence and severity of cognitive deficits in SLE patients and comparison between SLE patients with neuropsychiatric manifestations (NP-SLE) and without ones (non-NP-SLE).

Methods

93 out of 104 SLE patients, 57 with NP-SLE and 36 with non-NP-SLE underwent comprehensive neuropsychological examination. Tailor-made structured interview for neuropsychological assessment in SLE (SISLE) was used. Patients' emotional state was assessed by clinical interview and HADS.

Results

Cognitive dysfunction was identified in 57% of SLE patients, 48.4% in 1-3 tests, 8.6% (8 patients) in 4 or more tests (severe decline). Among impaired patients 15% had severe decline. In NP-SLE group 63.2% were impaired vs. 47.2% in non-NP-SLE group. All 8 patients with severe decline were NP-SLE. The dysfunction was irrespective of premorbid intellectual level, age, education, disease duration and steroid treatment. In NP-SLE significantly lower scores were observed in 8 tests (10 parameters).

Conclusion

Cognitive dysfunction is frequent in SLE patients. The majority of patients has mild deficits, but severe decline is also observed. The dysfunction is more frequent and more pronounced in NP-SLE. The study distinguished 8-test-first-choice-battery useful in detecting cognitive impairment in SLE and in case of severe decline – in preliminary differentiating NP-SLE and non-NP-SLE. Structured interview for psychological/neuropsychological examination of SLE patients is a useful and required tool for a standard patients' assessment.

Key words

systemic lupus erythematosus, cognitive disorders, neuropsychological tests.

Katarzyna Nowicka-Sauer, MD, MA Zenobia Czuszyńska, MD, PhD Żaneta Smoleńska, MD, PhD Janusz Siebert, MD, PhD, Professor

Please address correspondence and reprint requests to: Dr Katarzyna Nowicka-Sauer, Medical University of Gdansk, Department of Family Medicine, Debinki 2 Street, 80-211 Gdansk, Poland. E-mail: kpsauer@gumed.edu.pl

Received on October 4, 2010; accepted in revised form on December 15, 2010. © Copyright CLINICAL AND

EXPERIMENTAL RHEUMATOLOGY 2011.

Introduction

In the broad spectrum of the neuropsychiatric symptoms observed in SLE patients cognitive deficits are present both in adult (1-3) and in paediatric patients (4). In a quite numerous group of patients, cognitive impairment is the first symptom of the disease (5). Moreover, cognitive decline when observed as one of the initial symptoms - leads to early diagnosis of SLE (6). According to American College of Rheumatology (ACR) (7), making a diagnosis of neuropsychiatric lupus requires evaluation of cognitive functioning by objective neuropsychological testing. Thus neuropsychological assessment seems to be one of important diagnostic procedures in SLE.

Although reliability and validity of the ACR test battery has already been established (8) it is still worth continuing the assessment of its usefulness in SLE patient populations. Moreover, it is vital for the researchers and clinicians to have a possibility to use alternative, proven and standardised methods of detecting cognitive decline in case of lack of normalisation data for a particular country population or lack of appropriate language version of a given test. There is no doubt that comprehensive neuropsychological test batteries are necessary for full assessment of patients' functioning but they are time-consuming and tiring for the participants. So it seems vital to create the battery especially useful for quick, but still proper evaluation of cognitive functions in SLE patients in which standard screening tools are not sensitive enough. It is crucial to realise that the results of neuropsychological examination are connected with definite diagnosis and followed by further diagnostic decisions as well as therapeutic management.

The prevalence of cognitive impairment varies between researchers from 21% to 80% (9, 10) when comparing studies in the years 1986-2003. Research reports published after the establishment of ACR classification, case definition and diagnostic directives present similar results reporting the prevalence of cognitive deficits between 52-80% (9, 11-13). The latest studies also confirmed

that cognitive dysfunctions remain the most frequent neuropsychiatric symptom (14-17). As it emerges from the literature, prevalence study results are still not completely concordant.

Another important fact is that cognitive deficits are observed both in SLE patients with neuropsychiatric symptoms and those without such manifestations (1-3, 18-25). Again, comparative study results differ in terms of prevalence of cognitive dysfunctions in patients with and without neuropsychiatric syndromes coexisting with SLE. However, in the majority of studies, more prevalent and more pronounced deficits are observed in patients with nervous system involvement (18, 21, 22, 26, 27). Comparative analysis of NP-SLE and non-NP-SLE is still an important research course tending to explain the specificity of cognitive dysfunction in patients with SLE.

