Perceptual Categorization: Applications for the Experimental Psychopathology of Schizophrenia

Ph.D. Thesis

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Papers related to the thesis:

I. Szabolcs Kéri, György Szekeres, Ogúz Kelemen, Andrea Antal, István Szendi, Zoltán Kovács, György Benedek & Zoltán Janka: Abstraction is impaired at the perceptual level in schizophrenic patients. *Neuroscience Letters* 1998, 243: 93-96.

II. Szabolcs Kéri, György Szekeres, István Szendi, Andrea Antal, Zoltán Kovács, Zoltán Janka & György Benedek: Category learning and perceptual categorization in schizophrenia. *Schizophrenia Bulletin* 1999; 25: 593-600.

III. Szabolcs Kéri, Andrea Antal, György Szekeres, István Szendi, Zoltán Kovács, György Benedek & Zoltán Janka: [Sensory inhibition in schizophrenia II.: Relationship with the attentional dysfunction]. *Psychiatria Hungarica* 1999; 14: 393-397.

IV. Szabolcs Kéri, Ogúz Kelemen, György Szekeres, Nóra Bagóczky, Rita Erdélyi, Andrea Antal, György Benedek & Zoltán Janka: Schizophrenics know more than they can tell: Probabilistic classification learning in schizophrenia. *Psychological Medicine*, in press

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1. General summary

Schizophrenia is one of the most devastating mental disorders, affecting more than two million new cases a year. The related psychopathology is definitely complex, including the impairment of perception, thinking, affect, and self-regulation (Andreasen & Carpenter, 1993; Andreasen, 1995). In the past decade, a number of experimental approaches emerged to explain the clinical signs and symptoms in the framework of different cognitive models. Perhaps the most influential of these approaches emphasized the characteristic deficit of categorization and abstraction, often relating these issues to the negative symptoms and thought disorder (Frith, 1992; Andreasen, 1997; Spitzer, 1997).

In this thesis, a series of experiments is reported in order to elucidate how different interrelated cognitive mechanisms and associated neuronal circuits participate in the schizophrenic categorization disturbances. In the first part of the thesis, we demonstrate that schizophrenic patients fail to learn simple categories of two-dimensional geometric shapes, especially when the category space is continuos. This impairment can be compensated by verbal definitions, which raises the possibility that the symbolic recoding of visual information is disrupted as a candidate example of frontal and temporal lobe dysfunction. In contrast, the mental representation of visual forms, which is induced by verbal descriptions, is similar in both normal control subjects and schizophrenic patients. In the second part of the thesis, we apply a specific categorization procedure that investigates both the neostriatal habit learning system and the medio-temporal explicit memory system (Knowlton et al., 1996). Habit learning can be measured as a gradual increase in performance through several training trials, while explicit memory can be assessed by asking the subject to consciously identify category exemplars. In this test, schizophrenic patients show a selective deficit for the explicit memory task, but not for the habit learning task.

In summary, these results indicate that the functional integrity of prefrontal and medio-temporal structures is insufficient, whereas neostriatal and sensory neocortical mechanisms underlying visual category acquisition are relatively preserved in schizophrenia. Our findings can be integrated into current neuropsychological and computational theories of categorization.

2. Introduction

2.1. Historical background: The Kraepelinian concept of schizophrenic categorization deficit

The term *démence précoce* was first used by Morel (1856) to describe patients with withdrawal, bizarre behavior, and delusional thinking. Later, the components of Morel's concept were described separately. Distinct clinical entities - Hecker's hebephrenia (bizarre and disorganized thinking and emotional responses), Kahlbaum's catatonia (stereotyped movements, mannerism or extreme negativism), and paranoia (delusions of persecution, intoxication, and reference) – were then integrated in the notion of *dementia praecox* by Kraepelin (1896). Emphasizing the heterogeneity of clinical phenomenology, Bleuler wrote about "the group of *schizophrenias*", in which the most prominent feature was the splitting and disconnection of psychic functions (1911).

The impairment of conceptual reasoning and associative processes is among the most important clinical symptom of schizophrenia. Formal thought disorder is characterized by loose, mediated, indirect, and oblique associations:

> "Disorganized thinking ("formal thought disorder", "loosening of associations") has been argued by some (Bleuler, in particular) to be the single most important feature of schizophrenia. (...) The person may "slip off the track" from one topic to another ("derailment" or "loose associations"); answers to questions may be obliquely related or completely unrelated ("tangentiality")." (American Psychiatric Association, 1994, p.276.)

The basic idea explaining schizophrenic thinking and reasoning derives from Kraepelin who hypothesized that the induction of abstract concepts had been disturbed in this disorder (1919). In his view, the boundaries of categories are poorly defined, hence distinct contents of thought may spread into each other, constructing overinclusive formations and abnormal categories of real-world knowledge (Meadow et al., 1953). Using the modern terminology of cognitive neuroscience, semantic memory impairment (i.e. the disorganization of factual-lexical knowledge of real world categories) was recently introduced as a model of thought disorder, emphasizing the pathology of left temporal lobe (Spitzer, 1997).

2.2. Semantic categorization, temporal lobe dysfunction, and thought disorder

There is a growing number of evidence from neuropsychology, neurophysiology, neuroimaging, and cellular-molecular pathology that the temporal lobes are impaired in schizophrenia (Buchsbaum, 1990; McCarley et al., 1993; Heckers, 1997; Lawrie & Abukmeil, 1998; Kegeles et al., 1998; Shannon-Weickert & Weinberger, 1998; Weinberger, 1999; Bruder et al., 1999; March et al., 1999). In functional terms, this manifests itself in three dimensions: (i) the pathology of medio-temporal structures leads to deficient explicit memory functions; (ii) the pathology of left temporal association neocortex results in an aberrant semantic network and language disturbances; (iii) the pathology of primary auditory cortex leads to abnormal perception of sound (Kolb & Whishaw, 1996a). Although a few studies have reported associations between auditory hallucinations and abnormal activity patterns in the paralimbic and primary auditory cortex (David, 1999; Frith, 1999), the most consistent observation suggests a connection between the impairment of semantic memory and thought disorder (Spitzer, 1997; Goldberg et al., 1998). Extensive neuropsychological investigations, using a variety of semantic categorization and priming procedures, revealed that the schizophrenic deficit is fundamentally different from that seen in Alzheimer's disease and fronto-temporal dementia. While in the latter conditions there is a substantial loss and degradation of semantic knowledge, the conceptual network of schizophrenic patients can be characterized by disorganized activity patterns, that is, the physiological inhibition on the boundaries and interconnecting pathways of separate concepts is weak or inadequate. This may induce pathologically arranged conceptual categories and oblique associations, similarly as originally hypothesized by Kraepelin (Chen et al., 1991; Shallice et al., 1991; Spitzer et al., 1993; McKay et al., 1996; Paulsen et al., 1996; Spitzer, 1997; Goldberg et al., 1998).

2.3. Strategy shifting and category retrieval are related to the prefrontal cortex

Most of our semantic memories are automatic. Indeed, recent data suggests that separate mechanisms are necessary to guide the retrieval, combination, and shifting of stored concepts and categories to guide higher-level problem solving behavior. These executive and working memory functions are traditionally linked to the frontal lobes, another candidate for the pathology of schizophrenia (Weinberger et al., 1994; Goldman-Rakic & Selemon, 1997; Dehaene et al., 1999). In 1951, Fey reported that young schizophrenic patients displayed perseverative errors in the Wisconsin Card Sorting Test (WCST), which evaluates cognitive strategy shifting in a classification procedure (Fey, 1951). The impaired WCST performance is associated with hypoactivation and decreased dopamine D_1 receptor density in the

dorsolateral prefrontal cortex (Weinberger et al., 1986; Okubo et al., 1997). Clinically, the prefrontal dysfunction shows a correlation with the negative symptoms and reflects the prognosis of disease process (Green, 1996; Lysaker et al., 1997).

The left ventrolateral prefrontal area, together with the left temporal lobe, is also important in categorization, implicating the retrieval of phonological categories (i.e. words beginning with a particular letter) and semantic categories (i.e. words belonging in the same category) (Mesulam, 1990; Frackowiak, 1994; Kolb & Whishaw, 1996b). The latter is predominantly disrupted in schizophrenia, and the disorder of verbal working memory may play a crucial role in the psychopathology of some patients (Feinstein et al., 1998; Stevens et al., 1998).

2.4. The limitation of classification procedures

One can draw the following main conclusion from the above summary: verbal-semantic abilities and executive functions are deficient in schizophrenia, indicating the pathophysiology of fronto-temporal neuronal circuits (Friston & Frith, 1995). However, these observations provide an insufficient amount of information about the fundamental mechanisms of categorization and their characteristics in schizophrenia. In this thesis, we set out a series of experiments to examine three basic issues: (i) how categories with different feature characteristics are represented (the question of discrete and graded categories); (ii) how different types of category acquisition operate (the question of perceptual and verbal learning), and (iii) how non-frontal and non-temporal mechanisms of category learning are functioning in schizophrenia.

2.5. Discrete and graded categories

Categorization is one of the cornerstones of human cognition: perception, thinking, reading, and speaking are all based on categorical processes (Bruner, 1957; Harnad, 1987; Federmeier, 1997). During classification, instances of reality are grouped according to similarities and separated on the basis of dissimilarities (Gibson & Gibson, 1955; Pick, 1965; Homa & Chamblis, 1975). Considering the characteristics of common and distinctive features, well-defined (discrete) and ill-defined (graded) categories can be distinguished (Neisser, 1967; Medin & Barsalou, 1987). Discrete categories (DCs) can be described with features defining the category membership in an all-or-none fashion. If the feature is detected, exemplars can be classified quickly with few errors. In contrast, graded categories (GCs) can not be defined in an all-or-none fashion (Figure 1). The decision of category-membership for a pattern is not

absolute; it is based on a "statistical" comparison between the new pattern and the stored memory trace of categories. If the similarity achieves a predefined level, the new item can be sorted into the category (Carpenter & Grossberg, 1993). Classification of GC exemplars is accompanied by an exponential learning curve and higher error rates.

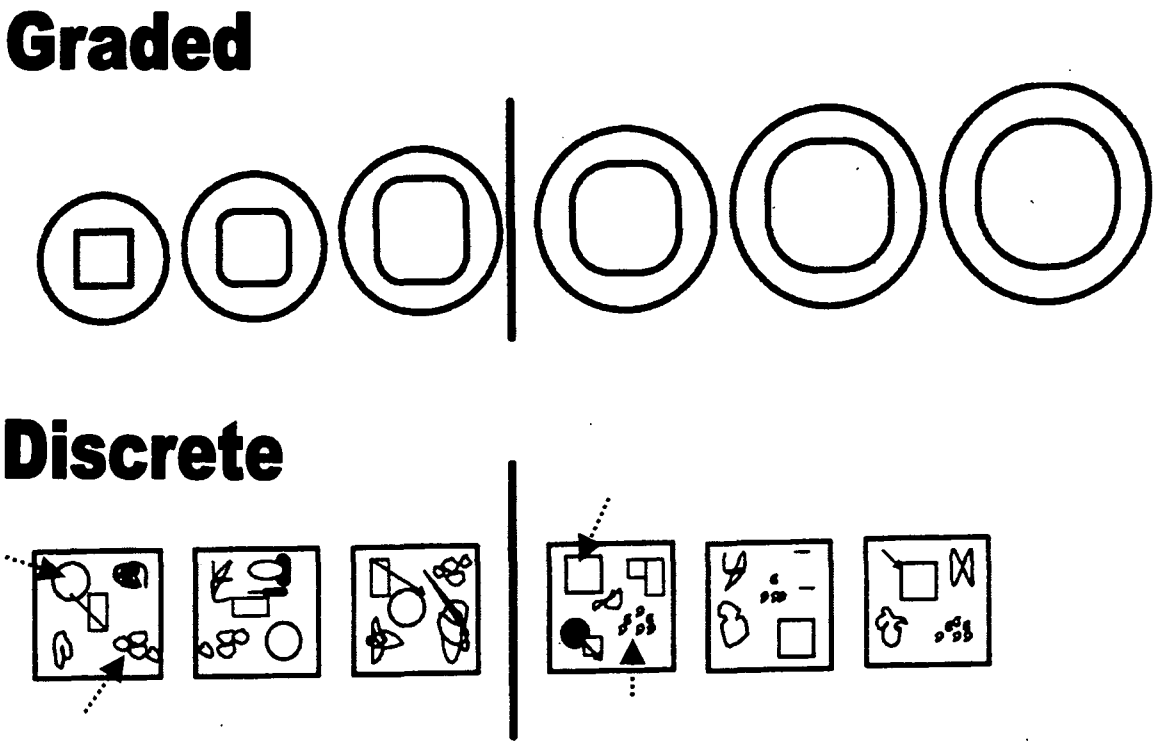

Figure 1. Exemplars of graded categories (GC) and discrete categories (DC) (upper and lower parts, respectively). [In DC1 circles and large spots were the common features, while in DC2 they were squares and triangles consisting of small spots (see dotted arrows). GC1 was the category of „smaller circles with square-like shapes in the middle", whereas GC2 included "larger circles with circle-like shapes". Note that for GCs, category membership can not be defined in an all-or-none fashion.]

