Assessment of visuo-spatial memory in patients with schizophrenia using the Location Learning Test.

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ABSTRACT: Recent studies give good evidence that memory impairment is one of the most profound cognitive deficits in schizophrenia. Multiple meta-analytic studies have demonstrated impairments especially in working and episodic memory including both its verbal and visual aspects. The scope of the present study was to examine the short and long term visuo-spatial memory in free immediate and delay recall conditions in patients with schizophrenia. We used Learning Location Test (LLT), a brief test designed initially to measure visuo-spatial recall and learning in older adults with possible dementia, as a new approach to the assessment of visuo-spatial memory and learning impairment in schizophrenia. We studied 30 patients with schizophrenia in comparison with 30 normal subjects matched with socio-demographic parameters. Patients with schizophrenia performed significantly lower in all tasks of LLT compared to the healthy subjects. The comparison between the two diagnostic groups of patients (paranoid and non paranoid patients) did not show any statistically significant difference regarding the three main index of LLT. Furthermore, the results indicate that patients have a tendency to form two separate groups: one achieving "good scores" and one achieving "very bad scores". In order to enhance the validity of the test and to reveal the characteristics of the two subgroups, further study in this population is needed.

Key Words: Schizophrenia, Visuo-spatial memory, Immediate and delay recall, Location Learning Test.

INTRODUCTION

Cognitive impairment is recognised as an important and primary aspect of schizophrenia[1]. The average patient with schizophrenia performance on cognitive tests falls statistically lower than the general population[2]. The main cognitive domains that show greater deficits in schizophrenia are memory and learning, executive functions, attention and general intellectual deficit[3,4,5].

These deficits have been shown to be present in first-episode patients who are antipsychotic drugs naïve[6] and in patients in clinical remission as well as in the acute clinical state[7]. Cognitive impairments impact patients on virtually every aspect of function, interfere with patients' ability to engage in real-world tasks, affect long-term outcome[8] and possibly contribute to some of the cognitive problems that characterize the clinical presentation of schizophrenia such as distractibility, forgetfulness, inattentiveness and concrete thought[9].

Memory has been regarded as one of the major areas of cognitive deficit in schizophrenia[10] and some researchers have proposed that some aspects of memory are selectively impaired relative to other neuropsychological functions in individuals with schizophrenia[11]. On the other hand few researchers have even referred to schizophrenia as an "amnesic syndrome"[12]. More over verbal and visual memory deficits considered as a prominent trait marker for schizophrenia, with impairments also observed in first-degree relatives of schizophrenic patients[13] .

Multiple meta-analytic studies have demonstrated that specific impairments of episodic memory are among the most profound memory deficits in schizo-

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phrenia, including both its verbal and visual aspects[14,15]. In a recent study[16] using the Visual Reproduction tasks of the Wechsler Memory Scale test reported a significant impairment in immediate and delay recall for visual material in schizophrenic patients.

Another aspect that has drowned special attention is the working memory (WM) deficit in patients with schizophrenia. WM is the capacity to hold mental representations on line transiently and to manipulate these representations[17]. According to older theories, WM is divided into a number of more or less independent subsidiary slave systems supervised by a central executive coordinator. Visuo-spatial memory (or else visuo-spatial sketchpad) is one component of the WM, responsible for situating the location of objects in space and is organized into two subsystems: the "object" and the "spatial" WM subsystems that can be segregated functionally and anatomically within the cortex It is suggested that both, object and spatial visual WM are affected in schizophrenia and the coordinator system as well[18]. In an extensive review of 33 studies (from 1992 to 2005) on spatial WM in schizophrenia Piskuilic et al[19] reported that from the quantitative data analysis there is strong evidence that patients with schizophrenia are impaired on the spatial WM measures and these impairments may be related to social disability and explain some cognitive deficits that characterize the clinical presentation of schizophrenia.