According to the above-mentioned aspects of neuropsychological studies in SLE the aim of the study was to evaluate the usefulness of neuropsychological diagnostic tests, focusing on distinguishing the most sensitive first-choice methods that facilitate quick diagnosis of cognitive decline in SLE. Additionally, the aim was to make a between-group comparison of SLE patients with and without neuropsychiatric manifestations.

Patients and methods

Patients

The participants were 104 patients with SLE (99 women and 5 men). All of them were patients of the Rheumatology, Internal Medicine and Connective Tissue Diseases Outpatient Clinic of the University Clinical Centre of the Medical University of Gdansk. All the patients fulfilled the revised ACR diagnostic criteria for SLE (28). Each patient was informed about the aim of the study and agreed to participate in it. The study project was approved by the independent ethics committee of the Medical University of Gdansk.

Due to objective reasons (hospitalisation, personal reasons) or exclusion criteria (head trauma) from the initial group of 104 patients who underwent the first part of the examination, 93 pa-

Competing interests: none declared.

tients (88 women, 5 men) underwent a complete, comprehensive neuropsychological examination. The mean age was 41.78 years (range: 19–71).

According to the ACR nomenclature and case definition for neuropsychiatric manifestations (7), and on the basis of physical examination and medical files, the physician classified the participants into two study groups: the first group consisted of patients with SLE with neuropsychiatric symptoms (NP-SLE) and the second, SLE patients without neuropsychiatric manifestations (non-NP-SLE). The physician verified 18 ACR syndromes with exclusion of cognitive dysfunction because the diagnosis of this condition was the object of the present study. Finally, 57 patients were classified as NP-SLE (53 women, 4 men) and 36 patients as non-NP-SLE (35 women, 1 man).

Structured interview

Detailed information for proper neuropsychological evaluation was collected using a tailor-made structured interview for SLE patients (SISLE). The following data were collected using the SISLE: past learning problems; past/current cognitive subjective complaints and results from past neuropsychological assessment if available; past brain and/or head injury; substance abuse/addiction; past psychiatric, neurological or psychological consultation (including psychotherapy); past/current psychiatric or neurological disorders; past/current pharmacological treatment of psychiatric or neurological conditions; disease duration (from making final diagnosis) and duration of neuropsychiatric problems in the NP-SLE group; information on past and current pharmacological treatment of SLE, especially steroid treatment. The questionnaire also contained items related to current pain complaints (especially chronic daily headache) and sleep disturbances. We also investigated factors which might interfere with the examination and its results such as problems of vision and hearing, hand motor impairment, e.g. connected with arthritis that can be observed in lupus patients. With respect to these factors, not only quantitative but also qualitative assessment of the test results was made when needed. Demographic data required for description of study participants were also collected.

Neuropsychological examination

It is worth noting that patients' subjective cognitive complaints are important and can indicate real deficits. However, the clinical diagnosis of cognitive dysfunction can only be made by objective, formal neuropsychological testing. In the present study, neuropsychological tests were administered and interpreted by the clinical psychologist trained in neuropsychology (K.N-S). The assessed cognitive functions, standardised tests used (including these recommended by the ACR) (7) and parameters evaluated in a particular test (29, 30) are presented in Table I.

Premorbid IQ estimation and cognitive impairment criteria

The knowledge of patient's premorbid level of functioning is an important component of cognitive deficit evaluation (31). Diagnosis of cognitive deficits, especially in the case of suspicion of secondary dysfunction, should be made on the basis of comparison between the present and premorbid level of intellectual functioning (premorbid IQ) (31). In the ACR case definition of cognitive dysfunction, the necessity of knowledge concerning premorbid intellectual abilities is mentioned; moreover, it is emphasised that making a diagnosis of cognitive decline demands comparison between present and premorbid functioning (7). In most cases, data from previously taken formal examination of intellectual level are not available, thus several procedures for estimation of premorbid level of intellectual functioning were developed and they are accepted by researchers and clinicians worldwide, e.g. the New Adult Reading Test, best performance method, methods using results obtained in the Wechsler Adult Intelligence Scale, most stable tests ("hold tests") or equations based on demographic data (29-31). In the present study, premorbid IQ was estimated using Nelson and McKenna's regression equation based on WAIS-R Vocabulary aged graded score (32).