2.6. Categories can be induced by serial exemplar presentation, feedback, and verbal definition

Learning about categories involves the extraction of common and distinctive features of exemplars. This procedure includes three levels: iconic representation (IR), categorical representation (CR), and symbolic representation (SR) (for comprehensive theoretical summaries, see Harnad, 1976, 1987, 1990). IR is a point-to-point reflection of physical reality. If we have a dog in our visual field, a detailed representation is formed and stored in a temporary memory buffer. When we perceive another dog, the integration of iconic images takes place, extracting the frequent common features and abandoning rare details. In this way the level of CR is completed. This is category induction by serial presentation of exemplars. However, there are other ways to construct categories. Suppose that not only items of a single category, but intermixed items of several categories are presented, and the observer is requested to decide about class membership. In this case, the experimenter should provide feedback signals to indicate whether category-decisions were correct or not. This procedure is called feedback learning. Finally, categories can be described verbally (SR). Verbal description of structural features allows quick top-down learning without perceptual demands (Harnad, 1990). In the case of DCs, SR provides a complete representation. For example, if the exemplars contain green circles as a common feature, SR gives the whole CR since the critical feature can be verbalized perfectly (Medin & Brasalou, 1987). In contrast, GCs can not be defined completely by SR. The formation of category boundaries depends on a perceptual learning procedure – the symbolic mode can provide only an approximate representation (Gibson & Gibson, 1955).

3. Overview of the thesis

3.1. Questions of the thesis

1. As discussed above, several aspects of higher-level and semantic categorization functions have been shown to be impaired in schizophrenia. However, alterations in fundamental mechanisms of categorization are less known. Our general aim was the exploration of this question.
2. The representations of DCs and GCs are different. The question is intuitive: Is there any difference between DC and GC learning in schizophrenia?
3. We intended to investigate three different types of category learning in schizophrenic patients: serial exemplar presentation, feedback learning, and verbal definition.

4. It is often reported that schizophrenia is featured by prominent general cognitive disturbances. Therefore, we examined the relationship between categorization abilities and general intellectual dysfunctions.
5. Recent neuropsychological evidence raised the possibility that, beyond the frontal and temporal lobes, the neostriatum may play an important role in category learning (Ashby et al., 1998). We examined how this non-frontal – non-temporal component of categorization operate in schizophrenic patients.

3.2. Arrangement of experiments

First, we tested category learning abilities of schizophrenic patients and control subjects for DCs and GCs. DC learning was evaluated by serial presentation of exemplars, in which subjects learned about categories with the observation of successively presented category members. The same learning paradigm was used for GCs (*Experiment 1*). For GCs, two additional paradigms were applied: learning by verbal definition and feedback (*Experiment 2* and *3*). In a separate set of experiments, specific methodological strategies were used to explore the role of generalized cognitive impairment and attentional dysfunction in schizophrenic categorization functions (*Experiment 4*). Finally, in a probabilistic classification learning task, we investigated distinct types of category acquisition mediated by the neostriatal habit learning system and the medio-temporal explicit memory system (*Experiment 5* and *6*).

4. General setup for Experiment 1-4

4.1. Stimuli

4.1.1. Discrete category (DC) exemplars

The exemplars of DCs consisted of five internal parts, each subtending 2° x 2°. In the members of the first category, circles and large spots appeared, while in the second category cue features were squares and triangles. The position of cues altered randomly. Stimuli subtended 8.9° in the horizontal and 6.8° in the vertical direction (Figure 1). The stimuli of *Experiment 2* used for the evaluation of minimal number of successive stimulus presentation (MNP) were 6.8° x 6.8° degrees in size and contained trapeziums and triangles as invariant features. The stimuli used for measurements of critical stimulus duration (CSD) had the same size and contained circles or squares as common features.

4.1.2. Graded category (GC) exemplars

Two-dimensional perceptual categories were applied with size and shape as dependent factors. The exemplars of GCs were interpolated images appearing in a stimulus area of 6.8°x 6.8°. To construct a continuous category space, a small circle with a square in the middle was transformed into a large circle with a circle in the middle (Brennan, 1985). In *Experiment 1* and *2*, the continuum was divided into 30 parts, 15 for the first and 15 for the second category (GC1 and GC2). In *Experiment 3* and *4*, the continuum was divided into 200 parts in a similar manner. The position of each point on the lines that defined shapes was randomized (5 dot pitches in both horizontal and vertical directions) (Figure 1).

4.2. Stimulus presentation and data collection

Stimuli were presented on a Sampo monitor controlled by a Pentium P54 CX personal computer. To guide the gaze of subjects, a small dot was placed in the middle of the screen. The viewing distance was 1 meter. The luminances of the fixation area (20 cd/m^2) and the stimulus area (140 cd/m^2) were constant. All tasks included a two-alternative forced choice paradigm, in which participants were requested to decide whether the presented stimulus belonged in category A or category B. Category decisions were indicated with pressing the category-associated keys on a computer keyboard. Categorization performance was defined as the percentage of correct responses. All participants were provided enough time to familiarize the setup and to practice decision making.

5. Experiment 1: Learning of discrete and graded categories

5.1. Subjects

Twenty patients (14 males, 6 females) who met the DSM-IV criteria of schizophrenia participated in the study (American Psychiatric Association, 1994). The current symptoms were assessed with the Positive and Negative Symptom Scale (PANSS) (Kay et al., 1987). The social functioning was evaluated with the Global Assessment of Functioning (GAF) scale of DSM-IV (American Psychiatric Association, 1994). All patients lived in the community, and were regularly checked by expert psychiatrists. Neurological and ophthalmological illnesses, substance abuse, and a history of electroconvulsive therapy were general exclusion criteria. Demographical and clinical data are shown in Table 1.

The control group comprised 20 subjects (14 males, 6 females) without any history of neurological or psychiatric disorders. They were members of the university staff or their relatives. The mean age was 36.2 years (SD=10.4), and the mean years of education was 11.1 (SD=2.9). All subjects had normal or corrected to normal visual acuity. The groups were matched for age and for duration of education (t-tests, $p>0.5$).

Table 1. Demographical and clinical data of schizophrenic patients (n=20; 14 males, 6 females)

	Mean	SD
Age (years)	38.7	11.9
Years of education	11.6	3.0
Age of onset	30.1	10.5
Number of hospitalization	4.0	2.6
GAF	46.6	18.7
PANSS – Global symptoms	48.1	12.1
PANSS – Positive symptoms	19.1	9.3
PANSS – Negative symptoms	21.8	8.2
Chlorpromazine-equivalent antipsychotic dose (mg/day)	285.1	183.8
Anticholinergic medication (procyclidine, mg/day)	3.6	7.5

GAF – Global Assessment of Functioning, PANSS – Positive and Negative Symptom Scale

5.2. Procedure

Exemplars of DC1 and then DC2 were presented sequentially, and subjects were asked to find the initially unknown category-relevant key elements. The exposure time was 700 ms. The required numbers of presentation for the two DCs were averaged. In the testing phase, previously unseen intermixed exemplars of DC1 and DC2 were presented, each for 28

ms. The number of presentations was 45 for each category. Participants were asked to categorize with pressing the category-associated keys. Exemplars of DC1 containing triangles or squares and exemplars of DC2 with large spots or circles were also intermixed as distracting elements.

In the GC learning phase, exemplars of GC1 and then GC2 were presented, each for 700 ms. The number of presentations was identical to that required for the detection of common elements of DCs (minimal number of presentation for feature extraction (MNP)). After the training procedure, subjects were informed that the presented stimuli belonged in two categories of geometrical shapes. Category knowledge was assessed with the exposition of new exemplars. The number of presentations was 45 for each category, the exposure time was 700 ms. Participants made category judgements as in the DC phase.

5.3. Results

The schizophrenic patients required more stimulus presentations (mean: 10.5, SD=4.7) for the detection of category-relevant elements of DCs than did the controls (mean: 6.7, SD=2.9) ($F(1,38)=9.57$, $p<0.005$). A two-way analysis of variance (ANOVA) (group (schizophrenics, controls) x category type (DC, GC)) conducted on the categorization performance indicated significant main effects of group ($F(1,38)=6.61$, $p<0.02$) and category type ($F(1,38)=116.23$, $p<0.0001$). There was also a two-way interaction ($F(1,38)=9.97$, $p<0.005$). Scheffé's tests revealed that schizophrenic patients were significantly impaired in the GC task ($p<0.005$), but not in the DC task ($p=0.98$) (Figure 2).

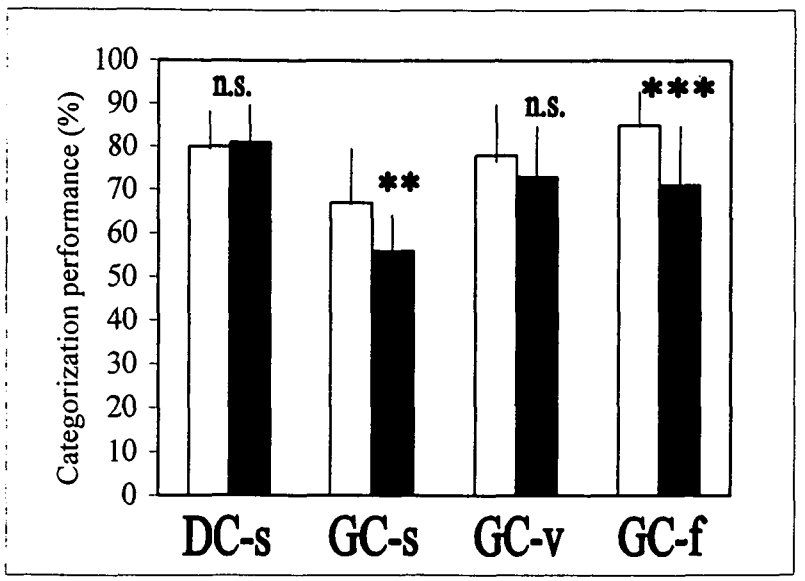

Figure 2. Mean categorization performance of the schizophrenic patients (filled bars) and control participants (open bars). [s – serial presentation, v – verbal definition, f – feedback, n.s. – non-significant, **p<0.005, ***p<0.0001; Error bars indicate standard deviations (SDs).]

A significant negative correlation was found between the GC performance and the scores of the cognitive component of PANSS (conceptual disorganization, disorientation, difficulty of abstract thinking, mannerism, posturing, and poor attention) (mean: 17.9, SD=8.7) ($r=-0.66$, $p<0.05$) (Lindenmayer et al., 1995). No other clinical and demographical parameters revealed significant correlations or covariances.

5.4. Discussion

The data presented above demonstrated that the DC performance was spared, whereas the GC performance was impaired in schizophrenic patients. This showed a negative correlation with the cognitive component of PANSS, which includes several items from both positive and negative symptoms. In other words, schizophrenic patients can learn about visual categories that are well-defined (DCs) in contrast to ill-defined categories (GCs). It must be emphasized that patients required more presentations of DC exemplars to find the cue, which can be attributed to their attentional impairment (Braff, 1993).

Several caveats may appear in connection with our results. First, it is possible that the DC performance appeared intact because the task was easier than the procedure for GC learning. To minimize this possibility, we used a very short exposure time for DCs and intermixed distracting elements. However, after the serial presentation the performance for GCs was still lower in comparison with DCs. Pilot studies revealed that further practice did not increase the DC performance in healthy subjects (data not shown), whereas for GCs a definite improvement was observable (see also *Experiment 1*). Therefore, psychometric matching is quite difficult because of the different kinetics of DC and GC learning. The performance increases rapidly to the maximum for a DC if key features are found, while in GCs the improvement is gradual.

The second problem comes from the different reliabilities of DC and GC tests. Reliability defines the magnitude of chance factors (noise) that contribute to the measured data. It has been demonstrated that schizophrenics are less impaired in test with lower reliability (Chapman & Chapman, 1978). In our case, the DC test was slightly more reliable (α: 0.62) than the GC test (α: 0.59). This suggests that the differential deficit is not due to chance factors.

It has been demonstrated that in unsupervised learning conditions such as serial exemplar presentation, subjects make efforts to verbalize the structure of categories (Medin et al., 1987). The success of categorization largely depends on the ability to find this verbal code. It is possible that the failure of schizophrenic patients to learn GCs is a result of the

deficient verbal recoding of ambiguous visual information. To test this hypothesis, we examined how verbal description affects GC performance. Additionally, we tested the perceptual learning of GCs guided by external feedback signals.

6. Experiment 2: Learning of graded categories by verbal definition and feedback

6.1. Subjects

The same population participated as in *Experiment 1* (Table 2).

6.2. Procedure

After the serial presentation of GCs (*Experiment 1*), the experimenter provided a verbal description of GC structure with standardized sentences. The definition was repeated slowly once. This was a non-perceptual modification of the structural representation of categories, which was established in the previous learning phase. The effect of verbal correction was measured by repeating the testing procedure used in *Experiment 1*.

In the feedback learning, subjects continued the categorization of GC exemplars similarly to the testing phase, but incorrect responses were followed by an immediate sound signal from the computer. The effect of feedback learning was assessed with repeating the testing phase without feedback.

