

COGNITIVE PSYCHOPATHOLOGY IN SCHIZOPHRENIA: COMPARING MEMORY PERFORMANCES WITH OBSESSIVE-COMPULSIVE DISORDER PATIENTS AND NORMAL SUBJECTS ON THE WECHSLER MEMORY SCALE-IV

Davide Maria Cammisuli¹ & Marco Timpano Sportiello^{1,2}

¹Department of Surgical, Medical, Molecular and Critical Area Pathology,
Pisa University School of Medicine, Pisa, Italy

²Hospital Psychology, Area vasta Nord Ovest Toscana, Pisa, Italy

received: 11.1.2016;

revised: 12.3.2016;

accepted: 29.3.2016

SUMMARY

Background: Memory system turns out to be one of the cognitive domains most severely impaired in schizophrenia. Within the theoretical framework of cognitive psychopathology, we compared the performance of schizophrenia patients on the Wechsler Memory Scale-IV with that in matched patients with Obsessive-compulsive disorder and that in healthy control subjects to establish the specific nature of memory deficits in schizophrenia.

Subjects and methods: 30 schizophrenia patients, 30 obsessive-compulsive disorder patients and 40 healthy controls completed the Wechsler Memory Scale-IV. Schizophrenia symptom severity was assessed by the Positive and Negative Syndrome Scale (PANSS). Performances on memory battery including Indexes and subtests scores were compared by a One-Way ANOVA (Scheffé post-hoc test). Spearman Rank correlations were performed between scores on PANSS subscales and symptoms and WMS-IV Indexes and subtests, respectively.

Results: Schizophrenia patients showed a memory profile characterized by mild difficulties in auditory memory and visual working memory and poor functioning of visual, immediate and delayed memory. As expected, schizophrenia patients scored lower than healthy controls on all WMS-IV measures. With regard to the WMS-IV Indexes, schizophrenia patients performed worse on Auditory Memory, Visual Memory, Immediate and Delayed Memory than Obsessive-compulsive disorder patients but not on Visual Working Memory. Such a pattern was made even clearer for specific tasks such as immediate and delayed recall and spatial recall and memory for visual details, as revealed by the lowest scores on Logical Memory (immediate and delayed conditions) and Designs (immediate condition) subtests, respectively. Significant negative correlations between Logical Memory I and II were found with PANSS Excitement symptom as well as between DE I and PANSS Tension symptom. Significant positive correlations between LM II and PANSS Blunted affect and Poor rapport symptoms as well as DE I and PANSS Blunted affect and Mannerism and Posturing symptoms, were found too.

Conclusions: Memory damage observed in schizophrenia patients was more severe and wider than that of patients with obsessive-compulsive disorder, except for visual working memory. Memory dysfunction, mainly related to episodic memory damage and reduced efficiency of central executive, is intimately connected to the specific psychopathological processes characterizing schizophrenia. Implications for therapeutics and cognitive remediation techniques are discussed.

Key words: schizophrenia - obsessive-compulsive disorder – cognition - memory deficit - Wechsler Memory Scale

* * * * *

INTRODUCTION

Cognitive psychopathology is a relatively new research field that aims to investigate how neuro-cognitive deficits commonly reported in psychiatric patient populations reveal cognitive phenotypes specifically characterizing mental disorders, in order to build up new theoretical models and to suggest how residual cognitive abilities can be improved by remediation techniques.

According to Lesh et al. (2011), cognitive impairment has been considered a core feature of schizophrenia since its first theoretical formulation (Kraepelin 1919) and it occurs across a number of domains (Bowie et al. 2006, Fioravanti et al. 2012). The group of experts in MATRICS (Measurement and Treatment Research to

Improve Cognition in Schizophrenia) supported by the National Institute of Mental Health (NIMH) developed a reliable and valid neuropsychological battery to be used in clinical trials and to facilitate drugs development. As a result, they have found that processing speed, attention, working memory, verbal and visual learning, abstract thinking and problem solving, and social cognition represent the cognitive domains most frequently impaired in schizophrenia (Nuechterlein 2004). Cognitive disorders are usually correlated to negative symptoms and disorganization (Schuepbach et al. 2002), they are relatively stable throughout the course of the illness in the majority of patients (Green et al. 2004) with different extent and strongly linked to functional impairment (Keefe & Harvey 2012), with negative implications in social, marital and work matters.

In relation to memory abilities in schizophrenia, working memory that seems to mostly influence the ability to find and keep a job (Bowie et al. 2008), has been observed to negatively affect treatment adherence as well as verbal long-term memory (Bhanji et al. 2004). A meta-analysis of Forbes et al. (2009) reported deficits in working memory subdomains (cfr. Baddeley 1992) without clear differences among them. A consistent association between illness duration, antipsychotic medication or symptom profile and working memory has not been found in schizophrenia, while dorsolateral prefrontal cortex has been identified as a critical brain region for central executive functioning (Lett et al. 2014).

Episodic memory damage is present in the majority of patients with schizophrenia (Cirillo & Seidman 2003) along with executive dysfunction (Lesh et al. 2011) and represents a hallmark of cognitive impairment. Episodic memory engages prefrontal, medial temporal and parietal regions which alteration has been implicated in pathophysiology of schizophrenia, with deficits occurring during encoding and retrieval phases in both visual and verbal tasks (Francis et al. 2015). Particularly, schizophrenia patients show poor recall of verbally learned information (Bowie et al. 2006). Verbal memory deficit does not represent an accessory but an intrinsic element of the disorder, it is not necessarily correlated to institutionalization and antipsychotic treatment (Sharma & Antonova 2003) and it has been reported in first-degree relatives of schizophrenia patients, too (Lesh et al. 2011). Neuropsychological data from some studies using the Judgment of Line Orientation Test (Benton 1983) and the Rey-Osterrieth Complex Figure (Rey 1941) also suggest a visuospatial memory impairment in schizophrenia due to difficulties in visuospatial discrimination, organizational strategies and retention (Hardoy et al. 2004, Seidman et al. 2003).