The aim of the estimation of premorbid IQ was not only to evaluate the level of premorbid intellectual functioning in order to investigate the homogeneity of compared groups in terms of IQ level, but also to determine cognitive deficits in the study group according to accepted diagnostic criteria. In our study the following criteria of cognitive impairment were used:

- Significant decline in test performance was stated when the result obtained was 2.0 or more standard deviation (SD) below estimated premorbid IQ.
- Cognitive deficit was diagnosed if there was significant decline (over 2.0 or more SD) in at least one test or one domain.

If there was decline in 4 or more tests or domains, dysfunction was classified as severe.

Emotional state

Hospital Anxiety and Depression Scale (HADS) (33) is a test used to assess the emotional state level, especially in patients with somatic diseases. HADS consists of two separate subscales assessing depressive and anxiety symptoms. A score between 0 to 7 points is in a normal range, 8–10 is a border score, 11 points and more represent an abnormal level of depressive/anxiety symptoms. The emotional status, severity of anxiety and depressive symptoms were also verified using a clinical interview by the clinical psychologist.

Examination procedure

Psychological examination lasting approximately 3–4 hours and was performed during two appointments. The examination conditions were the same in every case with no third person presence.

Statistical analysis

For statistical analysis, STATISTICA PL v. 6.1 was used. Results are reported as mean values with standard deviation (SD) and as proportions in case of qualitative (categorical) variables. For statistical analysis of categorical data, χ^2 test was used and parametric Student *t*-test was used for data measured on a

Cognitive impairment in SLE / K. Nowicka-Sauer et al.

Table I. Cognitive	functions assessed	, tests and	parameters used	l in pre	esent study.
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WAIS-R* Digit Span Forward [age-graded score]		
WAIS-R Digit Span Backward [age-graded score] Trail Making Test, Part B (TMT B) [time]		
WAIS-R Block Design [age-graded score] WAIS-R Object Assembly [age-graded score] Rey-Osterrieth Complex Figure (RCF) copy [time, type, score]		
Benton Visual Retention Test (BVRT) [number-correct, number-errors, type of errors] Rey-Osterrieth Complex Figure (RCF) 3 min. delayed recall [time, type score] WAIS-R Picture Completion [age-graded score]		
Auditory Verbal Learning Test (AVLT) [5-trial total score, visual and auditory recognition, number of intrusions and perseverations]		
WAIS-R Block Design [age-graded score] WAIS-R Picture Arrangement [age-graded score]		
WAIS-R Comprehension [age-graded score] WAIS-R Similarities [age-graded score]		
Stroop Color-Word Interference Test (Stroop Test) - Interference [time, number of errors] Trail Making Test, Part B (TMT B) [time]		
Trail Making Test, Part A (TMT A) [time] Stroop Color-Word Interference Test (Stroop Test) - Reading [time] WAIS-R Digit Symbol [age-graded score]		

nominal scale. To make a direct comparison between various test results and to diagnose deficits according to accepted criteria, each test score was transformed into a z-score. The cut-off point between norm and pathology, *i.e.* "normal cognitive function" or "cognitive deficits", respectively, was 2 SDs. The point of reference was a premorbid IQ estimated based on WAIS-R Vocabulary as mentioned above. We used $p \le 0.05$ as significance level.

Results

The demographic and clinical characteristics of patients, considering the classification based on the presence of neuropsychiatric manifestations are presented in Table II. As indicated in the table, there were no statistical differences between non-NP-SLE and NP-SLE patients according to sex distribution, estimated IQ, age, education level or disease duration and steroid treatment. The two study groups differed in terms of employment status: in the NP-SLE group, the percentage of patients on disability pension was higher. In the NP-SLE patients, the mean time of the appearance of neuropsychiatric

symptoms was 4.25 years, ranging from 1 to 21 years. Among clinical data, we noted significant differences between NP-SLE and non-NP-SLE in the prevalence of pain complaints and depressive as well as anxiety symptoms measured by HADS (Table II). The aforementioned symptoms were more severe in NP-SLE patients.

Cognitive deficits.