6.3. Results

A two-way ANOVA with a 2 (group: controls, schizophrenics) x 2 (type of learning: serial presentation, verbal definition, feed-back) design revealed significant main effects of group ($F(1,38)=10.05$, $p<0.005$) and the type of learning ($F(2,76)=113.15$, $p<0.0001$). The two-way interaction was also significant ($F(2,76)=5.71$, $p<0.005$). Scheffé's post hoc tests indicated that the verbal definition increased the performance significantly in both the schizophrenic and control groups ($p<0.0001$). After the verbal definition of GCs, the significant difference between the controls and schizophrenics was not observable ($p=0.09$) (Figure 2).

Following the feedback learning of GCs, the performance of schizophrenic patients was again below that of the controls ($p<0.0001$). In the schizophrenic group, the feedback

learning did not improve the categorization performance significantly ($p=0.99$), whereas did so in the control group ($p<0.02$) (Figure 2).

6.4. Discussion

Verbal-symbolic representation is usually considered in relation to associative and meaning-based conceptual operations, although words can also describe structural and physical properties with the exception of fine perceptual details. We investigated the effect of verbal description of visual appearance and found that schizophrenic patients were able to compensate their impaired perceptual category acquisition in this way. It is possible that they were unable to establish a verbal representation of GCs on the basis of visual observation of exemplars. The verbal recoding of visual information may require a preserved functional integrity of frontal lobes, especially the left ventrolateral regions, and the superior left temporal area (Mesulam, 1990; Frackowiak, 1994; Ashby et al., 1998). The failure of our schizophrenic participants to complete the task may stem from the dysfunction of these areas (Stevens et al., 1998).

Feedback paradigm is a stimulus-driven method for the learning of small physical details, which are critical in discriminating similar exemplars near to the category boundary. In this case, a significant increase in performance was found only in the control group, which shows that patients were not able to modify and refine their perceptual representations and to distinguish category exemplars with small physical differences. This finding is consistent with previous reports, suggesting impaired error correcting behavior in schizophrenia (Malenka et al., 1982).

In conclusion, the most important finding of *Experiment 2* is that after verbal definition the difference diminished between schizophrenics and controls. Although several studies have provided evidence for a verbal dysfunction in schizophrenia (Andreasen, 1979; Crow, 1997), the present results indicate that patients can successfully use their linguistic aptitude in the description of perceptual features of simple categories. However, verbal definition served as a modification of previous knowledge rather than a de novo category induction. In *Experiment 3*, we used verbal definition as the first induction process of GCs in a different patient population.

7. Experiment 3: Primary induction of graded categories by verbal definition

7.1. Subjects

Twenty schizophrenic patients (12 males and 8 females) and 20 control subjects (12 males and 8 females) participated in *Experiment 3*. For the principles of diagnosis and patient evaluation, see *Experiment 1*. The mean age of control subjects was 35.7 years (SD=4.9), the mean duration of education was 13.3 years (SD=7.4). These latter demographical parameters did not differ significantly between the schizophrenics and controls (t-test, $p>0.5$) (Table 2).

Table 2. Demographical and clinical data of schizophrenic patients (n=20; 12 male, 8 female)

	Mean	SD
Age (years)	34.6	8.5
Years of education	15.1	8.2
GAF	43.4	16.5
PANSS – Global symptoms	45.6	12.2
PANSS – Positive symptoms	20.8	12.4
PANSS – Negative symptoms	25.2	12.4
Chlorpromazine-equivalent antipsychotic dose (mg/day)	287.7	80.6

GAF – Global Assessment of Functioning, PANSS – Positive and Negative Symptom Scale

7.2. Procedure

The stimuli and the experimental parameters were the same as in previous testing phases. Subjects were told that they would see geometrical shapes presented successively and were asked to respond only if the actual stimulus appeared "a smaller circle with a square-like shape in the middle". It is important that before the experiment, participants were not exposed

to stimuli to exclude perceptual familiarization. Performance was defined as the percentage of presented stimuli judged as a small circle with a square in the middle.

7.3. Results

Figure 3 shows the categorization performance of the schizophrenic patients and control subjects. The difference remained below the level of statistical significance (t-test, $p>0.5$). Similarly, correlation and covariance analyses with the clinical parameters provided negative results ($r<0.2$).

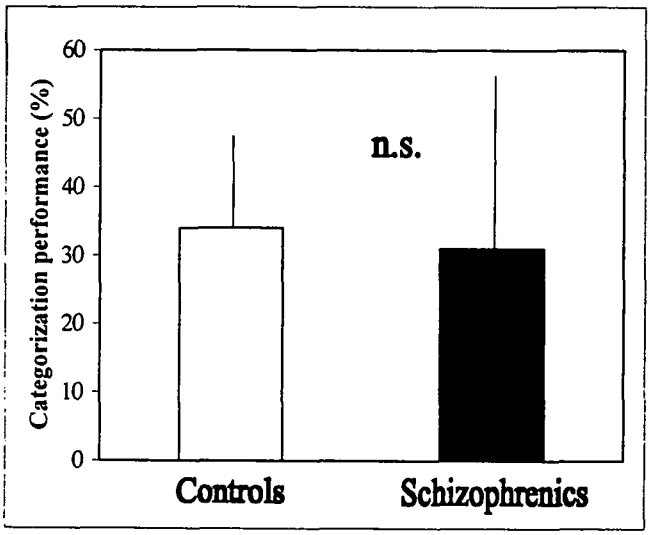

Figure 3. Mean categorization performances of the schizophrenic patients and control subjects after primary verbal definition. [n.s. – non-significant; Error bars indicate standard deviations (SDs).]

7.4. Discussion

The data from *Experiment 3* suggest that the mental representation of GCs, as induced by verbal definition, is similar in both groups, although the higher standard deviation in the schizophrenic group may point to larger individual differences. The possible effect of different symptom-predominances must be taken into consideration. For example, it is possible that the presence of a definite thought disorder may flaw between-group differences. However, from *Experiment 3* no evidence emerged for such a phenomenon, since there was no significant correlation between the categorization performance and clinical parameters. It seems that thought disorder is specifically related to the abnormality of semantic categories.

In summary, the above data confirms and extends the results of *Experiment 2*, revealing that schizophrenic patients are able to use verbal codes not only for the correction of category knowledge, but for the de novo induction of perceptual categories. However, the specificity of this effect remained unclear, similarly to the problem of generalized cognitive

deficit. First, it can not be excluded that further practice with serial exemplar presentation may also improve the GC performance of schizophrenic patients. Second, categorization dysfunction may be the consequence of a generalized cognitive disturbance present in most schizophrenic patients. *Experiment 4* was designed to examine these possibilities.

8. Experiment 4: The specificity of graded category impairment

8.1. Subjects

Twenty schizophrenic patients (14 males, 6 females) and 20 healthy control subjects (14 males and 6 females) participated in the study. For the principles of diagnosis and patient evaluation, see *Experiment 1*. The groups were matched for gender, age (controls: 38.1 years (SD=18.5)), and the level of education (controls: 12.4 years (SD=9.2)) (Table 3).

Table 3. Demographical and clinical data of schizophrenic patients (n=20; 14 male, 6 female)

	Mean	SD
Age (years)	35.1	11.2
Years of education	10.7	8.9
GAF	39.4	9.8
PANSS – Global symptoms	51.5	22.3
PANSS – Positive symptoms	19.2	8.4
PANSS – Negative symptoms	27.9	15.0
Chlorpromazine-equivalent antipsychotic dose (mg/day)	301.1	150.2

GAF – Global Assessment of Functioning, PANSS – Positive and Negative Symptom Scale

8.2. Procedure

Attentional abilities were determined by measurements of the critical stimulus duration (CSD) and the minimal number of stimulus presentation for feature extraction (MNP). CSD was defined as the minimum exposure time that was necessary for eight consecutive identifications of the cue element (circle or square). In this phase, a forced-choice staircase method was used with increments/decrements of 14 ms in the case of incorrect/correct responses (Braff & Saccuzzo, 1985).

In the measurement of MNP, stimuli were presented successively. The exposure time was 20 times longer than the previously measured CSD. In this task, subjects were asked to respond if they found the two common cue elements (triangle and trapezium) represented in each stimulus. The required number of stimulus presentation (=MNP) was recorded. Overall, the method of MNP measurement was similar to DC learning. Evaluations of CSD and MNP served as basic tests for attentional abilities. In further experiments, these parameters were used to counterbalance the attentional differences between the controls and schizophrenics.

In the training phase, subjects learned about two GCs by serial presentation of exemplars. The number of presentation was identical to the MNP, the exposure time was 20 times the CSD. In the testing phase, category knowledge was assessed with presenting new exemplars of GCs. The number of presentations was 40 for each category, the exposure time remained the same as in the previous phase. Other parameters were identical to those in *Experiment 1*. Finally, the training and testing phases were repeated to evaluate further practice effects on GC performance.

8.3. Results

The CSD was significantly prolonged in the schizophrenic group as compared to the controls (one-way ANOVA: $F(1,38)=9.91$, $p<0.005$) (Figure 4). In addition, schizophrenic patients needed more presentations to extract category relevant cues (one-way ANOVA: $F(1,38)=21.90$, $p<0.0001$) (Figure 5). Regarding the GC performance, a 2 (group: controls, schizophrenics) x 2 (practice: first and second study phases) ANOVA revealed main effects of group ($F(1,38)=8.24$, $p<0.01$), practice ($F(1,38)=131.01$, $p<0.0001$), and a two-way interaction ($F(1,38)=4.38$, $p<0.05$). Separate one-way ANOVAs indicated that schizophrenics had lower performances after the first ($F(1,38)=9.10$, $p<0.005$) and second training phases ($F(1,38)=98.01$, $p<0.0001$) (Figure 6).

8.4. Discussion

Experiment 4 replicated the results of *Experiment 1* in a different patient population. Despite the fact that attentional demands were counterbalanced regarding stimulus duration and number of presentation, the GC performance was significantly lower in the schizophrenic group. Schizophrenic patients required a longer time for stimulus detection (CSD) and more presentations to find common features (MNP). These data provide further evidence for attentional impairment in schizophrenia (Braff, 1993).

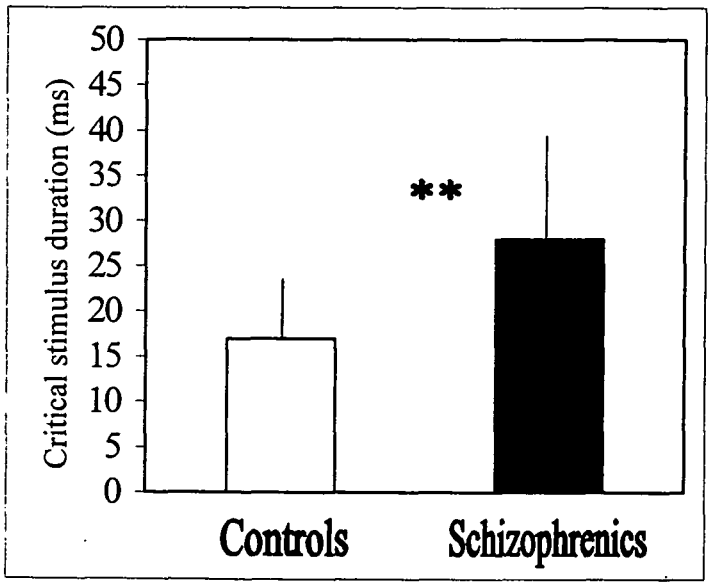

Figure 4. Mean critical stimulus duration in the schizophrenic and control groups. [**p<0.005; Error bars indicate standard deviations (SDs).]

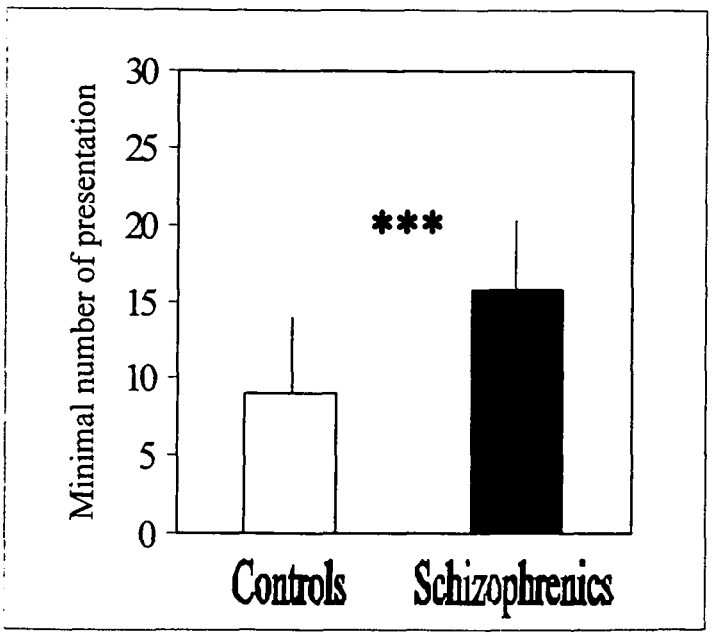

Figure 5. Mean number of stimulus presentation for feature extraction in the schizophrenic and control groups. [***p<0.0001; Error bars indicate standard deviations (SDs).]