Obsessive-compulsive disorder (OCD) patients typically show memory deficits different from schizophrenia (SCH) ones and most related to visuospatial domain (Boone et al. 1991, Christensen et al. 1992, Dirison et al. 1995, Deckersbach et al. 2000). However, episodic memory dysfunction seems to be involved more than other memory subdomains in maintaining OCD symptomatology. According to Muller and Roberts (2005), episodic memory deficits may account for doubts and uncertainties of OCD patients evolving into obsessions that, in turn, leading to compulsive checking. Sher et al. (1984) had previously observed that a verbal memory deficit on the Logical Memory subtests of the Wechsler Memory Scale was associated to checking.

Particularly, OCD patients clinically present the tendency to semantically encode fragments of events when stories are processed in memory of prose tasks, a peculiar feature of memory processing similar to that occurring in schizophrenia patients (Danion & Marczewsky

2000). Such a qualitative approach in analyzing performances on neuropsychological tests may further help clinicians and researchers to yield more information about how cognitive disturbances support development, maintenance and recurrence of symptomatology in different psychiatric populations and to set up tailored cognitive remediation exercises.

Given this and as urged by some authors (Keefe 2008, Šoštarič & Zalar 2011) who have pointed out the necessity to improve neuropsychological investigation in schizophrenia versus other psychiatric disorders, we decided to compare memory performances of SCH patients, OCD patients and healthy controls by the most complete and newest memory battery currently available and not previously used in such a way, the Wechsler Memory Scale-Fourth Edition (Wechsler 2009a) with the aim of establishing the specific nature of memory deficits in schizophrenia, suggesting their contribution in sustaining symptomatology and pointing out specific deficiency of memory subdomain on which cognitive remediation techniques should be based. In particular, we sought to clarify the nature of memory impairment in schizophrenia according to the refinement of the concept of episodic memory proposed by Tulving (2002), as directly linked to subjective time sense, auto-noetic awareness and self.

SUBJECTS AND METHODS

Subjects

In this observational study, sixty psychiatric patients were recruited from the Mental Health Service of Pisa (Area vasta Nord Ovest Toscana, Italy). All the patients met the criteria of the Diagnostic and Statistical Manual of Mental Disorder Fourth Edition Text Revision (APA, 2000) for schizophrenia (SCH, n=30) and obsessive-compulsive disorder (OCD, n=30). The diagnoses were confirmed independently by two senior psychiatrists also by using chart reviews and family interviews. None of the patients had a current history of drugs or alcohol abuse, they had no history of neurological diseases, other diseases involving the Central Nervous System or serious medical conditions, they had no significant head injuries or mental retardation. In addition to the clinical groups, a group of healthy control subjects (CG, n=40) was recruited from the community and met the same criteria as the clinical groups to be included in the study. The groups were matched according to age, education and gender. The SCH patients received typical and atypical antipsychotic drugs while the OCD patients were treated by SSRI/tricyclic antidepressant and benzodiazepines during the time of memory assessment. All the participants gave written consent after appropriate and clear oral information about the study, which was approved by the Medical Ethics Committee of Pisa.

Methods

Memory system evaluation

The assessment was performed by three experienced psychologists in a quiet hospital environment by the administration of the Wechsler Memory Scale-Fourth Edition (WMS-IV) (Wechsler 2009a). The WMS-IV includes two batteries for individuals aged 16-69 (Adult Battery) and a shorter version (Older Adult Battery) for individuals aged 65-90. In our study, we used the Adult version according to the ages of individuals constituting our samples. The WMS-IV takes about one hour and half to be administered to normal subjects. The experienced psychologists maintained a steady pace of administration with psychiatric patients and were alert for their changes in mood and cooperativeness during testing. Some flexibility was necessary to balance the need of patients with the maintainance of the standard administration procedures (e.g. not to exceed maximum elapsed time of 20-30 minutes from immediate to delayed conditions).

The WMS-IV provides a deep assessment of memory and it consists of seven subtests which evaluate specific aspects:

- a general cognitive screening: Brief Cognitive Status Examination;
- a memory of prose task: Logical Memory (LM), Immediate (LM I) and Delayed (LM II);
- a learning test of verbal memory for associated word pairs: Verbal Paired Associates (VPA), Immediate (VPA I) and Delayed (VPA II);
- a spatial memory for unfamiliar visual material: Designs (DE), Immediate (DE I) and Delayed (DE II);
- a non verbal memory task: Visual Reproduction (VR), Immediate (VR I) and Delayed (VPA II);
- a visuospatial working memory task: Spatial Addition (SA);
- a visual working memory task: Symbol Span (SSP).

For our study we decided not to administer optional subtests (i.e. Brief Cognitive Status Examination, Word Recall from VPA and Copy Design from VR) in order to reduce psychiatric patients' fatigue, maximize their effort and maintain a good relationship during the administration. A considerable amount of time was spent by the experienced psychologists to build introductory rapport prior to the test administration.

Raw subtests scores are transformed into appropriate age-adjusted scaled scores (Mean=10; SD=3), which are summed up to create Indexes scores (Mean=100; SD=15). Indexes scores providing information about examinees' performance on memory domains are the following: 1) Auditory Memory Index (AMI): LM I and II, VPA I and II; Visual Memory Index (VMI): DE I and II, VR I and II; Visual Working Memory Index (VWMI): SA and SSP; Immediate Memory Index (IMI): LM I, VPA I, DE I, and VR I; Delayed Memory Index (DMI): LM II, VPA II, DE II and VR II.