Comparison between NP-SLE and non-NP-SLE patients

Cognitive deficits were common in SLE patients (Table III). 57% (53 patients) fulfilled the accepted criteria for cognitive impairment. We observed a decline in 1-3 tests in 48.4% (45 patients) and severe impairment (decline in 4 or more tests) in 8.6% (8 patients). Among SLE patients with diagnosed impairment (53 patients), 85% had mild deficits and 15%, severe ones. As indicated in Table III, the prevalence of cognitive impairment in the NP-SLE group reached 63.2% and was higher than in the non-NP-SLE patients (42.7%). All 8 patients with severe decline were NP-SLE. The differences between NP-SLE and non-NP-SLE groups were statistically significant ($p \le 0.05$). Additional analysis of the percentage of patients with an impairment revealed that the percentage of NP-SLE patients was higher in every quantitative category (from 2 to 11 tests) but this tendency did not reach statistical significance ($p \le 0.05$) (data not shown).

First-choice tests in cognitive

function assessment of SLE patients

The results of the cognitive tests were analysed in two different ways. The prevalence of impaired performance when referencing to premorbid IQ being the first type (1st), and the analysis of mean scores being the second one (2nd), which was used to compare the patients with NP-SLE and non-NP-SLE. The 1st type of analysis revealed insignificant decline in most WAIS-R tests. Not many impaired performances were observed in WAIS-R Object Assembly and Digit Span Backward. Among the remaining test results, significant decline was observed in AVLT, RCF, TMT and Stroop Test (data not shown). The comparison of the prevalence of decline according to the 1st analysis type between NP-SLE and non-NP-SLE patients indicated significant differences in the following tests: AVLT, TMT, Stroop Test, WAIS-R Object Assembly and WAIS-R Picture Completion. Verbal tests form WAIS-R did not differentiate NP-SLE and non-NP-SLE groups (data not shown). The betweengroups comparison of the mean scores (2nd analysis type) revealed 8 tests (10 parameters among them) in which significant differences between NP-SLE and non-NP-SLE were noted (Table IV). Patients with NP-SLE had significantly lower mean scores in these tests.

Discussion

Many studies revealed that cognitive dysfunctions are often observed in SLE patients but the prevalence is not accordant between studies and ranges from 20% to 57.4% (1, 13, 15 19, 20, 23, 34, 35). In our study, cognitive deficits defined as a decrease from premorbid estimated IQ of at least 2 SDs in at least one test or domain, was observed in 57% of SLE patients. The similar prevalence ranged from 52% to 55%

Table II. Demographic and clinical data of SLE study groups.

	SLE (n=93)	non-NP-SLE* (n=36)	NP-SLE** (n=57)	<i>p</i> -value
Gender, n				NS
Female	88	35	53	
Male	5	1	4	
Estimated premorbid IQ, $x \pm SD$	105.3 ± 8.5	106.9 ± 7.9	104.3 ± 8.8	NS
Age, years, x ±SD NS	41.78 ± 12.67	40.94 ± 15.45	42.31 ± 10.67	
Education, n (%)				NS
Primary	13 (13.9)	6 (16.7)	7 (12.3)	
Vocational	18 (19.4)	6 (16.7)	12 (21.1)	
High school	44 (47.3)	17 (47.2)	27 (47.4)	
University	18 (19.4)	7 (19.4)	11 (19.3)	
Employment status, n (%)				< 0.01
Disability pension	51 (54.8)	15 (41.7)	36 (63.2)	
Retired	7 (7.5)	4 (11.1)	3 (5.3)	
Employed	26 (28)	9 (25.0)	17 (29.8)	
Student	9 (9.7)	8 (22.2)	1 (1.8)	
Disease duration, years, x±SD	8.1 ± 6.7	7.2 ± 7.1	8.7 ± 6.4	NS
Under steroid treatment, n (%)	87 (93.5)	33 (91.7)	54 (94.7)	NS
Maintenance dose	71 (76.3)	28 (77.8)	43 (75.4)	
Therapeutic dose	16 (17.2)	5 (13.9)	11 (19.3)	
HADS Depression, x±SD	6.24 ± 4.54	3.80 ± 3.3	7.78 ± 4.52	0.000
HADS Anxiety, x±SD	8.76 ± 4.91	6.00 ± 3.9	9.96 ± 4.97	0.000
Pain complaints, n (%)	45 (48.4)	11 (30.6)	34 (59.6)	0.006

NS: not significant, $p \ge 0.05$.