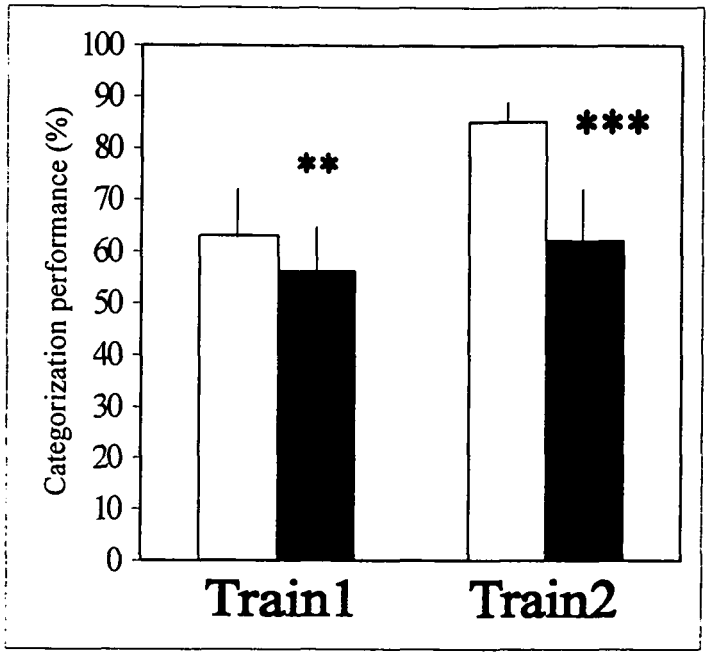

Figure 6. Mean categorization performances of the schizophrenic patients (filled bars) and control subjects (open bars) after two consecutive training phases with serial exemplar presentation. [**p<0.005, ***p<0.0001; Error bars indicate standard deviations (SDs).]

An important observation is that practice by serial exemplar presentation did not improve the performance of schizophrenic patients. This suggests that the prominent positive effect of verbal definition can not be replaced by a more extensive perceptual learning procedure, which is not efficient enough to promote the verbal recoding of visual information.

Considering further issues on the specificity of GC impairment, we used a method that helps distinguish between deficits due to a generalized cognitive dysfunction and specific impairments (Miller et al., 1995). In a task we can choose two levels of difficulty or training level where the performances of control subjects are located at equal distances from the 75% (e.g. performance levels of 85% ("easy") and 65% ("difficult")). If the differences between the controls and patients are similar at the "easy" and "difficult" conditions, the impairment may come from a general cognitive deficit of patients as a psychometric artifact. From the inspection of Figure 4, it is clear that in the "easy" condition (after the second study phase) the between-group difference was larger as compared to the "hard" condition (after the first study phase) (t-test, $p<0.05$). This indicates that the GC impairment reflects a specific cognitive impairment of schizophrenic patients.

Although our experiments provided a number of details about category learning in schizophrenia, few speculations are possible concerning the associated neuronal mechanisms. It has been suggested that verbal recoding of visual information is a function of frontal lobes (Kolb & Whishaw, 1996b). At the same time, it is likely that basic mechanisms of visual

memory and decision making are spared, since in some conditions our patients were able to perform categorization tasks. To gain more insight into the fundamental mechanisms of categorization, we applied a now classic test of Knowlton and her associates (1996), which has been extensively used in different patient populations.

9. Experiment 5: Are schizophrenic patients able to make probabilistic inferences?

9.1. Subjects

Participants were 40 schizophrenic patients (29 males, 11 females) and 20 comparison subjects (15 males, 5 females). For the principles of patient selection and diagnosis, see *Experiment 1*. The patients were evaluated with the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1983a), the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1983b), the Mini-Mental State Examination (MMSE) (Folstein et al., 1975), and the Global Assessment of Functioning scale (GAF). A low score in the MMSE (<25) was a general exclusion criterion (Table 4).

9.2. Procedure

In the probabilistic classification learning (PCL) task, which was a pen-and-paper version of the original test (Knowlton et al., 1994; Knowlton et al., 1996; Reber et al., 1996), subjects were asked to decide whether a pattern of cues predicted rain (category 1) or sunshine (category 2). Four cues were used, each comprising geometrical forms. Each cue was associated with a particular weather outcome with a certain probability. For instance, the circle predicted sunshine with a high probability and rain with a low probability, whereas the square had the inverse meaning. In a trial, the experimenter presented 1, 2, or 3 cues (Table 5). The cues were presented on separate cards and their left-to-right sequence was randomised in each trial. Subjects were asked to respond by deciding whether the cue(s) indicated rain or sunshine. After each trial, the experimenter provided a verbal feedback. If no response was made within 5 s, subjects were asked again to predict the weather outcome. All participants were able to make decisions in this forced-choice paradigm. Altogether 50 trials were included (5 blocks of 10 trials). Performance was defined as the percentage of correct responses, that is, selection of the weather outcome that was most probably associated with

the presented cue(s). Cue patterns associated with rain and sunshine with equivalent probabilities were excluded from the data analysis (Table 5).

Table 4. Clinical and demographical characteristics of the participants

	Schizophrenics (n=40)	Controls (n=20)
Age (years)	33.9 (9.6)	35.6 (10.4)
Education (years)	12.2 (3.1)	12.6 (6.9)
MMSE	27.8 (1.9)	28.7 (1.4)
Duration of illness (years)	6.5 (4.2)	-
SAPS	21.1 (5.5)	-
SANS	22.6 (5.4)	-
GAF	64.9 (8.3)	-
Mean atipsychotic dose	251.3 (249.9)	-

The Table depicts mean values (SD). The schizophrenic and control groups were matched for age, duration of education, and the MMSE (t-test, $p>0.2$). The dose of antipsychotics (mg/day) is given in terms of chlorpromazine-equivalents.

9.3. Results

A 2 (groups) x 5 (trial blocks) ANOVA revealed a significant main effect of trial blocks ($F(4,232)=10.96$, $p<0.0001$). The effect of group and the group by block interaction remained non-significant ($p=0.22$ and $p=0.49$, respectively). Newman-Keuls tests confirmed the ANOVA results, demonstrating no significant difference between the schizophrenic patients and the control subjects for any blocks ($p>0.2$). Separate linear regression analyses were conducted in the control and schizophrenic groups. These analyses indicated significant relationship between trials and categorization performance in the control group (R: 0.44, R^2: 0.19, $F(1,98)=22.84$, $p<0.0001$) and in the schizophrenic group (R: 0.32, R^2: 0.10, $F(1,198)=22.28$, $p<0.0001$) (Figure 7). Correlation and covariance analyses including the clinical parameters revealed negative results.

9.3. Discussion

The unexpected preservation of PCL in our schizophrenic patients suggests that basic mechanisms of perceptual categorization are spared. From a point of view, classification learning can be considered as a stimulus-response habit formation. On the basis of this assumption, one can expect that the neostriatum may play a crucial role in this process (Lawrence et al., 1998). Indeed, experimental evidence revealed that PCL is impaired in basal ganglia disorders such as Parkinson's disease and Huntington's chorea.

Table 5. Probabilistic structure of category cue(s)

Cue(s) representing test stimuli	Frequency	Sunshine	Rain	$P_{sunshine}$
●◆	4	4	0	1.00
●◆▲	1	1	0	1.00
●	7	6	1	0.86
●▲	4	3	1	0.75
◆	5	3	2	0.60
●■	2	1	1	0.50
◆▲	2	1	1	0.50
●▲■	2	1	1	0.50
●◆■	2	1	1	0.50
▲	5	2	3	0.40
◆■	4	1	3	0.25
■	7	1	6	0.14
◆▲■	1	0	1	0.00
▲■	4	0	4	0.00
Total	50	25	25	

Frequency refers to how many times a certain stimulus occurred during the test. Sunshine and Rain refer to how many times a stimulus indicated sunshine/rain. $P_{sunshine}$ is the probability that the weather outcome was sunny for a particular stimulus ($P_{rain} = 1 - P_{sunshine}$). As an example, stimulus ●▲ (row 4) consisted of 2 cues (2 geometrical forms) and was presented 4 times during the test (3 times sunshine, 1 time rain). Thus, ●▲ predicted sunshine with 75% probability.

In contrast, patients with circumscribed lesions to the medio-temporal structures or to the dorsolateral prefrontal cortex show intact learning rate in this task (Knowlton et al., 1996; Lawrence et al., 1998). In other words, abilities to consciously encode informations (explicit

memory) or to perform cognitive strategy shifting (working memory), which are dysfunctional in schizophrenia, are not indispensable to solve the weather prediction task. Hence, the spared PCL is understandable, providing evidence for a relatively intact neostriatal habit learning system in schizophrenia. However, a few studies suggested that neostriatal functions might be deficient in schizophrenia (Graybiel, 1997).

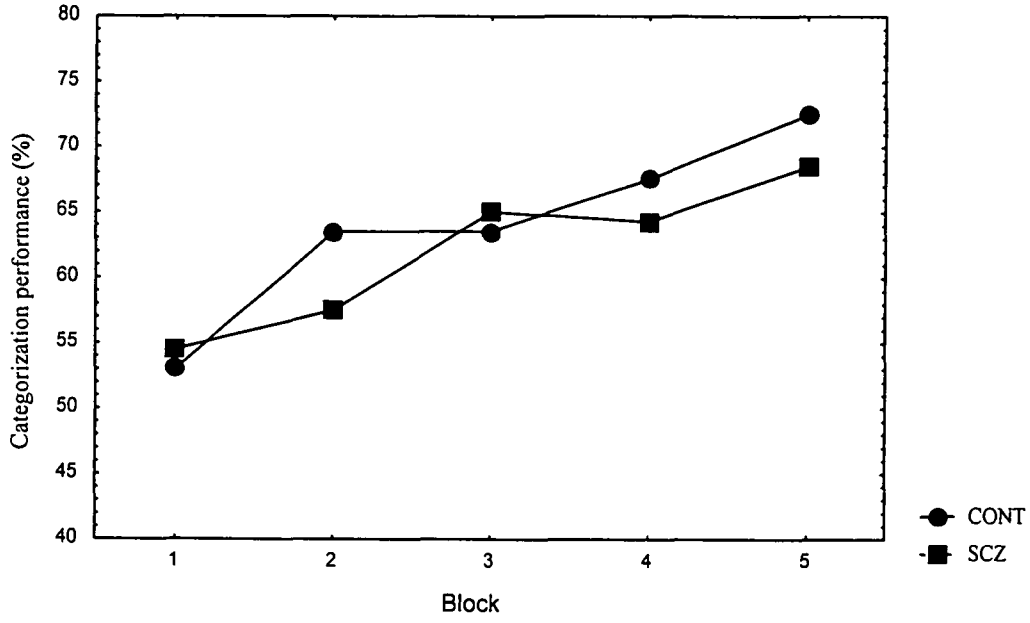

Figure 7. Mean categorization performances of the schizophrenic patients (SCZ) and control subjects (CONT) thorough the 5 blocks of the weather prediction task. [All between group differences are non-significant. Error bars are not shown.]

In the Wisconsin Card Sorting Test (WCST), stimuli had to be categorized according to their color, shape or the number of geometric shapes. Only one sorting strategy is correct at a time, and the participant has to find out that on the basis of feedback signals from the experimenter (Heaton, 1981). Finding the correct strategy is equivalent with the PCL paradigm, and schizophrenic patients do not show a prominent deficit in this case (Elliott et al., 1995). In further phases of WCST, the experimenter unexpectedly changes the rule of categorization (e.g. from color to shape) and the participant has to adapt to this new strategy. In this phase, schizophrenics display a perseverative tendency: they continue the categorization according to the former, incorrect rule (Fey, 1951; Weinberger et al., 1986; Weinberger et al., 1994; Elliott et al., 1995).

Data from animal studies revealed that lateral prefrontal lesions led to the impairment of shift learning (i.e. changing sorting strategy), whereas habit learning remained preserved. Lesion to the ventral prefrontal areas resulted in the opposite pattern of functional disturbance (Dias et al., 1996). Anatomically, the lateral prefrontal cortex is connected with dorsal neostriatal regions, while the ventral prefrontal cortex projects to ventral portions of neostriatum, comprising integrated parallel functional units (for a review, see Lawrence et al., 1998). Therefore, our results, together with previous findings from studies using the attentional set-shifting test of the CANTAB (Cambridge Automated Neuropsychological Test Battery), indicate that the ventral fronto-striatal system is relatively spared in some schizophrenic patients (Elliott et al., 1995; Elliott et al., 1998). On the other hand, a significant amount of neuropsychological and functional imaging data suggests the dysfunction of the dorsal fronto-striatal circuits. The well-known dorsolateral prefrontal deficit of schizophrenic patients has been extensively demonstrated in the form of perseverative WCST errors and planning disabilities in Tower-type tasks (Weinberger et al., 1994; Elliott & Sahakian, 1995; Morice & Delahunty, 1996; Pantelis et al., 1997; Goldman-Rakic & Selemon, 1997). In accordance with these considerations, a recent positron-emission tomography (PET) study found a prominent dysfunction in the dorsal and lateral neostriatum of schizophrenic patients performing a serial verbal learning test (Shihabuddin et al., 1998).