Clinical Assessment

The Positive and Negative Syndromes Scale (PANSS) (Kay et al. 1987) was used to measure severity of symptoms in SCH patients. It consists of three subscales for the evaluation of Positive Symptoms (7 items: Delusions, Conceptual disorganization, Hallucinatory behaviour, Excitement, Grandiosity, Suspiciousness/persecution, Hostility), Negative Symptoms (7 items: Blunted affect, Emotional withdrawal, Poor rapport, Passive/apathetic social withdrawal, Difficulties in abstract thinking, Lack of spontaneity and flow conversation, Stereotyped thinking) and General Psychopathological Symptoms (16 items: Somatic concern, Anxiety, Guilt feelings, Tension, Mannerism and posturing, Depression, Motor retardation, Uncooperativeness, Unusual thought content, Disorientation, Poor attention, Lack of judgement and insight, Disturbance of volition, Poor impulse control, Preoccupation, Active social avoidance). Each item is rated on a 7-point scale that ranges from 1 (symptom is absent) to 7 (symptoms is extremely severe).

Statistical analysis

The data were analyzed by using the SPSS 20 (IBM) statistical package. Sociodemographic characteristics of the samples were compared by Independent Samples T-Test while for categorical variables a Pearson's chi-square test was used. Differences in WMS-IV performances were calculated by a One-Way ANOVA with a Scheffé post hoc test to determine the direction of the differences among schizophrenia, obsessive-compulsive disorder and control groups. Statistical significance was reached for a p value <0.01.

Pearson correlations were made between illness duration in SCH and OCD patients and WMS-IV Indexes and subtests scores. Non parametric Spearman Rank correlations were used between scores on PANSS subscales and WMS-IV Indexes and between PANSS symptoms and WMS-IV subtests.

RESULTS

Sociodemographic characteristics of the clinical samples

Participants were demographically matched in terms of age (42.9±10.8 in SCH, 42.6±13.7 in OCD, 41.9±11 in CG) (SCH vs OCD, $t=0.062$, $p=0.951$; SCH vs CG, $t=0.345$, $p=0.731$; OCD vs CG, $t=0.189$, $p=0.851$), education (10.6±2.8 in SCH, 9.5±2.5 in OCD, 10.8±2.4 in CG) (SCH vs OCD, $t=1.158$, $p=0.254$; SCH vs CG, $t=-0.292$, $p=0.771$; OCD vs CG, $t=-1.528$, $p=0.135$) and gender (M:F in SCH=22:8; M:F in OCD=18:12; M:F in CG 30:10, $\chi^2=4.62$, $p=0.202$). Mean illness duration was 26(±8) for SCH patients and 17(±8) for OCD patients.

Table 1. Mean performance of SCH patients, OCD patients and controls on WMS-IV and inter-group comparisons

	SCH n=30 Mean (SD)	OCD n=30 Mean (SD)	CG n=40 Mean (SD)	F
Indexes				
AMI	71.6 (19.3)	92.6 (14.9)	97.1 (12.2)	18.9
VMI	68.1 (15.6)	84.3 (13.6)	101.2 (13.9)	36.6
VWMI	74.4 (12.8)	84.3 (11.9)	101.3 (13.8)	29.7
IMI	67 (16.8)	86.2 (15.8)	98.2 (11.1)	33
DMI	67.4 (16.9)	88.5 (12.2)	100.3 (17.4)	28.7
Subtests				
LM I	4.9 (3.4)	9.4 (2.7)	9.9 (2.3)	22.7
LM II	5 (3)	9 (3.1)	9.3 (2.6)	17.9
VPA I	5.7 (3)	7.9 (2.4)	9.5 (2.4)	13.1
VPA II	5.7 (3.8)	8.3 (2.6)	9.2 (2.4)	8.6
DE I	4.4 (2.8)	7.5 (3.6)	9.6 (2.1)	25.6
DE II	5.1 (2.1)	7.4 (3)	10.1 (3)	24.3
VR I	5.4 (3.3)	6.8 (3.2)	10.3 (2.7)	17.8
VR II	4.9 (3.2)	7.9 (2.6)	10.7 (3.1)	24.8
SA	6 (2.4)	6.8 (2.2)	10.3 (2.3)	23.9
SSP	5.3 (1.9)	7.8 (2.9)	10 (3.1)	20

Note: SCH: Schizophrenia patients; OCD: Obsessive-compulsive disorder patients; CG: Control group; F= Values of F Fisher; AMI: Auditory Memory Index; VMI: Visual Memory Index; VWMI: Visual Working Memory Index; IMI: Immediate Memory Index; DMI: Delayed Memory Index; LM I: Logical Memory Immediate Recall; LM II: Logical Memory Delayed Recall; VPA I: Verbal Pairs Associates Immediate Recall; VPA II: Verbal Pairs Associates Delayed Recall; DE I: Design Immediate Recall; DE II: Design Delayed Recall; VR I: Visual Reproduction Immediate Recall; VR II: Visual Reproduction Delayed Recall; SA: Spatial Addition; SSP: Symbol Span

Table 2. Scheffé post-hoc comparisons between groups

	SCH vs CG	OCD vs CG	SCH vs OCD
Indexes			
AMI	0.000	0.721	0.001
VMI	0.000	0.004	0.005
VWMI	0.000	0.001	0.082
IMI	0.000	0.047	0.001
DMI	0.000	0.126	0.001
Subtests			
LM I	0.000	0.882	0.000
LM II	0.000	0.963	0.000
VPA I	0.000	0.244	0.067
VPA II	0.001	0.740	0.055
DE I	0.000	0.081	0.005
DE II	0.000	0.018	0.035
VR I	0.000	0.006	0.397
VR II	0.000	0.031	0.019
SA	0.000	0.000	0.568
SSP	0.000	0.063	0.036