*non-NP-SLE: patients with SLE without neuropsychiatric manifestations; **NP-SLE: patients with SLE with neuropsychiatric manifestations.

Table III. Comparison of the prevalence of cognitive dysfunction in non-NP-SLE* and NP-SLE** patients.

	SLE (n=93)	non-NP-SLE (n=36)	NP-SLE (n=57)	p-value
Normal cognitive function, n (%)	40 (43)	19 (52.8)	21 (36.8)	
Cognitive dysfunction, n (%)	53 (57)	17 (47.2)	36 (63.2)	
Impaired in 1-3 tests, n (%)	45 (48.4)	17 (47.2)	28 (49.1)	
	85#			0.041
Impaired in 4 or more tests, n (%)	8 (8.6) 15 [#]	0 (0.0)	8 (14.0)	

*non-NP-SLE: patients with SLE without neuropsychiatric manifestations; **NP-SLE: patients with SLE with neuropsychiatric manifestations; *Percentage in the group of patients with cognitive dysfunction (n=53).

was observed by others (11, 27, 36). Higher prevalence was enriched by Carbotte (1) (66%) and Denburg (37) (71%). The cause of the difference may lie in methods of analysis used. Similarly to our study, these authors used premorbid IQ as a reference point but the premorbid IQ was estimated by the best performance method which often overestimates intellectual functioning (30). Indeed, literature review suggests that one of the main factor that may cause prevalence discrepancy is a difference in accepted criteria of cognitive decline (*e.g.* different cut-off points, premorbid IQ *vs.* norms as a reference point). The lower prevalence than the one indicated in our study was observed by researchers who used more rigorous criteria of cognitive impairment (23, 38, 39). In the later study, more rigorous criteria were used and, admittedly, although the same diagnostic tests were administered, there was no comparison between current and premorbid level of functioning. A study by Hay (40), in which – similarly to ours – the criterion was a decline in at least one test, revealed identical percentage of impaired patients.

Another factor determining the prevalence discrepancy is the number of tests used to assess cognitive functions. Individual tests differ in the spectrum of assessed domains and the level of sensitivity in detecting deficits. Sanna et al. (25) observed an impairment in 29% SLE patients using Mini Mental State Examination which is a standard screening tool used rather for general population and not sensitive enough for SLE patients' population. The same authors assessed the same patients' group on another occasion using different methods and they noted cognitive impairment in 74.5% of patients (13). These two studies clearly documented that prevalence analysis made using different neuropsychological tests influences the results indeed. Moreover, it is clear that studies without standardised comprehensive neuropsychological examination may underestimate the prevalence of cognitive deficits (25, 41). On the other hand, comprehensive examination may sometimes overestimate the prevalence of cognitive dysfunctions by detecting patients with a slight decline but, what is crucial from a clinical point of view, the failure to recognise clinically important decline by such examination is obviously less probable. It is worth mentioning that according to clinical rules, cognitive impairment should not be "diagnosed" on the basis of subjective patient's complaints or clinician's impression or suspicion. In every case, diagnosis of cognitive deficits requires prior objective examination and should be done even independently of patients' complaints. Taking into account methodological rules, patients with perceived cognitive deficits or subjective complaints not proved by neuropsychological examination, should not be included in the prevalence studies or other clinical data analysis or comparisons.

The other cause of prevalence differences is obviously patients' selection. Our study group consisted of SLE patients with and without neuropsychiatric manifestations and the prevalence was higher than in study by Kozora (42), in which selected patients without neuropsychiatric symptoms were examined. We observed lower prevalence

Table IV. Tests and parameters which differentiate patients with non-NP-SLE* and NP-SLE**.