From the results of *Experiment 5*, it is unclear whether schizophrenic patients gained a conscious explicit insight into the sorting strategy or they performed implicitly and automatically. In *Experiment 6*, we examined how the medio-temporal explicit memory system contributes to category learning in schizophrenia.

10. Experiment 6: Do schizophrenic patients predict consciously?

10.1. Subjects

The participants were identical as in *Experiment 5*.

10.2. Procedure

The explicit knowledge relating to the cue probability was evaluated after the 50 trials had been completed. In this phase, all cues were presented together in a randomised sequence. Subjects were asked 2 questions: "What if you knew it was going to be rainy (sunny) and one card was showing? Which card would be most likely to be showing?" Such questions were

repeated, the subjects being asked which 2 and then which 3 cues were most probably visible. The sequence of questions about a rainy or a sunny outcome was counterbalanced across participants. Performance was graded on a 1-to-4 scoring system. In the single-cue selection task, a score of 1 was given if the subject was able to select the most probable cue (e.g. circle for sunny weather), a score of 4 was given for the selection of the least probable cue (e.g. square for sunny weather), and scores of 2 and 3 for the intermediate cues (rhombus and triangle for sunny weather, respectively). In the two-cue selection task, the selected cards were scored separately (e.g. for a circle and a square the scores of 1 and 4 were assigned, respectively), and the sum of the scores was calculated. The sum of the scores was then recalculated from the obtained 3-to-7 range to a 1-to-4 range ([0.75 x sum] - 1.25). In the three-cue selection task, a score of 1 was assigned to the best pattern (e.g. circle-rhombus-triangle for sunny weather), 2 and 3 for the intermediates (circle-rhombus-square and circle-triangle-square for the sunny weather, respectively), and 4 for the worst alternative (e.g. rhombus-triangle-square for sunny weather) (Table 5). In these tests, lower scores were associated with better explicit memory function.

10.3. Results

A 2 (group) x 3 (number of cues presented) ANOVA performed on the cue selection scores demonstrated a main effect of group ($F(1,58)=13.25$, $p<0.001$). The effect of cue and the group by cue interaction did not reach the level of statistical significance ($p=0.10$ and $p=0.23$, respectively). Newman-Keuls tests yielded that the schizophrenic patients had significantly higher scores (i.e. lower recall performances) when 2 and 3 cues had to be selected ($p<0.005$ and $p<0.0005$, respectively) (Figure 8). Correlation and covariance analyses including the clinical parameters revealed negative results.

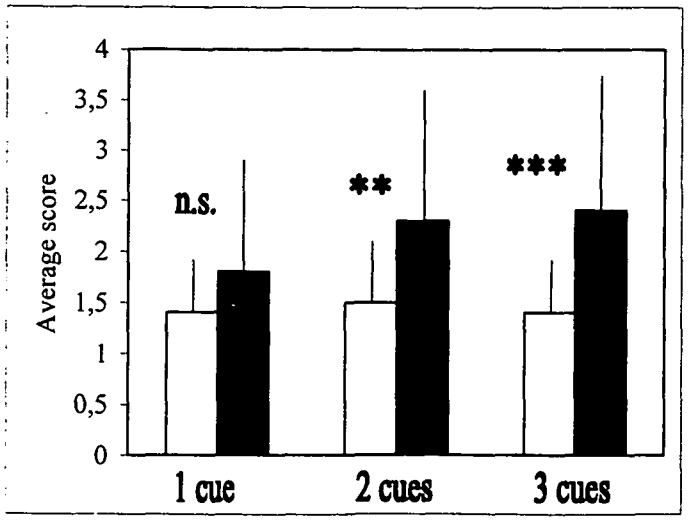

Figure 8. Average scores in the schizophrenic group (filled bars) and control group (open bars). [**p<0.005, ***p<0.0005; Error bars indicate standard deviations (SDs).]

10.4. Discussion

The results revealed that in the case of schizophrenic patients, category-knowledge did not reach the level of consciousness. Although they were able to achieve significant improvement in the PCL task, they failed to identify category exemplars. This pattern of performance is identical to that seen in amnesic patients with damage to the medio-temporal structures and represents a mirror image of the performance of Parkinson's disease patients who were impaired in the habit learning procedure, but showed intact performance in the explicit memory task (Knowlton et al., 1996). It is notable that schizophrenic patients were impaired only when 2 and 3 cues had to be selected. It can be hypothesized that the explicit representation of associations of cues is damaged, rather than the knowledge of single cues.

In summary, our data obtained from *Experiments 5* and *6* are consistent with the results of numerous studies reporting intact implicit memory (repetition priming and skill learning) and deficient explicit memory in schizophrenic patients (McKenna et al., 1990; Clare et al., 1993; Duffy & O'Carroll, 1994; Friston et al., 1994; Elliott & Sahakian, 1995; Brébion et al., 1997; Heckers et al., 1998). It must be noted, however, that in some patients with negative and delusive symptoms, there were alterations in skill learning, which suggests a more pronounced basal ganglia and implicit memory impairment (Schroder et al., 1996).

11. General discussion

11.1. Overview

The major results of our six experiments can be summarized as follows:

- Schizophrenic patients are impaired in the perceptual learning (serial exemplar presentation, feedback) of two-dimensional GCs (Figure 2).
- Basic mechanisms of categorization are spared in the case of DCs (Figure 2).
- The GC impairment can be compensated using verbal descriptions (Figure 2).
- The representations of GCs, which are primarily induced by verbal descriptions, is similar in both schizophrenic patients and healthy control subjects (Figure 3).
- The GC impairment is not the consequence of a generalized cognitive dysfunction (Figure 6).
- Category acquisition, which is based on implicit habit learning, is preserved schizophrenia (Figure 7).

- The explicit knowledge of categories acquired during habit learning is deficient (Figure 8).

For possible neuronal mechanisms of different aspects of categorization and their status in schizophrenia, see Table 7 (Kolb & Whishaw, 1996a,b; Knowlton et al., 1996; Damasio et al., 1996; Ashby et al., 1998; Lawrence et al., 1998; Fletcher et al., 1999).

In the following sections, we discuss three models of categorization and concept formation to demonstrate how our results can be integrated into global hypotheses to explain schizophrenic cognition. These models are as follows:

1. The COVIS (COmpetition between Verbal and Implicit Systems) hypothesis of Ashby et al. (1998);
2. The ART (Adaptive Resonance Theory) of Carpenter and Grossberg (1993);
3. The SBCF (Spatially Based Concept Formation) model (Mandler, 1988, 1992).

11.2. The COVIS (COmpetition between Verbal and Implicit Systems) hypothesis

This neuropsychologically based model provides the most clear-cut explanation of schizophrenic categorization disturbances. The model proposed two closely related neuronal systems for categorization: the first is explicit and based on verbal representations, whereas the second is an implicit system with predominantly perceptual representations (Ashby et al., 1998) (Figure 9).

In the implicit system, visual features of category exemplars such as form and color are processed in the ventral occipito-temporal cortex. Via connections between the ventral visual stream and neostriatum, each stimulus is associated with a certain category outcome. In other words, neostriatal networks divide the perceptual space according to certain response properties. For the occipito-temporal cortex, it does not count whether a stimulus contained a circle or a square – these features are both equal subjects for the analysis of form. In contrast, the neostriatum links different outcomes to these features: circles signify category A, whereas squares signify category B. Ashby and his colleagues (1998) also hypothesized that after the striatal decision, units in the prefrontal cortex are activated via striato-thalamo-cortical pathways. The implicit system plays an important role in classification processes when the rules of categorization are difficult to verbalize and the learning process is supervised (i.e. driven by feedback as a contrast of serial exemplar presentation). The PCL task is a good example for this type of category learning, placing a burden on the ventral cortico-striato-frontal circuits. This function was spared in schizophrenic patients but not in patients with basal ganglia disorders (Knowlton et al., 1996; Lawrence et al., 1998) (*Experiment 5*).

Table 7. Neuronal mechanisms of categorization and their status in schizophrenia

NEURONAL STRUCTURES	FUNCTION
PREFRONTAL CORTEX	• *verbal rule selection (anterior cingulatum)*↓ • *abstraction from exemplars (left lateralized)* ↓ • *symbolic recoding (left inferior regions)* ↓ • strategy shifting (dorsal regions with the dorsal striatum) ↓ • contextual representation↓
MEDIO-TEMPORAL REGIONS	• *explicit representation of categories*↓ • multimodal integration↓
TEMPORAL ASSOCIATION NEOCORTEX	• semantic-lexical categories (temporal pole, posterior-ventral regions, temporo-parieto-occipital junction) ↓
VENTRAL NEOSTRIATUM	• *automatic abstraction from exemplars*✓ • *habit learning*✓
OCCIPITO-TEMPORAL VISUAL CORTEX	• *encoding the form and color*✓ • *representation of categorical information*✓

Functions targeted in the present experiments are written in italics. ↓ - impaired in schizophrenia, ✓- spared in schizophrenia

The explicit system is based on the anterior attentional area of Posner and Petersen (1990) and the working memory network of Goldman-Rakic (1987) and Fuster (1990). Ashby and his associates argue that the anterior cingulatum plays a crucial role in the selection of verbal categorization rules (e.g. to find out that cards must be sorted according to their color in the WCST), whereas the dorsal fronto-striatal circuits mediate strategy shifting (e.g. to switch from color to shape) (see also Owen et al., 1993; Lawrence et al., 1998). Therefore, the neostriatum participates in both implicit and explicit categorization procedures, supporting a good competition field between these systems. In schizophrenia, decreased dopamine level in the prefrontal cortex impairs switching and leads to perseverative errors. Recently, a close negative correlation was reported between the density of prefrontal D_1 receptors and the WCST perseverative errors. However, the selection of categorization rule is generally thought

to be spared in schizophrenic patients, despite the fact that the anterior cingulatum shows hypoactivity in category retrieval tasks, which is reversed by dopaminergic drugs (Dolan et al., 1995).

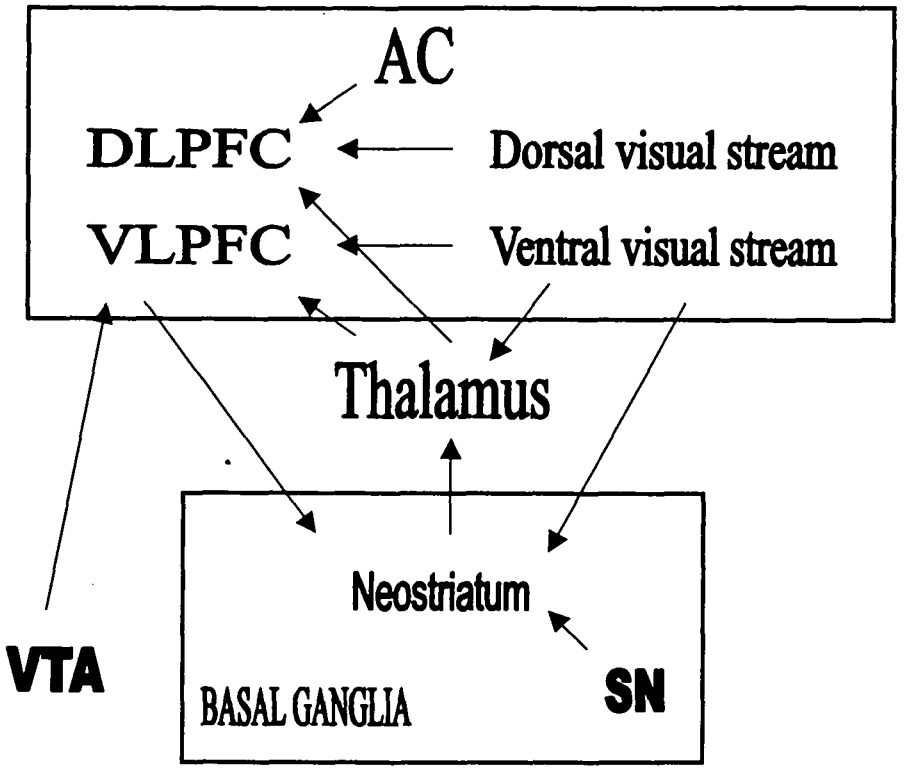

Figure 9. Neuronal circuitry of perceptual categorization. [DLPFC – dorsolateral prefrontal cortex, VLPFC – ventrolateral prefrontal cortex, AC – anterior cingulatum, VTA – ventral tegmental area, SN – substantia nigra]

Unsupervised category learning (e.g. serial exemplar presentation) urges verbal rule formation (Medin et al., 1987; Ahn & Medin, 1992; Wattenmaker, 1992). However, in the case of two-dimensional GCs used in our experiments, verbal rules are not optimal. One distinguished difficulty is that GC exemplars are defined by the conjunction of two perceptual dimensions: size and shape. It has been agreed that subjects tend to select unidimensional rules, i.e. they may believe that size or shape alone fully determines category membership (Ashby et al., 1998). Therefore, instead of thinking about categories of "smaller circles with a square-like shape" and "larger circle with an circle-like shape", they tend to think about "smaller circles" versus "larger circles" or "square-like shapes" versus "circle-like shapes". A functional imaging study found that a specific area in the dorsolateral frontal cortex was

activated when subjects categorized perceptual stimuli defined by feature-conjunctions (Rees et al., 1997). Hence, it is possible that schizophrenic patients were completely unable to establish such feature conjunction, which produced a prominent GC deficit after serial exemplar presentation and was resolved after verbal definition. An alternative explanation can be that the apparent ambiguity of GC rule selection exceeded the functional capacity of anterior cingulatum (Dolan et al., 1995). Finally, a dysfunctional lateralization of the frontal lobes can also account for categorization deficits. In an artificial grammar learning task, right prefrontal activation was associated with the processing of individual exemplars, whereas the left prefrontal cortex showed a pronounced activity when an abstract categorical structure emerged during the learning process (Fletcher et al., 1999). The prefrontal origins of schizophrenic categorization dysfunction are summarized in Table 6.