The presence of visuo-spatial learning and memory impairments in schizophrenia is supported also by fMRI studies. During spatial WM tasks healthy subjects showed increased activation in right frontal, temporal and cingulate regions. Schizophrenic patients showed greater activation compared with control subjects in left frontal, temporal and parietal regions as well as in right frontal regions[20]. The investigators also observed increased memory errors in schizophrenic patients, associated with increased prefrontal activation.

Although verbal memory in patients with schizophrenia has been extended studied, studies on visual memory are less numerous [13] On the other hand the literature examining delayed recall in schizophrenia is far less extensive and inconsistent than the immediate encoding studies. The goal of the present study is to examine the ability of short and long term visuo-spatial memory in free immediate and delay recall conditions in schizophrenic patients using the Learning Location Test (LLT). The LLT[21] is a brief test designed to measure visuo-spatial recall and learning that has been developed for use with older adults with possible dementia. LLT is a simple test, since it does not require fine motor control, verbal responses, or complex instructions. The LLT allows evaluation of the ability to learn the spatial location of a series of everyday objects and offers a measure of learning over trials. The LLt also offers a validation of delay recall (long term memory). From research literature we did not find any study applying LLT in patients with schizophrenia.

SUBJECTS - METHODS

We studied thirty inpatients from the 3rd university psychiatric department suffering from chronic schizophrenia in a clinically stable state, after remission of acute exacerbation. Diagnosis was based on ICD-10 criteria for clinical research[22] As an indicator of clinical stability, patients were studied just before their discharge of the psychiatric unit to independent accommodations in the community and they received the same dose of medications for at least 3 weeks. Patients were included to the study after review of their medical records and psychiatric interview by two of the investigators together with their treating clinicians. All patients were under medication treatment and were received 2nd generation antipsychotics with no anticholinergic agents.

The comparison group included 30 healthy volunteers with comparable socio-demographic status. All subjects were physically well and free of personal or family history of psychotic illness.

Exclusion criteria for all participants were head trauma resulting in loss of consciousness, alcohol or substance abuse and known organic brain disorder or medical conditions that may influence cognitive functions (e.g. thyroid function).

All participants provided written informed consent after receiving a full explanation of the test procedures. Finally the study protocol was approved by the Scientific and Ethical Committee of University General Hospital AHEPA.

The two groups were matched for age (patient's

Table 1. Demographic characteristics by group.

	Patients		**Controls**		
	N = 30		N = 30		***Significance***
	M	***SD***	**M**	***SD***	
Age	36.90	*10.14*	36.30	*10.73*	t = .222, ρ <.835
Education	12.43	*3.22*	15.27	*2.42*	t = - 3.381, ρ < .001
Gender (M/F)	19 / 11		15 / 15		x^2 = 0.297, *NS*

mean age: 36.90yrs, SD: 10.14; healthy controls mean age: 36.30yrs, SD: 10.73), but were significantly differed in educational years as assed by t-test (patient's mean: 12.3yrs, SD: 3.62, control's mean: 15.27yrs, SD: 2.42, t = 3.35, ρ < .001). Finally there is no difference on gender ratio (male - female) between the groups. (x^2 = 0.297, NS).

The demographic characteristics of the groups are presented in Table 1.

To all subjects was administered the LLT test, which includes the location learning task of 10 everyday objects which are located on a grid 5X5. After having observed the grid with the objects for 30 seconds, the subjects were asked to locate the cards with the objects in their original place, in a net grid. After 5 repetitions, a delayed trial (thirty minutes later) follows.