Note: SCH = schizophrenia patients; OCD = obsessive-compulsive disorder patients; CG = control group. Statistical significance was achieved at $p < 0.01$. AMI: Auditory Memory Index; VMI: Visual Memory Index; VWMI: Visual Working Memory Index; IMI: Immediate Memory Index; DMI: Delayed Memory Index; LM I: Logical Memory Immediate Recall; LM II: Logical Memory Delayed Recall; VPA I: Verbal Pairs Associates Immediate Recall; VPA II: Verbal Pairs Associates Delayed Recall; DE I: Design Immediate Recall; DE II: Design Delayed Recall; VR I: Visual Reproduction Immediate Recall; VR II: Visual Reproduction Delayed Recall; SA: Spatial Addition; SSP: Symbol Span

Inter-group comparisons analysis

Mean and standard deviations of the three groups on the WMS-IV Indexes and subtests were first reported in Table 1 with Fisher values by One-Way ANOVA.

Scheffé post-hoc comparisons indicated that SCH patients perform significantly more poorly than CG in

all Indexes and subtests scores ($p < 0.01$) as expected, while OCD show a statistical significant difference when compared to CG only in VMI ($p = 0.004$), VWMI ($p = 0.001$), VR I ($p = 0.006$), and SA ($p = 0.000$). SCH patients had significant lower performances than OCD patients in AMI ($p = 0.001$), VMI ($p = 0.005$), IMI ($p = 0.001$), DMI ($p = 0.001$), LM I ($p = 0.000$), LM II

($p=0.000$) and DE I ($p=0.005$). No correlation was found between SCH and OCD illness duration and WMS-IV Indexes and subtests scores (Table 2).

Correlations between psychopathological and memory measures

Means and standard deviations of Positive, Negative and General Psychopathology PANSS subscales were 19.6 ± 5.4 , 20.5 ± 9.7 and 33.6 ± 9.7 , respectively. No correlation was found between PANSS subscales and WMS-IV Indexes. Interestingly, significant negative correlations were found between LM I ($\rho=-0.72$, $p<0.01$) and LM II ($\rho=-0.66$, $p<0.01$) with PANSS positive symptom Excitement as well as between DE I and PANSS general psychopathology symptom Tension ($\rho=-0.62$, $p<0.01$). Significant positive correlations were found between LM II and PANSS negative symptoms Blunted affect ($\rho=0.54$, $p<0.05$) and Poor rapport ($\rho=0.55$, $p<0.05$) as well as DE I and PANSS negative symptom Blunted affect ($\rho=0.60$, $p<0.05$) and general psychopathology symptom Mannerism and Posturing ($\rho=0.50$, $p<0.05$).

DISCUSSION

According to the principles for interpreting performances on the WMS-IV (Wechsler 2009b), the examination of memory structural aspects highlights that SCH patients have mild difficulties on auditory and visual working memory tasks and compromised visual, immediate and delayed memory, whereas OCD patients show a more inhomogeneous profile mainly characterized by a reduced efficacy of visual memory, visual working memory and immediate memory. As corroborated by the comparison with the CG group, OCD patients had significantly lower scores in visual memory and visual working memory, especially in VR I and SA subtests that contribute to determine the VMI and VWMI scores, respectively. This finding is supported by evidence of declarative non verbal memory and visuospatial skills deficits in OCD patients (Kuelz et al. 2004, Muller & Roberts 2005).

Memory damage observed in schizophrenia patients is more severe and wider than that of patients with obsessive-compulsive disorder, except for visual working memory: the SCH group reported significantly lower scores than the OCD group in auditory, visual, immediate and delayed memory. With regard to auditory memory, many studies that have shown how SCH patients perform poorly on word list learning (Karilampi et al. 2007) and verbal delayed memory (Robles et al. 2008) are in line with our findings. Verbal memory tasks have been found to best discriminate SCH patients from normal subjects (Müller et al. 2004). Additionally, verbal memory impairment is associated with a volume reduction of the prefrontal-hippocampal circuit (Cirillo & Seidman 2003, Kraguljac et al. 2013). The dysfunction

of this circuit provokes the failure of information consolidation reflecting low scores on verbal memory tasks. Moreover, low verbal abilities affecting intelligence early occur in the life of schizophrenia patients from school age (O'Carroll 2000). This may represent a core feature of cognitive endophenotype in schizophrenia supporting that verbal memory is a vulnerable area of the pathological process (Golimbet et al. 2006). Furthermore, increasing evidences have indicated that verbal memory impairment is also underpinned by genetic factors in samples with high risk of developing schizophrenia (Hill et al. 2008). Parallel to performances on auditory memory, visual memory impairment has been documented in schizophrenia (Neuchterlein et al. 2004, Chang et al. 2014). Our results also confirm those of Gold et al. (1992, 2000) that have demonstrated an impairment of SCH patients on immediate and delayed recall on the previous versions of WMS.