In conclusion, most of the neuropsychological and functional imaging data can be adequately explained by the COVIS model, implicating that verbal mechanisms of categorization are deficient, whereas implicit functions are relatively intact in schizophrenia.

11.3. The ART (Adaptive Resonance Theory)

The ART was designed to explain recognition and categorization in both normal and pathological conditions (Grossberg, 1970, 1976; Carpenter & Grossberg, 1993; Aakerlund & Hemmingsen, 1998). The model consists of a feature layer and a category layer, which are organized by the attentional gain control and orienting subsystems (Figure 10).

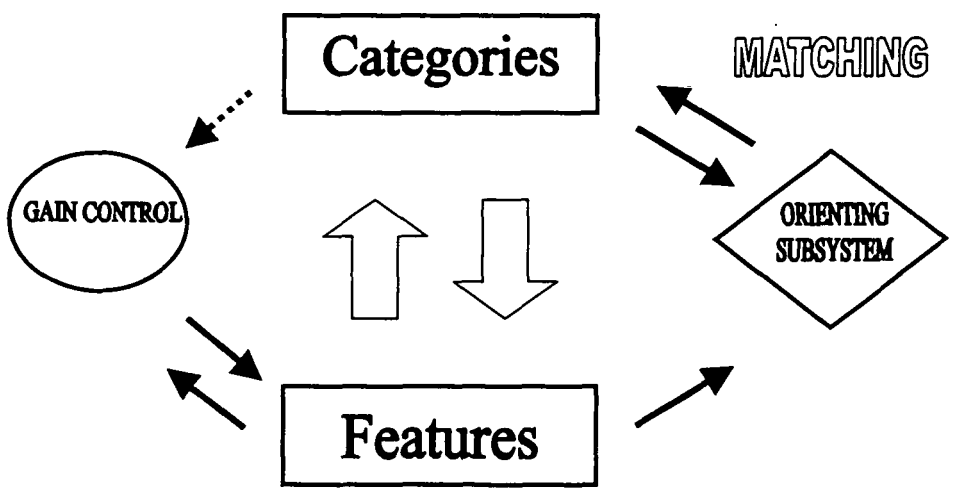

Figure 10. The structure of the ART. [The dotted arrow signify an inhibitory connection.]

The feature layer subserves elementary visual processing, concerning shape, color, spatial characteristics, and binocular disparity. These features are condensed and grouped in the category layer. For example, dogs have colors, shapes, surface textures etc., which are integrated to the percept of a dog. Moreover, all dogs have similar properties that make them members of the same category. These latter informations are represented in the category layer. The orienting subsystem is responsible for the comparison and matching of patterns provided by the feature layer and stored in the category layer. It is important to note that the set-point of acceptability is determined by the orienting subsystem. If the value of the set-point is low, less similar visual patterns are allowed to be included as members of a particular category, whereas in the case of higher set-points the criterion of decision is stricter. If we want to recognize our own dog, the set-point is extremely high, hence all other dogs are rejected. In contrast, if we want to categorize items around us as animals or non-animals, the set-point is low allowing a wider degree of generalization (Carpenter & Grossberg, 1993; Aakerlund & Hemmingsen, 1998).

Another important component of ART is the attentional gain unit. During the matching process, this subsystem must be inhibited by the category layer, otherwise the activity of positive feedback loops may stimulate the appearance of inadequate informations in the feature layer (Figure 8). Several studies, designed to determine the neurobiological correlates of ART, suggested that the feature layer is a computational equivalent for sensory neocortex, the category layer for fronto-temporal cortex, the orienting subsystem for hippocampus, and the attentional gain unit for the striato-thalamic system (Carpenter & Grossberg, 1993; Aakerlund & Hemmingsen, 1998). In comparison with the COVIS, note that the ventral visual system corresponds to the feature layer, whereas prefrontal and cingulate areas refer to the categorical layer. One substantial difference is that in the COVIS, neostriatum is directly connected to category induction, whereas in the ART it is included as an attentional filtering unit.

These considerations have heuristic values in understanding schizophrenia. First, abnormal inhibitory pathways from the prefrontal cortex to the striatum may induce pathological attentional filtering, which leads to activities in the sensory cortex that must not be present for a given external input (Robbins, 1990). Second, autonomous activations in the fronto-temporal areas (category layer) may result in inadequate internal mental operations in the absence of external sensory input. These mechanisms are hypothesized to be the bases of hallucinations and disrupted reality testing (Hoffman, 1999). Third, hippocampal impairment (orienting subsystem) can be accompanied by a deficient tuning of category set-points as a

candidate pathomechanism of overinclusive or even flattened concept activation. Recently, some aspects of schizophrenic WCST impairment have been successfully modeled in the framework of ART (Aakerlund & Hemmingsen, 1998).

The main conclusion concerning our experiments is that for simple perceptual categories the cornerstone of schizophrenic classification impairment is the abnormal representation. After the serial presentation of GCs, one can suppose that any level of categorization may be insufficient in schizophrenia: the formation of categorical representation (interaction between the feature and category layers), the orienting subsystem, or the attentional gain control unit. Neurobiological data allow any of them (see the Introduction). However, it is remarkable that after verbal definition, but not after extended training with serial exemplar presentation, schizophrenics displayed no significant difference from the controls. In other terms, if category representation was corrected, they appropriately used their orienting and gain control subsystems to classify novel exemplars. In addition, perceptual category learning in the PCL task was spared despite a marked medio-temporal deficit.

The assumption of specific representational abnormality, as explained in the mirror of ART, can be treated cautiously. First of all, the neurobiological skeleton of ART is highly theoretical. Secondly, it is less known how simple perceptual categorization is organized in the brain in comparison with more elaborate semantic processes, which heavily burden all components of the ART. These questions must be clarified before drawing final conclusions concerning the specific locus of schizophrenic categorization impairment.

11.4. Future directions: Spatially Based Concept Formation (SBCF)

A central question in cognitive neuroscience concerns the issue how concepts are developed and what makes the substantial steps in progressing from perceptual to semantic representations (Mandler, 1988, 1992). Consider, for example, the categories used in our experiments, which were geometrical shapes with minimal conceptual and meaning-based properties. It hardly can be stated that these stimuli provide special meaning as in the case of semantic categories. When infants first exposed with the wealth of sensory word, shape, color, and texture patterns of objects bear little meaning and importance for them. First, they learn how these patterns comprise coherent objects and categories of similar objects. Second, the objects and their classes begin to emerge as instances with a special functional meaning for the person: we learn what house, vehicles, and animals are. Here is the nucleus of the

problem: What does mediate the transition from perceptual to conceptual representation? What does barking instances with four legs make dogs?

One remarkable explanation for this question raises the possible role of spatio-temporal information processing, which may transcend percepts into concepts (Mandler, 1988, 1992). One of the most fundamental conceptual differentiations is the division of word into living and non-living things. How can a child discriminate between toy dogs and living dogs with similar size, shape, color, and surface texture? How can a child know that toys and living animals must be treated differently (e.g. a toy dog can be put in the washing machine, whereas a living dog has to be given something to eat)? During interactive learning processes, infants may observe that the patterns of movement of living and non-living instances are substantially different. A toy dog hardly can run itself (self-induced movements), and if it is set into motion by external sources, it runs in a straight line without any attempt to avoid a crush with the chair (linear motion). In contrast, living dogs are characterized by self-induced and rapidly changing movements. Similarly, essentially different motor patterns are associated with living and non-living things. In conclusion, different kinetics of movements and different motor behaviors might be the bases of concept formation (Mandler, 1988, 1992).

This hypothesis allows us to speculate about its possible role in schizophrenic conceptual disorganization. It is possible that the abnormal processing of spatio-temporal information and the deficiency of fine motor learning may lead to impaired concept formation and semantic memory dysfunction in schizophrenia. From the point of motion perception, a wealth of data supports this theory. A number of studies provided evidence that schizophrenic patients are prominently and specifically impaired in tasks in which spatial location, motion, trajectory, and high temporal/low spatial frequencies have to be processed (O'Donnel et al., 1996; Cadenhead et al., 1998; Kéri et al., 1998; Slaghuis & Curran, 1999; Chen et al., 1999). From a neurobiological point of view, spatially-oriented and object-oriented visual information processing are organized in two parallel, but closely interacting systems in the brain (Milner & Goodale, 1993; Ungerleider & Haxby, 1994). Analysis of motion, spatial location and visuo-motor coordination are linked to the dorsal stream (occipito-parietal cortex), while areas participating in the processing of color and form are located along the ventral stream (occipito-temporal cortex). Interestingly, the dorsal stream is heavily connected with the dorsolateral prefrontal cortex, whereas the ventral stream projects to the ventrolateral prefrontal areas (Kolb & Whishaw, 1996b). Petrides (1994) hypothesized that the ventral prefrontal areas play roles in the retrieval and active maintenance of information, whereas the spatially-oriented dorsal regions participate in the active manipulation and recombination of

representations to achieve adaptive problem solving strategies (for a recent validation, see Owen et al., 1999). These considerations fit well into the neuropsychological and functional imaging literature of schizophrenia (see also our *Experient 5*), which suggested a more pronounced insufficiency of dorsal regions, including both posterior and prefrontal cortices (Weinberger et al., 1994; Elliott & Sahakian, 1995). Therefore, we suppose that as an alternative hypothesis for the representational disability concept outlined in previous sections, spatio-temporal processing abnormalities may explain many aspects of schizophrenic conceptual malfunctions. Future studies are warranted to test this hypothesis.

12. References

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14. Appendix: Papers related to the thesis

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Abstraction is impaired at the perceptual level in schizophrenic patients

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Abstract

This study investigates category learning in schizophrenia in order to evaluate abstraction abilities at the perceptual level. The participants learned about two categories of geometric shapes. The category exemplars were presented successively. In the case of schizophrenic patients, longer exposure time and more stimulus presentations were used to counterbalance attention impairments. In spite of this, the perceptual category learning was significantly impaired in the patient group. In contrast, when the training procedure involved verbal category definition and not perceptual learning, the performance of schizophrenics was similar to that of the healthy controls. These findings suggest that the perceptual learning of categories, but not free classification judgements are impaired in schizophrenia, and that this impairment is not due to pure attentional disturbances. © 1998 Elsevier Science Ireland Ltd.

Keywords: Abstraction; Attention; Category learning; Perceptual; Schizophrenia

The loosening of associations and conceptual disorganization are among the most important symptoms of schizophrenia. Several studies on word association, semantic priming and categorization have investigated this problem with controlled laboratory methods [4,11,15–17]. These studies suggested that the categorical organization of semantic knowledge is impaired in schizophrenia. The theory of disconnected and hyperactivated semantic network suggests that the representation of distinct categories are abnormally connected in schizophrenia [5,16,17]. However, the characteristics of perceptual, but not semantic categorization abilities are not clear. In perceptual categorization tasks, stimuli with little meaning and conceptual-associative properties are applied, as in the case of simple geometric shapes [10,13]. The present three experiments were designed to evaluate perceptual classification abilities in schizophrenia. We investigated how patients could recognize simple structural-perceptual similarities and dissimilarities of different stimuli when the attentional demands were counterbalanced.

In the first experiment, the attentional abilities of the schizophrenic patients and control subjects (Table 1) were determined by measurements of the critical stimulus duration (CSD) and the minimum number of successive stimulus presentations (MNP), required for the detection of the common features between exemplars. The stimuli were presented on a Sampo monitor (0.28 mm dot pitch size) controlled by a Pentium P54 CX personal computer. The luminances of the fixation area (20 cd/m^2) and the stimulus area (140 cd/m^2) were constant. The stimuli consisted of five internal parts, which were different non-figurative shapes. Each stimulus contained one or two of the four cues (circle, square, triangle and trapezium). The position of cues within the whole stimulus altered randomly. Each stimulus subtended 6.8° in the horizontal and 6.8° in the

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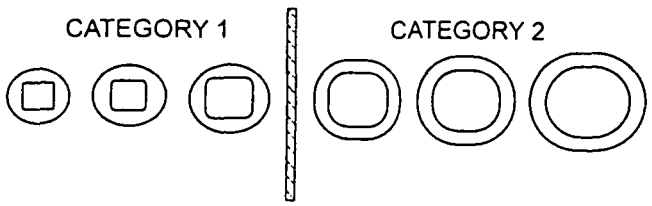

Fig. 1. The exemplars of the two categories. A small circle containing a square was transformed into a large circle containing a circle, and this stimulus continuum was divided into two parts: one for the first, and the other for the second category.

vertical direction, and each internal part subtended 2° in the horizontal and 2° in the vertical direction.

