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Are all forms of feature binding disturbed in schizophrenia? Evidence from a central vs. peripheral distinction in working memory

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ABSTRACT

In this study we investigated central and peripheral feature binding in a group of 24 high pre-morbid IQ patients with schizophrenia and 24 healthy controls. In particular, participants were asked to remember specific single (e.g., word, colour) or multiple features (e.g., coloured words) of experimental items with central (coloured word) vs. peripheral (a coloured frame) attributes in a working memory binding task. Performance of the patients was significantly inferior to that of controls, especially when required to remember the peripheral combination of multiple features. Results suggest that patients with schizophrenia may have difficulties in unitizing peripheral features in working memory.

1. Introduction

Episodic memory of any complex event typically includes many different types of information. Some of this information is more semantic in nature (e.g., the content of an event), while other types of information are more perceptual and/or contextual (e.g. the context in which the event was acquired). Most importantly, when perceiving the world around us, we must first simultaneously process separate features and subsequently bind them together in order to form unique and memorable objects, scenes, and/or episodes. Yet, the processes underlying this binding are still not completely clear. One way of conceptualizing this binding process was proposed by Graf and Schacter (1989), who introduced the concept of *unitization* to refer to the encoding of a certain number of different stimuli as a single unit. More recently, evidence (e.g., for a review see Mayes et al., 2007) suggests that there are different types of binding and that the form of binding involved in a task may vary depending on a combination of multiple factors, including data-driven (e.g., object complexity) and conceptually driven (e.g., involvement of long-term memory) processes. For example, intra-item associations (i.e., features that are unitized into one entity) may occur when different components (e.g., word and colour) are already bound into one entity (a coloured word) (Cycowicz et al., 2001). This creates a representation that is perceived, encoded and remembered as a single entity. Inter-item associations instead refer to bindings between items that can belong to the same (e.g., two unrelated words) or to different (e.g., word and colour, face and name) domains. Inter-item associations indicate that the items go together, but they do not form a single entity. Along the same line, cognitive researchers have proposed similar definitions. For example, Baddeley (1986) distinguished between intrinsic (unitized intra-item associations) and extrinsic contexts (e.g., non-unitized inter-item associations), while Moscovitch et al. (1995) distinguished between unitized intra-item associations vs. non-unitized organizational contexts. More recently, Zimmer et al. (2006) proposed an ulterior distinction between object tokens and episodic tokens. They claimed that object tokens represent intrinsic information and can be considered as a consolidated object file (unitized), while episodic tokens contain information about the context in which the object was originally acquired (non-unitized). Moreover, the literature on source monitoring and eyewitness testimony (Mammarella and Fairfield, 2008) also distinguishes between central (unitized) vs. peripheral (non-unitized) source attributes. Again, central source attributes refer to source information that is bound to, and consequently more directly connected with, the item itself. Differently, peripheral source information refers to source details that are not as tightly bound to the item because the features are external to the item itself as is the case with location and order information. In line with the Source Monitoring Framework (Johnson, 2006), the central vs. peripheral distinction will be used throughout this article because we feel it better highlights our underlying assumption that some details may be central with

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respect to the main scene or event (unitized), while others may represent more peripheral aspects that may be included and bound to that event later (to-be-unitized). Furthermore, long-term memory research showed that cognitive processes and neural correlates involved in intra-item and inter-item associations may vary (Mayes et al., 2007) and many studies have suggested that central source information requires less attention and intentional processing than peripheral source information (Moscovitch et al., 1995; Spencer and Raz, 1995; Troyer and Craik, 2000). Consequently, central and peripheral source details may differ in the degree of effortful processing required.

Further evidence comes from developmental, aging and schizophrenia research (Spencer and Raz, 1995; Ling and Blades, 2002). Interestingly, a large body of evidence highlights inter-item associative deficits in episodic memory in patients with schizophrenia (Aleman et al., 1999; Lepage et al., 2006) and it has been proposed that these difficulties may result from deficits in the ability to bind different types of contextual information in working memory that, in turn, disturbs the formation of integrated memory representations (Stone et al., 1998; Danion et al., 1999). Several studies have also reported impairments in binding processes in working memory in patients with schizophrenia, suggesting dysfunctions in their ability to establish links between the event's content and different contextual elements (Waters et al., 2004). In particular, schizophrenia patients seem to have difficulties in feature binding when they are asked to remember object–location combinations (Burglen et al., 2004; Salamé et al., 2006). However, Luck et al. (2008) found that this deficit may be linked to the nature of the to-be-bound feature, calling on a more general spatial processing deficit to explain poor performance in these binding tasks rather than binding processes per sé.

In line with the above findings, we expect the encoding of peripheral source information to be more resource consuming than the encoding of central source information and that schizophrenia patients should have particular difficulties in encoding peripheral source information. Results in this direction would be in line with numerous studies showing memory deficits in schizophrenia when more resource-demanding processes are involved (Lefèbvre et al., 2010; Achim et al., 2011).