Interestingly, our comparison between SCH and OCD patients does not show any statistical significance on visual working memory even if they significantly differed in comparison to CG, to testify in favour of a slight impairment in this memory subdomain in OCD patients. Some alterations related to executive functioning could explain this finding in a different way. In schizophrenia, the central executive weakness may account for the inability of maintenance over time internal representation of contextual information to be manipulated and processed. This would lead patients to have less attentional resources to be allocated to perform tasks. As is well-known, the prefrontal cortex has been identified as playing a critical role in working memory performance (Buchsbaum & D'Esposito 2008). Working memory tasks activate dorsolateral prefrontal cortex (Ranganath & Blumenfeld 2008), a region known to be disrupted in schizophrenia (Barch et al. 2001). Cognitive deficit in schizophrenia could be mainly due to the dysfunction of this brain area affecting central executive efficiency for attentional control (Lett et al. 2014). Otherwise, according to Chamberlain et al. (2005), in OCD patients the failure in cognitive inhibitory processes (i.e. control over internal cognitions disturbed by intrusive thoughts and ideas) associated with abnormalities in neural network connecting cortical to subcortical structures (particularly the lateral orbitofrontal loop), may explain memory deficits and abnormal behaviour. Moreover, anxiety in OCD patients represents an intrusive condition that prevents the efficacy of the central executive, by reducing inhibition on interference of irrelevant stimuli in achieving a goal.

Our study precisely points out the failure of SCH patients in the ability to remember visually presented information in comparison to OCD patients, especially for unfamiliar visual material in the immediate condition (DE I). This subtest provides a reliable assessment of memory for visual details and spatial location. Beyond previous investigations (Seidman et al.

2003, Kim et. al. 2008), we underline that visual memory disorder in schizophrenia may be due both to an impairment of simultaneous stimuli processing and a deficiency of strategic planning in sequencing actions to reproduce the correct items and location of items, stressing even more the role of the central executive in determining an integrated experience of consciousness on the workspace. Manifestations of pronounced fear, anxiety, stiffness, tremor, profuse sweating and restlessness as intrusive conditions greatly influencing central executive functioning may explain the negative correlation found between DE I and PANSS Tension symptom. We also suggest that a major difficulty in executive control seems to be associated to physical manifestations connected to affective tone flexion (i.e. a scarce emotional responsiveness and unnatural movements or posture), as revealed by the association between DE I and Blunted affect and Mannerisms/Posturing symptoms, respectively.

Moreover, as already reported by Danion et al. (1999), SCH patients do not show difficulties in retaining isolated aspects of an event but they usually failed in identifying it as a global experience, as observed by scores significantly worse on LM I and II than those of OCD patients. Such a task in which the number of correct items defining the story is recorded, is strongly influenced by the examinee's ability to organize verbal information in a consistent and logical scheme. In our sample, we noted a relatively preserved ability to perform a semantic encoding (no statistically significant difference between SCH and OCD in VPA scores) that allow patients to retain isolated aspects of an event but a damage of episodic memory hindering the unitary recomposition of different aspects of an event that would lead patients to live a fragmented, incoherent and chaotic experience of self. The tendency to process memories of events by a semantic encoding, also present in OCD, would be exacerbated in schizophrenia. Distortions of episodic memory can be interpreted as manifestations of a defective functioning of auto-noetic awareness consisting of conscious recall (cfr. Tulving, 1985, 2002) that would prevent the unitary recomposition of various aspects of a same event. Cognitive failures in episodic memory highlight auto-noetic awareness crumbling strongly characterizing the inability of SCH patients to present story elements in an organized and meaningful way and clearly differencing them from OCD ones. Moreover, performances on LM I and II may be negatively affected by accelerated motor behaviour, heightened responsivity to stimuli, hypervigilance or excessive mood lability, giving reason why of the negative correlation between these WMS-IV subscales and Excitement symptom. The sense of coherence (Happé and Frith 2006) and the sense of agency (Dimaggio et al. 2012) help to define the personal history of each individual (i.e. autobiographical memory). It is also determined by the ability to integrate spatiotemporal characteristics of experiences and it is

shaped by interpersonal relationships. A great contribution in the area of interpersonal neurobiology has been offered by Siegel (2001). He noted how brain cells from infancy respond to sensory events from external world and how development of "neural integration" - as the process in which distinct components come to be clustered into a functional whole- can be fostered or hindered by important interpersonal relationships and social interactions. With regard to our findings, manifestations of a SCH patients' inability in interpersonal relationships, such as a diminished emotional responsiveness, a lack of interpersonal empathy and of closeness in conversation might contribute to the formation of a poor neural integration, by confirming the association between low scores on verbal memory delayed recall tasks (LM II) and PANSS negative symptoms Blunted affect and Poor rapport.

Drug treatment as a covariable that may influence patients' performances on memory testing not taken into account and the non-use of common psychiatric interviews (e.g. SCID, MINI) for diagnostic ascertainment represent the main limitations of our study. It should also be implemented by the collection of more extensive data in order to give more robust and significant results.

In spite of these limitations, as far as we know, we have reported the first results from the comparison of performances of schizophrenia patients and obsessive-compulsive disorder patients on WMS-IV. This test represents an advantage since it provides an in-depth analysis of memory subdomains functioning, not simple to administer in the case of patients with mental disorders. In relation to its previous version, the Wechsler Memory Scale-III (Wechsler 1997), the WMS-IV presents many advantages. One of the WMS-IV development goal was to improve subtests reliability without dramatically increasing testing length. Another goal was the development of visual working memory tasks requiring mental manipulation of visual information. In addition to the creation of a Visual Working Memory Index (VWMI), another goal of the WMS-IV development was to improve the content of the Visual Memory Index (VMI), by minimizing the impact of visual-perceptual abilities, visuoconstruction skills and verbalization of visual stimuli on visual memory subtests. Finally, the overall index structure of the WMS-III provided 13 primary and supplemental index scores based on 11 subtests; by contrast, the WMS-IV has got a more simplified index structure with 7 subtests providing 5 index scores for the Adult Battery. Furthermore, the use of a comprehensive standardized battery instead of isolated memory tests commonly adopted in clinical practice (e.g. California Verbal Learning Test, Rey-Osterrieth complex figure), allows to evaluate memory as a complex cognitive system, ensures that all areas can be adequately assessed and points out strengths and weaknesses of each patient, in order to set up tailored exercises from cognitive

remediation techniques currently available. However, we recommend caution when WMS-IV Indexes and subtests score are interpreted because of numerous factors (e.g. visual-spatial processing, severe attentional problems) that might influence memory performance (cfr. Wechsler 2009b).