With this procedure we define the following index. First for each card we estimate the displacement score (DS). We sum up the displacement scores for all objects-cards and we estimate the displacement score for each trial (DS_1, DS_2 ect.). Then we calculate the total displacement score (TDS), adding the displacement scores of each trial (TDS = DS_1+ DS_2+ DS_3+ DS_4+ DS_5), which represent a measure of the mistakes the subject did. Second we calculate the Learning Index (LI) which derives from the sum of the ratio of improvement between the trials (a1, a2, ect.) divided by 4. The ratio of improvement between the 1st and 2nd trials e.g. a1 is done according to the formula a1 = DS_1 - DS_2 / DS_2. The LI indicates the ability to learn the visuo-spatial location of the objects throughout repetitions and is an index of subject's ability to form new memory records and to recall them in free conditions (maximum score 1). Finally after a delay of thirty minutes with no stimulus distraction, the subject is asked to put again the same cards-objects in their right place but this time without having observed the original grid. We measure again the displacement score of the trial (DS_d) and we estimate the delayed recall score (DRS) by subtracting the DS_d from DS_5. The DRS represents solely the free recalling ability after a certain period of time i.e. represents an index for long-term memory*.

STATISTICAL ANALYSIS

A statistical analysis was performed using SPSS version 11.5. Data analyzed between groups with t-test for independent samples as regards to the index TDS, LI and DRS. The group of patients was separated in two groups, one consisting of paranoid type schizophrenia and the other with the rest of types of schizophrenia in sum and the performance on LLT was directly compared between the groups.

Furthermore we examined the correlations in the patients' group with regard to education, age and gender. Correlations analyzed with Pearson's correlation coefficients.

RESULTS

1. *Between groups analysis*

Patients' group performed significantly lower compared to the healthy controls. The difference between two groups regarding the three studied index TDS, LI and DRS was statistically significant (t(58) = 4.702, 5.587, 2.535 for TDS, LI and DRS perspectively). The

* *More details concerning the instructions for the administration and scoring of LLT are presented in: Location Learning Test, Manual, Thames Valley Test Company, Bury St Edmunds, England, 2000.*

Table 2. Mean scores on LLT for both groups.

Parameters	Patients N = 30		Controls N = 30		*Significance*	
	Mean	***SD***	**Mean**	***SD***	**t**	**ρ**
TDS	45.33	*37.38*	11.90	*0.48*	4.702	< .0001
LI	0.48	*0.29*	0.84	*0.19*	5.587,	< .0001
DRS	2.45	*6.32*	0.10	*0.92*	2.535,	< .014

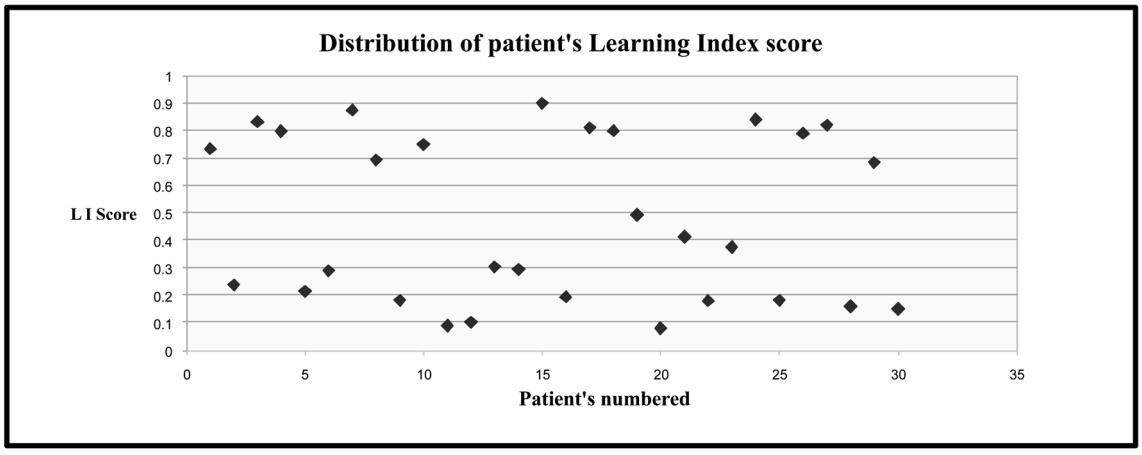

Figure 1. Distribution of patient's Learning Index score.

mean LI score for patient's group was 0.48 whereas controls subject's performance was 0.84 (with maximum score 1).