Accordingly, we adapted a long-term memory paradigm developed to study feature binding (Ecker et al., 2007a, 2007b) in order to investigate binding deficits for peripheral information. In particular, we asked participants to study a series of coloured words vs. words encased in a coloured frame, but always tested them on the coloured word. This type of test stimuli allowed us to directly compare working memory (WM) performance for intra-item or central associations (colour words) vs. between-domain inter-item or peripheral associations (words encased in a coloured frame) since we were primarily interested in investigating whether schizophrenia patients are as successful as controls at online unitizing or if they have particular difficulties manipulating between-domain features in order to achieve a new unitized representation in WM. We therefore compared WM for an already unitized representation (coloured word) vs. memory for a to-be-unitized representation (new unitized representation coming from a coloured frame and a word) by asking participants to discriminate between studied associations and unstudied associations that were always centrally manipulated at test. In this manner we varied encoding conditions but kept testing conditions constant. In line with previous studies (Burglen et al., 2004; Diaz-Asper et al., 2008), we expected schizophrenia patients to make more false alarms on central combination trials than on single feature trials.

In addition, when patients are not given an already unitized representation but are invited to form a unitized representation from two different features (peripheral condition), two patterns of performance may be found. First, if unitization is correctly completed at encoding, WM performance with peripheral combinations should be similar to that observed with central combinations. Second, if patients are not able to unitize or do not unitize items, then their WM performance should be poorer under peripheral compared to central combinations conditions.

To maximize the likelihood that information was in working memory, and thereby minimize the need for retrieval of information from long-term memory, each trial presented only three words studied sequentially for 2 s each and memory was tested after a retention interval of only 4 s. In this manner, discriminating whether an item was old or new after minimal encoding and very short retention intervals should primarily involve the evaluation of each item in working memory. In addition, participants were explicitly invited to memorize single features or combinations by inserting a study cue before stimuli presentation that informed participants of the to-be-remembered information. The idea was that by asking participants to intentionally focus on specific information (e.g. word, colour or combination), they might use specific encoding strategies in order to help create links between the words and the colours, and especially in peripheral combination trials.

2. Method

2.1. Participants

Demographic and clinical data are summarized in Table 1. This study included 24 high pre-morbid IQ patients with schizophrenia and 24 non-psychiatric comparison participants. Eligible participants were recruited following discharge from an acute psychiatric unit. Diagnoses were made according to the DSM-IV criteria, as determined by the the Structured Clinical Interview for DSM-IV (SCID; First e tal. ,1995), by a board-certified attending research team of psychiatrists. Subtype diagnoses were as follows: paranoid ($n=21$), disorganised ($n=1$), undifferentiated ($n=1$), and residual (n=1). All were relapsing, multiple-episode patients able to live in the community with on maintenance neuroleptic therapy. The mean length of illness was defined as current age minus age at onset of symptoms. All patients were receiving neuroleptic medication at the time of the study (13 on risperidone, 3 on haloperidol, 2 on amisulpiride, 2 on fluphenazine, 2 on olanzapine, 2 on aripiprazole, 2 on paliperidol, and 1 on quetiapine). Three patients were receiving a combination of two neuroleptics. Psychiatric symptoms were assessed using the 30-item Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987). Participants were tested just before discharge in remission phase. The clinical assessment was administered by psychiatrists and/or licensed research psychologists who were trained to a minimum interclass correlation of 0.80, as close as possible to the administration of the neuropsychological tests. The TIB (Brief Intelligence Test; Sartori et al., 1997), an Italian equivalent of the National Adult Reading Test (NART), was used as a putative measure of intellectual functioning. The TIB is widely used in clinical and research settings to estimate pre-morbid intellectual levels as it is relatively resistant to the effects of psychiatric disease. We evaluated the pre-morbid IQ in patients to avoid the possibility that poorer performance in patients with schizophrenia could be attributable to intellectual disability. The mean estimated IQ for patients was 102.99 (S.D.=9.39).

Table 1
Demographic and clinical characteristic (mean ± S.D.) of the groups.

	Patients ($n=24$)	Controls ($n=24$)
Sex (% male)	87 (%)	83 (%)
Age (years)	35.96 (6.75)	34.89 (6.38)
Education level (years)	10.88 (3.51)	11.37 (0.17)
Estimated IQ	102.99 (9.39)	
Duration of illness (years)	8.89 (7.36)	
PANSS		
Total PANSS score	60,09 (12.51)	
Positive Symptom Scale	16.52 (5.22)	
Negative Symptom Scale	13.59 (4.35)	
General Psychopathology Scale	29.98 (7.18)	
Chlorpromazine equivalent (mg/day)		
Typical antipsychotics	141.67 (95.29)	
Atypical antipsychotics	92.07 (67.84)	