Many studies have demonstrated that cognitive abilities of schizophrenia patients can be ameliorated thanks to cognitive remediation interventions that have relevant and durable implications for functional independence, work and social life (McGurk et al. 2007, Wykes et al. 2011). It has been reported that patients can benefit from interventions after 3-6 months and show maintenance effects for the majority of treated cognitive domains during time (Wykes & Reeder 2005). Empirical support for cognitive remediation in schizophrenia is well-documented (Barlatti et al. 2013, Thorsen et al. 2014). Neurocognitive gains are obtained thanks to the improvement of the underlying neuropsychological functions that help patients in cognitive restructuring such as attention, memory and executive functioning (Wykes & Reeder 2005). In the light of our results, SCH patients should undergo programs including strategy coaching (McGurk et al. 2007) that mainly targets memory and executive functioning, by teaching patients strategic information processing such as chunking information and semantic categorization and by requiring them to monitor and give a final evaluation of planned actions to perform memory tasks.

Cognitive psychopathology has become an important area of research in a number of psychiatric disorders. According to Trivedi (2006), research in this area has shed light on various aspects of psychiatric disorders, such as the association to biological underpinnings, the explanation of underlying psychopathology and issues related to course, outcome and treatment strategies. In particular, comparing neuropsychological performances of psychiatric patients may help in differentiating pathologies by the characterization of peculiar neurocognitive profiles and in better explaining the contribution of cognitive symptoms to clinical phenomenology of mental disorders.

We would stress that the most important frailty of memory system in schizophrenia patients can be traced back to episodic verbal memory accounting for a severely damaged sense of self (Sass & Parnas 2003) and a lack of auto-noetic awareness along with a decreased frontal efficiency in context-processing pointing out a central coherence deficit (cfr. Happé & Frith 2006). Such findings have some relevant implications for pharmacological treatment and psychotherapy. In fact, thanks to neurocognitive evaluation, psychiatrists are facilitated in selecting drugs for pharmacological treatment, starting from the knowledge of their effects on cognition (cfr. Kasper & Resinger 2003) while psychotherapists should take into consideration modalities of memory functioning in patients with schizophrenia to obtain better results. Further research in

cognitive remediation area is strongly encouraged, especially with the aim of improving cognitive remediation exercises tailored to specific weaknesses of SCH patients' neurocognitive profile thanks to personalized treatment protocols. Cognitive remediation techniques should also improve in distinguishing specific and not specific effects of an intervention, evaluating persistence and generalizability of observed improvements and estimating the influence of all the other factors that may interact with treatment outcomes, such as patients' motivation and adherence.

In comparison with published research in this domain, the present study used the WMS-IV as the most comprehensive and newest scale of its series to evaluate memory performance, allowing clinicians and researchers to depict memory profile of psychiatric patients, by specifically outlining deficits for each memory subdomain and improving quality of psychodiagnostic testing and research outcomes. Starting from the most relevant memory deficits showed by SCH patients, our findings particularly recommend the use of tests assessing verbal and visual memory as essential parts of a comprehensive neuropsychological battery when schizophrenia patients' performances are tested.

CONCLUSIONS

Memory deficits observed in schizophrenia patients were more severe and wider than that of patients with obsessive-compulsive disorder, except for visual working memory. Memory dysfunction, mainly related to episodic memory damage and reduced efficiency of central executive, is intimately connected to the specific psychopathological processes characterizing schizophrenia. Implications for therapeutics and cognitive remediation techniques are discussed.

Acknowledgements:

We gratefully acknowledge Susan Corrieri (Interdepartmental Linguistic Centre, University of Pisa) for the English editing of the article, Chiara Rossi and Cristiana Parrini for their help in collecting data.

Conflict of interest: None to declare.

References

1. *American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders 4th text revision. Author, Washington DC, 2000.*
2. *Baddeley A: Working Memory. Science 1992; 255:556-59.*
3. *Barch DM, Carter CS, Braver TS, Sabb FW, MacDonald A, Noll DC et al.: Selective deficits in prefrontal cortex function in medication-naïve patients with schizophrenia. Arch Gen Psychiatry 2001; 58:280-88.*