The results for both groups were presented on Table 2.

2. *Intergroup analysis*

2a. *Comparison of diagnostic groups*

The comparison between the two diagnostic groups of patients (group 1: N = 9, paranoids, group 2: N = 21, rest of schizophrenic types) did not show any statistically significant difference regarding the three index TDS, LI and DRS. Specifically, the Mann - Whitney U test for inter-type correlation returned negative results. (TDS: z = -.385, ρ < .722, LI: z = -.702, ρ < .504 and TDS : z = -1.308, ρ < .218).

2b. *Comparison according the distribution of patients LI score.*

The distribution of the patient's LI score, which indicate the ability to form new memory traits and to recall them in free conditions, revealed that our patient sample formed 2 separate groups (Figure 1): the first group (n = 13) performed within or near the range of healthy controls regarding the LI index, mean LI score: 0.79 (range 0.60 to 0.90), SD: 0,07 (control's LI: 0.84) were characterized as "good learners". The performance of the second patient's group (n = 15) was dramatically low with a mean LI score: 0.21 (range 0.08 to 0.37), SD: 0.09, "bad learners" patients. The rest two patients performed between the two groups ranges (LI index 0.48 and 0.41 respectively).

The comparison between the two groups of pa-

Table 3. Mean scores and statistical significance of the two groups of patients ("Good" and "Bad" learners) and healthy controls.

Parameters	**"Good" learners** N = 13		**"Bad" learners** N = 15		**Controls** N = 30		***Significance***	
	Mean	***SD***	**Mean**	***SD***	**Mean**	***SD***	**F(2,57)**	**ρ**
TDS	23.54*	*13.80*	62.40*	*44.17*	11.90	*0.48*	21.436	< .0001
LI	0.79*	*0.07*	0.20*	*0.09*	0.84	*0.19*	91.560	< .001
DRS	2.45	*6.32*	- 2.14	*5.33*	0.10	*0.92*	3.109	< .053

** Between the 2 groups of patients Mann - Whitney U test, TDS: z = - 2926, ρ < .005, LI: z = - 4.495, ρ < .0001) and DRS z = - 1.083, ρ < .302).*

tients (e.g. "good" and "bad" learners) revealed a statistically significant score for the TDS and LI index (Mann - Whitney U test, TDS: z = - 2926, ρ < .003 and LI: z = - 4.495, ρ < .0001) but not for the DRS (z = - 1.083, ρ < .302). Finally, from the analysis of variance between the 2 groups of patients and the control group we came to the same result. (ANOVA, TDS: F(2,57) = 21.436, ρ < .0001, LI: F(2,57) = 91.560, ρ < .001, DRS: F(2,57) = 3.109, ρ < .053). Table 3 presents the mean scores and statistical significance of the three groups.

2c. *Intergroup Correlation*

To find any possible effects of education, age and gender on LLT performance, we examined the relationship between these factors and LLT performance of patients. We found with Pearson's correlation that TDS, LI and DRS correlated significantly with education (TDS: r = 0,460, ρ < .001, LI: r = 0,548, ρ < .001 and r = 0,332, ρ < .01) but not with age.

Finally the comparison of a possible gender effect (t-test for independent samples) did not show any statistically important difference in both the patients group and the controls group. (Patients TDS: t(28) = - .436, ρ <.436, LI: t(28) = - 1.326, ρ <.196,. DRS: t(28) = - 646, ρ <.524, Controls TDS: t(28) = - 1.339, ρ <.191, LI: t(28) = 1.047, ρ <.304, DRS: t(28) = - 1.408, ρ <.170).

DISCUSSION

The important finding of the present study is that patients with schizophrenia as a whole group perform statistically lower on LLT test in comparison to normal controls and these findings concern all the learned index i.e. TDS, LI and DRS. The results reveal a deficit in the schizophrenic group concerning visuo-spatial learning, and visuo-spatial immediate and delayed recall in comparison with healthy volunteers.