Test – parameter	non-NP-SLE	NP-SLE	<i>p</i> -value
Benton Visual Retention Test – number of distortions	1.03 ± 1.11	1.88 ± 1.58	0.003
Trail Making Test, Part A – time	44.55 ± 14.94	56.27 ± 20.88	0.004
Auditory Verbal Learning Test - number of perseverations	2.09 ± 2.42	4.17 ± 4.28	0.005
Trail Making Test, Part B – time	95.09 ± 44.89	133.25 ± 85.0	0.011
WAIS-R Block Design – aged graded score	10.65 ± 3.01	9.21 ± 2.68	0.021
Benton Visual Retention Test - number of errors	3.44 ± 2.29	4.80 ± 2.97	0.022
Stroop Colour-Word Interference Test, Interference - time	64.38 ± 18.65	75.63 ± 26.40	0.027
Stroop Colour-Word Interference Test, Reading - time	23.32 ± 4.97	26.08 ± 6.36	0.038
Rey-Osterrieth Complex Figure Test, copy - time	134.20 ± 63.57	175.99 ± 107.92	0.043
WAIS-R Digit Symbol – age graded score	11.20 ± 3.40	9.62 ± 3.77	0.05

*non-NP-SLE: patients with SLE without neuropsychiatric manifestations; **NP-SLE: patients with SLE with neuropsychiatric manifestations.

than Sanna and co-workers (13). In the later study, only patients with subjective cognitive problems were examined dissimilarly to our study which included non-selected patients irrespectively of subjective complaints.

The results of the prevalence studies are still not fully accordant, nevertheless, it is worth pointing out that the establishment of case definitions and suggested tests battery by ACR was an undeniably important step in the progress of research on cognitive impairment in SLE patients.

As has arisen from our study and from research carried out by others, in the SLE population, mild cognitive deficits predominate over severe ones. In the present study, severe cognitive deficits were only observed in 8 (8.6%) of all SLE patients (15% out of 53 cognitively impaired patients) and this low prevalence is in accordance with other studies (3, 15, 18, 23, 43, 44). Our clinical observations and studies in this area suggest that more severe cognitive decline is observed in individual patients. Nevertheless, detection and treatment of such a profound impairment is vital due to the fact that cognitive deficits can be a mark of central nervous system involvement and sometimes co-exist with other nervous system manifestations. This thesis is accordant with the fact that in our study all severely impaired patients were those with NP-SLE. In addition, such profound decline significantly influences patients' emotional state and functioning. Nevertheless, mild and/or not numerous deficits cannot be disregarded, especially in patients with a high general intellectual level of functioning.

Similarly to other authors, we observed more frequent and more pronounced cognitive impairment in patients classified according to ACR case definitions as neuropsychiatric lupus (1, 13, 18, 20, 22, 23, 27, 40, 45). Not many studies were inconsistent with ours. Mulherin (43) revealed no differences between NP-SLE and non-NP-SLE in group of 21 SLE patients (9 were NP-SLE). These results, however, cannot be generalised due to small sample size. In another study (24) which did not reveal differences between the groups discussed, Mini Mental State Examination was used to compare NP and non-NP-SLE patients. As mentioned above, this test is not recommended for SLE patients.

The homogeneity of the NP-SLE and non-NP-SLE groups examined in our study according to premorbid IQ level, age, education and steroid treatment seems to prove that observed differences in cognitive functioning are the result of the disease itself and/or the co-existing involvement of the nervous system. Among factors influencing cognitive functioning in SLE patients, disease duration also seems to be of no importance, since cognitive deficits may occur at every stage of the disease, even very early in its course, as a first symptom. The noted difference in employment status (higher percentage of NP-SLE being unable to work) was expected since neuropsychiatric SLE is connected with more severe disease course, including disability.

The review of the research on cognitive functioning in SLE patients led us to a general conclusion that reporting the neuropsychological studies in SLE patients is vital to enclose the precise explanation of the inclusion study criteria, clear information of a performed neuropsychological examination with a precise description of methods and criteria used for diagnosis of cognitive dysfunction. The lack of such description can be deceptive and sometimes make betweenstudies comparisons impossible.

The latest European League Against Rheumatism (EULAR) 2010 recommendations for monitoring SLE patients include an assessment of cognitive functioning and emotional state (46). However, comprehensive neuropsychological examination is time-consuming, sometimes tiring and may not be necessary in every case. Taking these facts into consideration, the aim of the present study was to distinguish the possibly short but still sensitive and proper, group of tests that can be the first-choice battery for SLE patients. The present study allowed to distinguish the following tests which seem to fulfil the above-mentioned conditions and can be the first-choice battery, particularly useful for wide use and quick diagnosis of cognitive dysfunction in SLE patients (administration takes about 1 hour):

Trail Making Test, part A and B, Auditory Verbal Learning Test, Stroop Color-Word Interference Test, Rey-Osterrieth Complex Figure Test, Benton Visual Retention Test, WAIS-R Digit Symbol, WAIS-R Block Design WAIS-R Vocabulary for premorbid IQ estimation.