4. Barlati S, Deste G, De Peri L, Ariu C & Vita A: Cognitive remediation in schizophrenia: current status and future perspectives. *Schizophr Res Treatment* 2013; 2013:1-12.
5. Benton AL, Hamsher K, Varney NR & Spreen O: *Contributions to Neuropsychological Assessment*. Oxford University Press, New York, 1983.
6. Bhanji NH, Chouinard G & Margolese HC: A review of compliance, depot intramuscular antipsychotics and the new long-acting injectable atypical antipsychotic risperidone in schizophrenia. *Eur Neuropsychopharmacol* 2004; 14:87-92.
7. Boone, KB, Ananth J, Philpott L, Kaur A & Djenderedjian A: Neuropsychological characteristics of nondepressed adults with obsessive-compulsive disorder. *Cogn Behav Neurol* 1991; 4:96-109.
8. Bowie CR, Leung WW, Reichenberg A, McClure MM, Patterson TL, Heaton RK et al.: Predicting schizophrenia patients' real-world behavior with specific neuropsychological and functional capacity measures. *Biol Psychiatry* 2008; 63:505-11.
9. Bowie CR, Reichenberg A, Patterson TL, Heaton RK & Harvey PD: Determinants of real-world functional performance in schizophrenia subjects: Correlations with cognition, functional capacity, and symptoms. *Am J Psychiatry* 2006; 163:418-25.
10. Buchsbaum BR & D'Esposito M: *Short term and working memory systems*. *Learning and Memory: A Comprehensive Reference*. Elsevier, Oxford, 2008.
11. Chamberlain SR, Blackwell AD, Fineberg NA, Robbins TW & Sahakian BJ: The neuropsychology of obsessive compulsive disorder: The importance of failures in cognitive and behavioural inhibition as candidate endophenotypic markers. *Neurosci Biobehav Rev* 2005; 29:399-419.
12. Chang WH, Chen KC, Yang YK, Chen PS, Lu RB, Yeh TL et al: Association between auditory P300, psychopathology, and memory function in drug-naïve schizophrenia. *Kaohsiung J Med Sci* 2014; 30:133-38.
13. Christensen KJ, Kim SW, Dysken MW, Hoover, KM: Neuropsychological performance in obsessive-compulsive disorder. *Biol Psychiatry* 1992, 31:4-18.
14. Cirillo MA & Seidman LJ: *Verbal Declarative Memory Dysfunction in Schizophrenia: From Clinical Assessment to Genetics and Brain Mechanisms*. *Neuropsychol Review* 2003; 13:43-77.
15. Danion JM & Marczewsky P: Les objectifs et les methodes de la psychopathologie cognitive. In Xavier S & Van der Linden M (eds.): *Traité de neuropsychologie clinique*, pp. 9-17 Solal, 2000.
16. Danion JM, Rizzo L & Bruant A: Functional mechanisms underlying impaired recognition memory and conscious awareness in patients with schizophrenia. *Arch Gen Psychiatry* 1999; 56:639-44.
17. Deckersbach T, Otto MW, Savage CR, Baer L, & Jenike MA: The relationship between semantic organization and memory in obsessive-compulsive disorder. *Psychother Psychosom* 2000; 69:101-107.
18. Dimaggio G, Salvatore G, Popolo R, Lysaker PH: Autobiographical memory and mentalizing impairment in personality disorder and schizophrenia: clinical and research implications. *Front Psychol* 2012; 13:529.
19. Dirison S, Bouvard M, Cottraux J, Martin R: Visual memory impairment in patients with obsessive compulsive disorder: a controlled study. *Psychother Psychosom* 1995; 63:22-31.
20. Fioravanti M, Bianchi V & Cinti ME: Cognitive deficits in schizophrenia: an updated metanalysis of the scientific evidence. *BMC Psychiatry* 2012; 12:64.
21. Forbes NF, Carrick LA, McIntosh AM & Lawrie SM: Working memory in schizophrenia: a meta-analysis. *Psychol Med* 2009; 39:889-905.
22. Francis MM, Hummer TA, Vohs JL, Yung MG, Liffick E, Mehdiyouf NF & Breier A: Functional neuroanatomical correlates of episodic memory impairment in early phase psychosis. *Brain Imaging Behav* 2015; 1-11.
23. Golimbet VE, Alfimova MV, Kaleda GV, Lavrshina OM, Korovaitzeva GI, Lezheiko TV & Abramova LI: Verbal memory deficit in schizophrenia as a possible endophenotype of the disease: In Murray WH (eds): *Schizoaffective Disorders: New Research*, pp. 165-186, Nova Science Publishers, 2006.
24. Gold JM, Randolph C, Carpenter CJ, Goldberg TE & Weinberger DR: The performance of patients with schizophrenia on the Wechsler Memory Scale-Revised. *Clin Neuropsychol* 1992; 6:367-73.
25. Gold JM, Rehkemper G, Binks SW, Carpenter CJ, Fleming K, Goldberg TE et al.: Learning and forgetting in schizophrenia. *J Abnorm Psychol* 2000; 109:534-38.
26. Green MF, Kern RS & Heaton RK: Longitudinal studies of cognition and functional outcome in schizophrenia: Implications for MATRICS. *Schizophr Res* 2004; 72:41-51.
27. Happé F & Frith U: The weak coherence account: Detail-focused cognitive style in autism spectrum disorders. *J Autism Dev Disord* 2006; 36:5-25.
28. Hardoy MC, Carta MG, Catena M, Hardoy, MJ, Cadeddu M, Dell'Osso L et al.: Impairment in visual and spatial perception in schizophrenia and delusional disorder. *Psychiat Res* 2004; 127:163-66.
29. Hill SK, Harris MS, Herbener ES, Pavuluri M, & Sweeney JA. Neurocognitive allied phenotypes for schizophrenia and bipolar disorder. *Schizophr Bull* 2008; 34:743-759.
30. Karilampi U, Helldin L, Hjärthag F, Norlander T & Archer T: Verbal learning in schizopsychotic outpatients and healthy volunteers as a function of cognitive performance levels. *Arch Clin Neuropsychol* 2007; 22:161-74.
31. Kasper S & Resinger E: Cognitive effects and anti-psychotic treatment. *Psychoneuroendocrinology* 2003; 28:27-38.
32. Kay SR, Flszbein A, Opfer LA: The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull* 1987; 13:261.
33. Keefe RS: Should cognitive impairment be included in the diagnostic criteria for schizophrenia? *World Psychiatry* 2008; 7:22-8.
34. Keefe RS & Harvey PD: Cognitive Impairment in Schizophrenia. In Geyer MA & Gross G. (eds.): *Handbook of Experimental Pharmacology: Novel Anti-Schizophrenia Treatments*, 11-37. Springer-Verlag Berlin Heidelberg, 2012.
35. Kim MS, Namgoong Y & Youn T: Effect of organizational strategy on visual memory in patients with schizophrenia. *Psychiatry Clin Neurosci* 2008; 62:427-34.
36. Kraepelin E: *Dementia praecox and paraphrenia* (1919 R. M. Barclay, Trad.). Robert E. Krieger Publishing Co. Inc., Huntington NY, 1971.
37. Kraguljac NV, Srivastava A & Lahti AC: Memory deficits in schizophrenia: a selective review of functional magnetic resonance imaging (fMRI) studies. *Behav Sci* 2013; 3:330-347.