The patients make more mistakes regarding the normal subject in learn and recall the right positions of the objects - cards throw the trails as indicated from their low TDS score, the main index for mistakes. According to the LI index patients with schizophrenia manifest a learning deficit concerning visuo-spatial material which is evident both in learning through repetition and in recall in free conditions. The poor LI score gives important evidence for an alleged deficit in encoding new memories. On the other hand the patients as a whole group manifested a difficulty in long term visuo-spatial memory, as expressed by DRS score, which represents an impairment concerning recall ability after a certain period of time (long term memory).

The low performance of our group of patients is correlated with educational level, but not with age, subtypes of schizophrenia and gender. Bucks and Willison[21] in their original study of the development of

LLT in patients with dementia reported worse performances for the female subjects of their patient group, whereas we did not find such a correlation in our group of patients with schizophrenia.

Our results supporting the existence of visuo-spatial learning and memory deficits in patients with schizophrenia are consistent with studies investigated the memory function in the same group of patients, although it is difficult to compare direct our results to other studies in the literature, given that LLT has not previous used for the investigation of memory deficits in patients with schizopheria. Visuo-spatial memory deficits are replicated finding in many studies investigated cognitive function in schizophrenia[23] and the magnitude of these deficits ranges between 1 and 2 standard deviations[24].

In their meta-analysis conducted on 70 studies Aleman et al. [25] reported a significant memory impairment in schizophrenia for both immediate and 30 minute recall of verbal and visual materials, with effect sizes of d = 1.27 and 1.00 for immediate encoding and d = 1.2 and 1.09 for 30 minute recall in verbal and visual tasks, respectively. They concluded that the magnitude of memory impairment was not affected by age, medication, duration of illness, patient status, severity of psychopathology, or positive symptoms.

Skelley et al[16] administered the Wechsler Memory Scale-Revised (WMS-R) and subjects (patients with schizophrenic and normal controls) are presented with stories (Logical Memory subtest) and visual figures (Visual Reproduction subtest) on three recall stages: immediate encoding - recall, 30 minute delay recall, and 24 hour recall. They reported that patients with schizophrenia demonstrated marked recall impairments for both verbal and visual materials at all recall conditions intervals. Authors noticed that, visual recall and learning is impaired in schizophrenic patients in contrast with verbal memory, but not verbal learning.

Finally, Bozikas et al[26] reported that their Greek schizophrenic patients showed statistically significant deficits on nonverbal memory and visuospatial ability as measured with the Rey-Osterrieth Complex Figure Test (ROCF) and the Hooper Visual Organization Test (HVOT).

The most interesting finding of our study is that concerning the distribution of LI index the patients with schizophrenia we studied tend to be separated in two distinct subgroups according to their LI performance i.e. their ability to learn new visuo-spatial information. The first group preserve their learning ability for visuo-spatial tasks and they perform within or near the range of healthy controls, while the second group of patients performed very poor and indicate a serious deficit in visuo-spatial memory. This is in accordance with earlier findings regarding memory impairment in dementia and the existence of "good and bad learners", using LLT[21]. The comparison of the two groups of schizophrenic patients (good and bad learners) and the controls group showed a statistically difference for the indexes TDS and LI but not for delayed recall DRS. The question if the memory deficit in schizophrenic patients concerns the encoding or the retrieval procedure rests has not yet been answered. Our results thought give evidence for a more pronounced encoding deficit since the three groups of subjects (schizophrenic patients and healthy controls) differ on the encoding condition but not on the free recall condition.