The CSD was defined as the minimum exposure time necessary for eight consecutive identifications of the one cue element of stimuli (circle or square). In this phase, a forced-choice staircase method was used with increments/decrements of 14 ms in the case of incorrect/correct responses [2].

In the measurement of MNP, stimuli were presented successively. The exposure time was 20 times longer than the previously measured CSD. In this task, subjects were asked to respond if they found the two common cue elements (triangle and trapezium) represented in each stimulus. We recorded the required number of stimulus presentations [8]. The evaluation of CSD and MNP served as basic tests for attentional abilities. In the further experiments, these parameters were used to counterbalance the attentional differences between the controls and schizophrenics.

In the second experiment in the first (training) phase, subjects learned about perceptual categories. The exemplars were computer-interpolated images: a small circle with a square in the middle was gradually transformed into a large circle with a circle in the middle. This continuum was divided into 200 parts: 100 for the first and 100 for the second category. The stimuli subtended 6.8° in the horizontal and 6.8° in the vertical direction (Fig. 1). The exemplars of the first category, and then some of the second category were presented successively in a pseudorandomized order. In this way, the subjects learned about the two categories by the observation of similar category members. The number of presentations was the same as in the first phase (MNP), while the exposure time was 20 times longer than the CSD in both groups. These values were set individually. In the second (testing) phase, the category knowledge was measured by presenting new intermixed exemplars of the two categories. The number of presentations was 40 for each category, the exposure time remaining the same as in the previous phase. The participants categorized by pressing the category-associated keys on the computer keyboard. Feedback was not given in this phase. Finally, the training and testing phases were repeated to evaluate further practice effects on categorization performance.

In the third experiment the spontaneous and free similarity and classification judgements were investigated. The stimulus set and the parameters were the same as in the second experiment (testing phase), the clinical and demographic data are shown in Table 1. The subjects were told that they would see geometric shapes presented successively, and were asked to respond by pressing a key only if the actual stimulus appeared as a small circle with a square in the middle. The performance was given as the percentage of presented stimuli judged as a small circle with a square in the middle.

Table 2 summarizes the raw data of the first and second experiments, and also the one-way analysis of variance (ANOVA) comparisons. Concerning the second experiment, an additional 2 (group: controls, schizophrenics) ×2 (practice: first and second study phases of categorization) ANOVA on the categorization performances revealed the main effects of group ($F(1,38) = 8.24$, $P < 0.01$), practice ($F(1,38) = 131.01$, $P < 0.0001$) and also a two-way interaction ($F(1,38) = 4.38$, $P < 0.05$). The separate ANOVAs demonstrated that after the second study phase, the difference between the two groups increased. In the third experiment, the performance (%) of controls was 34.32 ± 9.24, while that of the schizophrenics was 31.17 ± 19.36. The *t*-test revealed that this difference was not significant.

Table 1
Clinical and demographical data of the participants (mean ± SD)

	First and second experiment		Third experiment	
	Schizophrenics ($n = 20$)	Controls ($n = 20$)	Schizophrenics ($n = 20$)	Controls ($n = 20$)
Age (years)	34.6 ± 8.5	35.7 ± 4.9	35.1 ± 11.2	38.1 ± 18.5
Education (years)	15.1 ± 8.2	13.3 ± 7.4	10.7 ± 8.9	12.4 ± 9.2
PANSS (global)	45.6 ± 17.8	–	51.1 ± 22.3	–
PANSS (positive)	20.8 ± 12.2	–	19.2 ± 8.4	–
PANSS (negative)	25.2 ± 12.4	–	27.9 ± 15.0	–
GAF	43.4 ± 16.6	–	39.4 ± 9.8	–
Antipsychotics	287.7 ± 80.6	–	301.1 ± 150.2	–

The diagnosis of the patients was based on the DSM-IV criteria [1]. The clinical symptoms were evaluated with the Positive and Negative Symptom Scale (PANSS) [7]. The social status was determined with the Global Assessment of Functioning (GAF) scale [1]. The doses of antipsychotics (mg/day) were converted to chlorpromazine equivalent doses.

Table 2
Critical stimulus duration (CSD), the minimum number of stimulus presentations for feature extraction (MNP) and the categorization performances after the first and second study phases (CAT 1 and CAT 2) in the schizophrenia and control groups

	Controls	Schizophrenics	$F(1,38)$
CSD (ms)	17.05 ± 6.21	27.90 ± 13.40	9.91, $P < 0.005$
MNP	9.10 ± 4.04	15.80 ± 4.97	21.90, $P < 0.0001$
CAT 1 (%)	63.45 ± 7.55	56.05 ± 7.96	9.10, $P < 0.005$
CAT 2 (%)	85.45 ± 2.91	61.80 ± 10.29	98.01, $P < 0.00001$

Data are the mean ± SD. Each value is compared by one-way ANOVA.

Our findings can be summarized as follows. Firstly, the CSD was longer and the MNP was higher in the schizophrenia group: the patients needed a longer time to detect stimuli and more presentations to find common features. These data provide further evidence of the attentional impairment in schizophrenia [3]. However, in the learning phase of perceptual categories, these parameters were counterbalanced individually. More exemplars were presented to the schizophrenic patients than to the controls, and the exposure time was also longer in their case. In spite of the attentional support, our patients had a marked perceptual categorization deficit, and the further practice was not effective. These findings suggest that schizophrenics were impaired at the perceptual level of abstraction and more dominantly in the correction and improvement of this knowledge. This impairment was not due to a pure attentional deficit. Furthermore, the differences between the two groups were not similar at the accuracy levels of controls located around nearly equal distances from the critical 75% performance level (CAT 1 and CAT 2, Table 2). This indicates that the categorization deficit was not a psychometric artifact, which could derive from the general cognitive disturbances of schizophrenic patients [12]. Finally, it was demonstrated that schizophrenics did not differ from controls in similarity and classification judgements when the learning involved no strict perceptual procedure. The mental representations of stimuli, induced by verbal definition, were similar in both groups. However, the standard deviation was larger in the patient group, which suggests wider interindividual differences.

Overall, it is concluded that classification/abstraction is impaired at the perceptual level, and not exclusively at the semantic level in schizophrenia. Furthermore, this seems to be a specific deficit, at least in the case of interpolated geometric images used in these experiments. It is noteworthy that for the present stimuli, the mental representations of categories were holistic-global rather than analytic, which reflects an earlier stage of cognitive organization [6]. Further studies should compare the category representations based on feature analysis and global structure in order to gain more insight into the nature of abstraction in schizophrenia. The Wisconsin Card Sorting Test (WCST), which is a popular method for the evaluation of prefrontal functions in schizophrenia, also includes a categorization procedure [20]. However, in this test a more complex and flexible usage, correction and reorganization of knowledge is required, and the stimuli have rather different physical properties. Since simple perceptual category learning is believed to be independent of the medio-temporal and prefrontal neuronal structures [9,18,19], our results raise the possibility that the basis of schizophrenic classification disabilities are connected with the disorder of modality-specific association cortex. On the other hand, it is also possible that perceptual category learning is mediated by neocortico-striatal loops, which are coordinated by the prefrontal cortex [14,19]. Thus, the categorization deficit may reflect the disorder of these neuronal structures. This latter may be congruent with the fronto-striatal hypothesis, which suggests that the connection between these cortical and subcortical structures is impaired in schizophrenia [14].

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Category Learning and Perceptual Categorization in Schizophrenia

by Szabolcs Kéri, György Szekeres, István Szendi, Andrea Antal, Zoltán Kovács, Zoltán Janka, and György Benedek

Abstract

The aim of this study was to evaluate category learning in schizophrenia on tests of perceptual abstraction. Participants learned to categorize simple geometrical shapes. The categories were either well-defined (discrete categories, or DCs) or ill-defined (graded categories, or GCs). In DCs, the cues defining category membership can be verbalized in an all-or-none fashion, while in GCs they cannot be defined unambiguously. Three types of learning were used successively: serial presentation of category-exemplars, verbal description, and feedback. After the serial presentation, schizophrenia patients showed a deficit for GCs ($p < 0.005$) but not for DCs ($p = 0.98$). After the verbal definition of GCs, the difference between schizophrenia patients and controls diminished ($p = 0.09$). Finally, after the feedback learning of GCs, a significant difference was observed again ($p < 0.0001$), suggesting that schizophrenia patients were impaired in this learning paradigm. The GC-learning impairment after the serial presentation displayed a relationship with the score of the cognitive component assessed with the Positive and Negative Syndrome Scale ($r = -0.66$). In conclusion, these results suggest that the perceptual stage of abstraction is impaired in schizophrenia. This impairment can be partially compensated by instructions via top-down verbal processes.

Key words: Category learning, cognitive deficit, perceptual representation, schizophrenia.

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The disorganization of semantic memory is an important aspect of the neuropsychology of schizophrenia (Spitzer et al. 1993; Chen et al. 1994; Clare et al. 1994; McKay et al. 1996; Spitzer 1997). Semantic memory is a factual representation of the world that involves both physical-perceptual and associative-conceptual features. Categorical organization is a central characteristic of semantic memory: similar facts are grouped together, while dissimilar ones are separated. This organization has two fundamental components: perceptual and conceptual (Caramazza 1996; Mandler 1996). For example, "bird" is a perceptual category, because sparrows, storks, eagles, and so forth all have structural-physical similarities. At the same time, "birds" have a common associative meaning, so they are also the members of the same conceptual category. In more general (superordinate) categories, such as "animal" or "man-made tool," little perceptual commonness can be found among the members (Medin 1983; Mandler et al. 1991; Mandler 1996). Finally, the perceptual and the meaning-based information seems to converge into a common integrated semantic network (Vandenberghe et al. 1996). In schizophrenia, both perceptual and conceptual aspects of categorization have been shown to be impaired (Shallice et al. 1991; Chen et al. 1994). For instance, the reaction times of schizophrenia subjects were longer when they had to decide whether "aeroplane" belongs in the category "bird" or not (Chen et al. 1994). In this case, healthy controls decide easily by considering the large conceptual difference, whereas patients hesitate because of the perceptual similarities between "aeroplane" and "bird." This hesitation may indicate a disturbance of the relationship between perceptual and conceptual categorization in schizophrenia. Shallice and colleagues (1991) also demonstrated impairments in both perceptual and conceptual aspects of categorization. For example, when a "plug" was briefly presented from an unusual view, schizophrenia patients categorized it as "candles in a church" (perceptual level) or a "switch" (conceptual level). The phenomenon of obscure and uncertain category boundaries is consistent with the theory of a hyperconnected and disorganized semantic network (Spitzer et al. 1993; David 1994; Paulsen et al.

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1996; Goldberg et al. 1998). However, in spite of extensive investigations of semantic memory, few data are available on simple perceptual category acquisition and organization in schizophrenia, although it is one of the fundamental principles of human cognition (Harnad 1987).

The first step in the present model of perceptual category learning, which is based on the original assumptions of Harnad (1987), is the presentation of a number of stimuli to enable the observer to extract the relevant features common in each exemplar. This generalized pattern is stored in the memory. After this learning phase, new stimuli are presented in a perceptual categorization task. The categorization of the new exemplars is determined by comparing the new stimuli with the stored representations (Carpenter and Grossberg 1993). Here we distinguish two kinds of perceptual categories, following Medin and Barsalou (1987). Discrete categories (DCs) are defined with features characteristic of the given category. The presence or absence of these features determines category membership in an all-or-none fashion. These well-defined categories are easy to verbalize (Homma and Vosburgh 1976; Medin and Barsalou 1987). In contrast, the representation of a graded category (GC) is an averaged central tendency, a summary representation of several individual exemplars (prototype). GCs are ill-defined because they are hard to verbalize and hard to define unambiguously. At higher levels of representation, categories can be labeled and described verbally. This symbolic representation allows quick cognitive (top-down) learning, but nonproportional information such as fine perceptual skills cannot be represented properly in this way: here the sensory-perceptual channels have an indispensable advantage (bottom-up learning) (Mandler 1996).

The aim of the present study was to examine category learning and perceptual categorization of DCs and GCs in schizophrenia, so as to gain more insight into the functioning of basic processes of abstraction in this disorder.

Methods

Subjects. Twenty patients (6 women and 14 men) who met the *DSM–IV* (American Psychiatric Association 1994) criteria of schizophrenia participated in the study. The current symptoms were assessed with the Positive and Negative Syndrome Scale (PANSS; Kay et al. 1987). The social functioning was evaluated with the Global Assessment of Functioning scale of *DSM–IV*. Two of the patients were drug-free, and only 4 of the 20 were on anticholinergic medication. Demographic and clinical data are shown in table 1.

The control group comprised 20 subjects (6 women and 14 men) without any history of neurological or psychiatric disorder. The control subjects were members of the university staff. The mean age was 36.25 years (standard deviation [SD] ± 10.42), and the mean years of education was 11.10 (SD ± 2.86). All subjects had normal or corrected-to-normal visual acuity. The two groups were matched for age ($F(1,38) = 0.48$, $p = 0.49$) and for duration of education ($F(1,38) = 0.23$, $p = 0.63$). The educational levels of the controls and of the parents of the schizophrenia subjects were also comparable (mean 10.95 years, SD ± 2.19) ($F(1,38) = 0.03$, $p = 0.85$).