38. Kuelz AK, Hohagen F & Voderholzer U: Neuropsychological performance in obsessive-compulsive disorder: A critical review. *Biol Psychol* 2004; 65:185-236.
39. Lesh TA, Niendam TA, Minzenberg MJ & Carter CS: Cognitive control deficits in schizophrenia: mechanisms and meaning. *Neuropsychopharmacology* 2011; 36:316-38.
40. Lett TA, Voineskos AN, Kennedy JL, Levine B & Daskalakis ZJ: Treating working memory deficits in schizophrenia: a review of the neurobiology. *Biol Psychiat* 2014; 75:361-70.
41. McGurk SR, Twamley EW, Sitzer DI, Mchugo GJ, Mueser KT, et. al: A meta-analysis of cognitive remediation in schizophrenia. *Am J Psychiatry* 2007; 164:1791-1802.
42. Muller J & Roberts JE: Memory and attention in Obsessive-Compulsive Disorder: A review. *J Anxiety Disord* 2005; 19:1-28.
43. Müller BW, Sartory G & Bender S: Neuropsychological deficits and concomitant clinical symptoms in schizophrenia. *Eur Psychol* 2004; 9:96-106.
44. Nuechterlein KH, Barch DM, Gold JM, Goldberg TE, Green MF & Heaton RK: Identification of separable cognitive factors in schizophrenia. *Schizophr Res* 2004; 72:29-39.
45. O'Carroll R: Cognitive impairment in schizophrenia. *Adv Psychiat Treat* 2000; 6:161-168.
46. Ranganath C & Blumenfeld RS: Prefrontal cortex and memory. In Byrne JH & Eichenbaum H (eds.): *Learning and memory: A comprehensive reference: Memory system*, 261-279. Elsevier Science, 2008.
47. Rey A: L'examen psychologique dans les cas d'encéphalopathie traumatique. *Arch Psychol* 1941; 28:215-285.
48. Robles O, Blaxton T, Adami H, Arango C, Thaker G & Gold J: Nonverbal delayed recognition in the relatives of schizophrenia patients with or without schizophrenia spectrum. *Biol Psych* 2008; 63:498-504.
49. Sass LA & Parnas J: Schizophrenia, Consciousness, and the Self. *Schizophr Bull* 2003; 29:427-444.
50. Schuepbach D, Keshavan MS, Kmiec JA & Sweeney JA: Negative symptom resolution and improvements in specific cognitive deficits after acute treatment in first-episode schizophrenia. *Schizophr Res* 2002; 53:249-61.
51. Sharma T & Antonova L: Cognitive function in schizophrenia: deficits, functional consequences, and future treatment. *Psychiatr Clin of North Am* 2003; 26:25-40.
52. Sher KJ, Mann B, Frost R.O.: Cognitive dysfunction in compulsive checkers: further exploration. *Behav Res Ther* 1984; 22:493-502.
53. Seidman LJ, Lanca M, Kremen WS, Faraone SV & Tsuang MT: Organizational and visual memory deficits in schizophrenia and bipolar psychoses using the Rey-Osterrrieth complex figure: effects of duration of illness. *J Clin Exp Neuropsychol* 2003; 25:949-64.
54. Siegel DJ: Toward an interpersonal neurobiology of the developing mind: Attachment relationships, "mind-sight," and neural integration. *Infant Ment Health J* 2001; 22:67-94.
55. Šoštarič M & Zalar B: The overlap of cognitive impairment in depression and schizophrenia: A comparative study. *Psychiatr Danub* 2011; 23:251-56.
56. Thorsen AL, Johansson K & Løberg EM: Neurobiology of cognitive remediation therapy for schizophrenia: a systematic review. *Front Psychiatry* 2014; 5:103.
57. Trivedi JK: Cognitive deficit in psychiatric disorders: Current status. *Indian J Psychiatry* 2006; 48:10-20.
58. Tulving E: Memory and consciousness. *Can Psychol* 1985; 26:1-12.
59. Tulving E: Episodic memory: from mind to brain. *Annu Rev Psychol* 2002; 53:1-25.
60. Wechsler D: Wechsler memory scale-third edition. The Psychological Corporation, San Antonio TX, 1997.
61. Wechsler D: Wechsler Memory Scale UK (WMS-IVUK) 4th ed. Person Education, London, 2009a.
62. Wechsler D: Wechsler Memory Scale-Fourth Edition (WMS-IV) technical and interpretive manual. Pearson, San Antonio TX, 2009b.
63. Wykes T, Huddy V, Cellard C, McGurk SR & Czobor P: A meta-analysis of cognitive remediation for schizophrenia: methodology and effect sizes. *Am J Psychiatry* 2011; 168:472-485.
64. Wykes T & Reeder C: *Cognitive Remediation Therapy for Schizophrenia. Theory and Practice*. Routledge Taylor & Francis Group, London, 2005.

Correspondence:

Daive Maria Cammisuli, MD, PhD
Department of Surgical, Medical, Molecular and Critical Area Pathology,
Pisa University School of Medicine
2 Via Paradisa, 56124 Pisa, Italy
Email: d.cammisuli@med.unipi.it