Studies using the delayed matching-to-sample (DMTS) task from the Cambridge Neuropsychological Test Automated Battery (CANTAB)[27], which tend to discriminate encoding from retrieval aspects of visuo-spatial memory[28] revealed conflicting results. Investigation of DMTS performance in adults with early phase and chronic adult-onset schizophrenia has revealed encoding deficits[29], while encoding and retrieval deficits have been suggested in first episode adult-onset schizophrenia and those at risk for adult-onset schizophrenia[30]. The second study where the patients with schizophrenia were younger gives strength to the hypothesis that the encoding and retrieval deficits in the younger patients with schizophrenia may be developmental stage dependent[31]. We have to mention that our patients were older (mean age 36.9 ysr) and they suffer from chronic schizophrenia.

The limitation of our study includes the small sample, the use of only one memory instrument and the gross presentation of psychopathological aspects (we formed only two groups of paranoid and nonparanoid schizophrenic patients).

Our study was a first attempt to apply LLT schizophrenic patients. In conclusion, regardless the small

patient's sample, we replicated the findings of previous studies which indicated that patients with schizophrenia are characterized by visuo-spatial memory deficits. More over we found out that schizophrenic patients may form two distinguished group according to the magnitude of these deficits; a group performed similarly with healthy subjects, while the second group presents very serious deficits. Further research is needed to specify the characteristics of the two subgroups.

Although LLT test has not been designed for such patients suffering from schizophrenia presents certain advantages for use in this population. It has very simple instructions and demands short time in its administration procedure that might compromise performance due to coexisting attentional deficits and fatigue burden. The use also of everyday objects for recall minimizes the semantic burden of the performance. Hence the use of LLT test in such patients may reveal a possible visuo-spatial memory deficit per se.

Abbreviations

LLT: Learning Location Test
WM: Working Wemory
DS: Displacement Score
TDS: Total Displacement Score
LI: Learning Index
DRS: Delayed Recall Score

Μελέτη της οπτικοχωρικής μνήμης σε ασθενείς με σχιζοφρένεια με το Location Learning Test.

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ΠΕΡΙΛΗΨΗ: Σύγχρονες έρευνες υποστηρίζουν την παρουσία διαταραχών των γνωστικών λειτουργιών στη σχιζοφρένεια και ειδικώτερα της λεκτικής και οπτικοχωρικής μνήμης. Σκοπός της εργασίας ήταν η μελέτη της οπτικοχωρικής μνήμης σε ασθενείς με σχιζοφρένεια. Χρησιμοποιήθηκε το Location Learning Test (LLT), μία συνοπτική δοκιμασία εκμάθησης της θέσης σειράς καθημερινών αντικειμένων στο χώρο και η άμεση και καθυστερημένη ανάκλησή τους. Μελετήθηκαν 30 ασθενείς με σχιζοφρένια κατά τη διάρκεια της νοσηλείας τους και 30 υγιή άτομα. Οι ασθενείς είχαν στατιστικά σημαντικά χαμηλότερη επίδοση σε όλους τους δείκτες αξιολόγησης της δοκιμασίας LLT συγκριτικά με τους υγιείς. Οι διαγνωστικές υποομάδες των ασθενών (παρανοϊκοί και μη παρανοϊκοί ασθενείς) δεν διέφεραν ως προς τις επιδόσεις στη δοκιμασία. Δεν διαπιστώθηκε συσχέτιση με το φύλο και την ηλικία αλλά μόνον με το μορφωτικό επίπεδο. Η κατανομή των τιμών του Δείκτη Εκμάθησης στην ομάδα των ασθενών διαμόρφωσε δύο διακριτές ομάδες. Η επίδοση της πρώτης ομάδα βρίσκεται μέσα ή κοντά στο εύρος διακύμανσης τιμών των υγιών, ενώ η δεύτερη ομάδα παρουσιάζει δραματικά χαμηλή επίδοση. Απαιτείται περαιτέρω διερεύνηση των χαρακτηριστικών των δύο ομάδων.

Λέξεις Κλειδιά: Σχιζοφρένεια, Οπτικοχωρική μνήμη, Άμεση και καθυστερημένη ανάκληση, Location Learning Test.

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