Moreover, in all of the above tests, except WAIS-R Vocabulary, patients with NP-SLE obtained significantly worse results than patients without neuropsychiatric manifestations. The most profound impairment was observed in complex attention, visual-spatial abilities, nonverbal memory, mental flexibility and psychomotor speed. Similar results were observed in other studies (1, 2, 12, 20, 23, 24, 26, 47, 48). Thus,

presented battery, especially in case of diagnosis of severe decline, can be useful in a diagnostic process of neuropsychiatric form of SLE.

The lack of decrease in test performance and lack of differences between NP-SLE and non-NP-SLE patients in WAIS-R Vocabulary, Comprehension, Similarities, Picture Arrangement and Picture Completion proved that the level of general intellectual functioning in patients with SLE, remains unchanged. This result was anticipated due to the fact that some of the abovementioned methods are "hold tests" (29, 30). Except WAIS-R Vocabulary, these tests do not seem to be useful in cognitive assessment of SLE patients.

In neuropsychological assessment it is indispensable to evaluate the patient's emotional state. Hospital Anxiety and Depression Scale used in the present study, verified by clinical review, turned out to be a useful tool in detecting patients with more pronounced depressive and/or anxiety symptoms as well as SLE patients with co-existing neuropsychiatric manifestations. Moreover, using HADS which evaluates both depressive and anxiety level is justified in SLE patients since our study results pointed out that anxiety symptoms were more pronounced than depressive ones in these patients.

Due to the fact that making diagnosis of cognitive impairment required not only neuropsychological assessment, but also gathering data vital for differentiating primary and secondary impairment connected with basic disease itself, we consider the structured interview tailor-made for SLE patients used in our study (SISLE) as a required tool facilitating diagnostic process.

As mentioned above, the evaluation of neuropsychological functioning and emotional state, reappeared in this year EULAR recommendations for SLE patients. Cognitive deficits observed in SLE patients are the most frequent NP symptoms, most probably being the manifestation of SLE itself and the signal of central nervous system dysfunction (19, 34) which can be detected very early by cognitive testing (49). Buća and co-workers (14) concluded that every SLE patient should undergo neuropsychological examination due to the fact that cognitive decline may be the predictor of brain structural abnormalities. That is why, it is justifiable that psychological, including neuropsychological, assessment should remain a standard element of a clinical judgment, care and monitoring of the disease course. Moreover, our results suggest that psychological examination, including cognitive deficits assessment, especially when severe decline is detected, can be a helpful tool in detecting neuropsychiatric manifestation of SLE. This conclusion is in accordance with Monov's (17). Such examination, besides its proven sensitivity in detecting central nervous system involvement, is also available, and is neither invasive nor expensive.

A strength of this study is that we examined the large non-selected group of SLE outpatients which consists of those with and without neuropsychiatric manifestations. Each patient was evaluated in terms of neuropsychiatric SLE manifestations according to ACR recommendations and they all underwent comprehensive neuropsychological examination performed and interpreted by a clinical psychologist. The emotional state was evaluated not only by psychometric tests but also by a clinical interview. Additionally, a structured, tailormade interview for the cognitive functioning evaluation in SLE was used. In summary, our research revealed that cognitive dysfunctions are frequently observed neuropsychiatric symptoms in SLE patients and they are more common and more pronounced in patients with nervous system involvement. In these terms, the present study constitutes confirmation of previous studies in this area. Furthermore, the analysis of the results obtained made it possible to distinguish the short, first-choice neuropsychological battery useful in quick, early detection of cognitive deficits in SLE. The WAIS-R Vocabulary test is useful in the assessment of premorbid intellectual functioning (premorbid IQ) in SLE patients. Severe decline was observed in SLE patients with neuropsychiatric manifestations, thus, according to our results, such profound impairment can lead to a suspicion of a neuropsychiatric form of SLE.

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Cognitive impairment in SLE / K. Nowicka-Sauer et al.

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