Stimuli

Discrete categories. The 30 instances of DCs consisted of five internal parts that were nonfigurative shapes. DC1 was defined with a coexisting circle and large spots, while in DC2 the cue features were a square and an irregular triangle consisting of small spots. The positions of category-relevant cues altered randomly in each stimulus.

Table 1. Demographic and clinical data of the schizophrenia group ($n = 20$, 6 women/14 men)

	Mean	± SD	Range
Age, years	38.70	11.85	27–67
Education, years	11.55	3.02	8–18
Age at onset	30.05	10.45	17–59
Number of hospitalizations	4.00	2.59	1–10
GAF score	46.55	18.74	21–80
PANSS scores			
Global symptoms	48.10	12.07	27–67
Positive symptoms	19.10	9.30	7–47
Negative symptoms	21.80	8.15	9–40
Neuroleptic dose (chlorpromazine-equivalent), mg/day	285.10	183.79	0–900
Anticholinergic dose (procyclidine), mg/day	3.62	7.49	0–30

Note.—SD = standard deviation; GAF = Global Assessment of Functioning; PANSS = Positive and Negative Syndrome Scale.

Each DC member subtended 8.9 degrees in the horizontal and 6.8 degrees in the vertical direction, and each internal part subtended 2 degrees in the horizontal and 2 degrees in the vertical direction (figure 1).

Graded categories. The exemplars of GCs were computer-interpolated images of simple geometrical shapes: each point of the initial shape (a small circle with a square in the middle) passed toward its new position (a large circle with a circle in the middle) so as to depict a continuum between these extreme configurations (Brennan 1985). The continuum was divided into 30 parts, 15 for the first and 15 for the second category (GC1 and GC2). Each stimulus area subtended 6.8 degrees in the horizontal and 6.8 degrees in the vertical direction. The position of each point on the lines outlining the shapes was randomized (5 dot pitches in both horizontal and vertical directions). This randomization of the shape of GC exemplars was category-irrelevant noise. Note that we used simple geometrical shapes as category exemplars with little functional and associative content, minimizing conceptual levels of information processing (figure 1).

Procedure

General design. There were four consecutive phases of category learning in the same sequence in each subject. After each phase, the actual categorization performance was determined. The first phase was DC learning by sequential presentation of category exemplars; three different types of GC learning followed: sequential presentation of exemplars, verbal definition, and feedback.

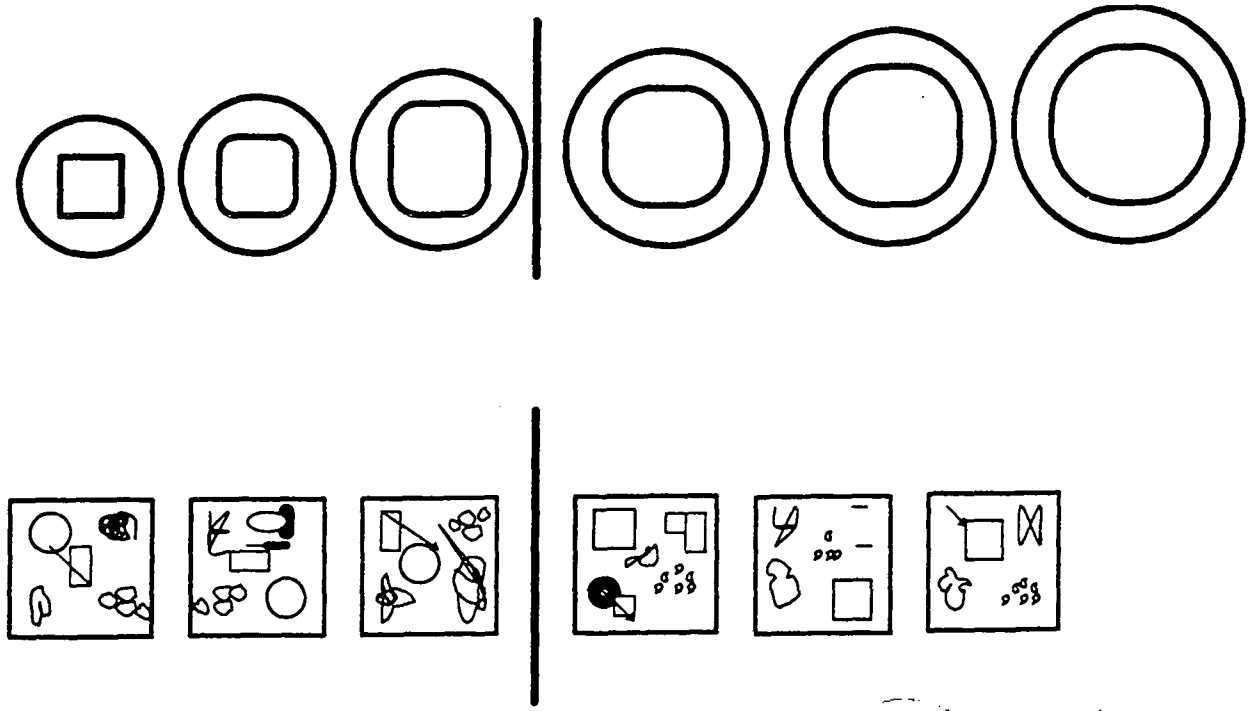
DC learning by successive presentation of exemplars. The subjects first learned the two DCs by the sequential presentation of some category exemplars of DC1, and then of some DC2. In this phase, the task was to find the invariant, category-relevant key elements, and the subjects were asked to respond if they found these common features. The required presentations of DC1 and DC2 exemplars for the detection of key elements were counted and averaged for each subject individually.

The stimuli were presented on a Sampo monitor (0.28 mm dot pitch size) controlled by a Pentium 82430 FX/P54 CX personal computer. The exposure time was 700 ms. To guide the gaze of subjects, a black dot appeared on the screen. The subjects sat 100 cm from the computer screen.

In tests of the DC performance, previously unseen intermixed exemplars of DC1 and DC2 were presented, each for 28 ms. Participants were asked to categorize the new stimuli by pressing the previously learned category-associated keys on the computer keyboard. The number of presentations was 45 for each category. In this testing session, exemplars of DC1 containing a triangle or a square, and exemplars of DC2 with large spots or a circle were intermixed in the stimulus set as distracting elements.

The DC learning served as a basic test for measurement of the attentional abilities of schizophrenia patients

Figure 1. Exemplars of graded categories (circles) and discrete categories (squares)



during the detection of perceptual-structural commonness and the execution of categorization tasks. The task evaluated the number of required presentations of exemplars in order to detect category-relevant cues, and also the categorization performance at a brief exposure time. Data from DC learning revealed that schizophrenia patients can execute these tasks successfully (see "Results"), which suggests that the learning and storing of category-relevant cues, the detection of cues, and the category decisions were not below the general abilities of patients. Thus, the same parameters were used in further tests with one exception: the exposure times in the testing phases were longer, in order to definitely exclude any attentional overloading effect.

GC learning by successive presentation of exemplars. Exemplars of GC1 and GC2 were presented, each for 700 ms, exactly as in the DC learning phase. The number of presentations was the same as the individual average value in the previous phase. Subjects were told that the previously seen forms belonged in two different groups of shapes. Category knowledge was tested by presenting 45 new exemplars for each category at an exposure time of 700 ms. Participants made category judgments as in the DC learning phase.

In both DC and GC learning phases, half the subjects began with the first category, and the other half with the second category. Performances of the groups in which learning began with the first categories (DC1/GC1) were not significantly different from the performances of the groups who began with the second categories (DC2/GC2). This was true for both the schizophrenia group and the control group ($p > 0.6$ in each case).

GC learning by verbal definition. Following the learning by serial presentation of GC exemplars, the complete verbal descriptions of GCs were given to the participants by the same author, with the same standardized sentences. The definition was repeated slowly once, as a nonperceptual modification of the former structural representation of categories gained in the previous phase. The effect of the verbal correction of category knowledge was measured by repeating the testing procedure used in the previous phases.

GC learning by feedback. In the feedback learning phase, subjects continued the categorization of GC members with the design applied in the previous testing phases, but incorrect responses were followed by a sound signal from the computer. The effect of feedback learning was assessed by repeating the testing phase without feedback.

Data Analysis. First, a one-way analysis of variance (ANOVA) was conducted to compare the number of required category exemplars for the detection of cue features in the control group and in the schizophrenia group. Second, a 2 (group: schizophrenia patients, controls) × 2 (category type: DC, GC) repeated measures ANOVA was performed on the categorization performances measured after the serial presentation of DCs and GCs. Third, an additional 2 (group) × 3 (type of learning: serial presentation, verbal definition, feedback) ANOVA was performed on the GC performances. For post hoc analysis, Scheffé's test was used.

Results

DC and GC Learning by Successive Presentation of Exemplars. The data were normally distributed. Schizophrenia patients required more stimulus presentations (mean 10.45, SD ± 4.65) to detect category-relevant elements of DCs than did the controls (mean 6.65, SD ± 2.92) ($F(1,38) = 9.57$, $p < 0.005$). The repeated measures ANOVA on the DC and GC performances after the serial presentation indicated main effects of group ($F(1,38) = 6.61$, $p < 0.02$) and category type ($F(1,38) = 116.23$, $p < 0.0001$). There was a significant interaction between group and category type ($F(1,38) = 9.97$, $p < 0.005$). Scheffé's test revealed that the schizophrenia patients were significantly impaired in the GC task ($p < 0.005$) but not in the DC task ($p = 0.98$) (table 2).

GC Learning by Verbal Definition and Feedback. The two-way ANOVA revealed significant main effects of group ($F(1,38) = 10.05$, $p < 0.005$) and the type of learning ($F(2,76) = 113.15$, $p < 0.0001$). There was also a two-way interaction ($F(2,76) = 5.71$, $p < 0.005$). The post hoc analysis indicated that, after the verbal definition of GCs, the significant difference between controls and schizophrenia patients was not observable ($p = 0.09$). The verbal definition increased the performance significantly in both the schizophrenia and control groups ($p < 0.0001$) (figure 2; table 2). However, after the feedback learning of GCs, the performance of the schizophrenia subjects was again below that of the controls ($p < 0.0001$). In the schizophrenia group, the feedback learning did not change the categorization performance significantly ($p = 0.99$), whereas it did so in the control group ($p < 0.02$) (table 2).

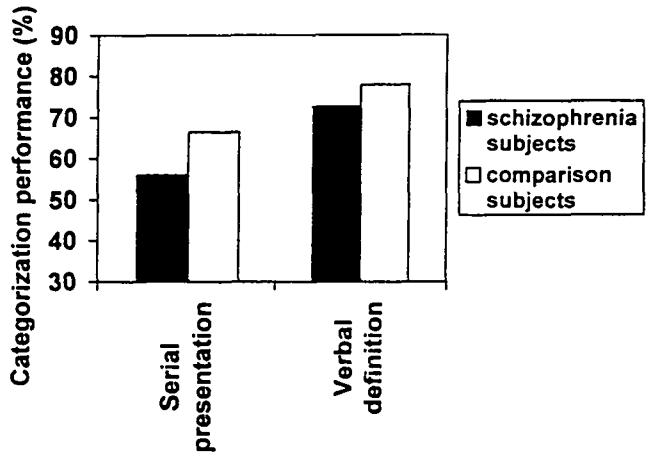
Correlation Between Test Performances and Clinical Data. For comparison of the test performances and PANSS scores, Spearman's correlation coefficients were calculated. A significant negative relationship was found between the categorization performance after the serial presentation of GC exemplars and the scores of the cognitive component assessed with PANSS—conceptual disorganization, disorientation, difficulty of abstract thinking,

Table 2. Categorization performances of the control and schizophrenia subjects after serial presentation, verbal definition, and feedback learning

	Control subjects			Schizophrenia subjects		
	Mean performance (%)	Range	± SD	Mean performance (%)	Range	± SD
Serial DC	80.20	69–96	7.88	81.10	70–95	6.76
Serial GC	66.50	50–85	9.79	56.05	36–72	7.69
Verbal GC	77.90	56–91	9.14	72.55	41–86	10.93
Feedback GC	84.65	56–96	7.88	71.35	35–87	12.66

Note.—SD = standard deviation; DC = discrete categories; GC = graded categories.

Figure 2. Mean categorization performances of the schizophrenia patients (n = 20) and the comparison group (n = 20) after serial presentation of graded category (GC) exemplars and after verbal definition



mannerism, posturing, and poor attention; (mean 17.91, SD ± 8.68; $r = -0.66$, $n = 20$, $p < 0.05$) (Lindenmayer et al. 1995).

Discussion

The present study examined two aspects of category learning in schizophrenia. First, it has been suggested that the perceptual learning of DCs may be intact, while that of the GCs is impaired. However, the main finding of our study is that the verbal definition of GCs may compensate for impaired perceptual learning abilities in schizophrenia.

After the serial presentation of exemplars, the DC performance of schizophrenia patients appeared normal, while their GC performance was impaired. This suggests that schizophrenia patients can learn and store information about simple, well-defined (i.e., DC) visual categories, and are able to compare new information with these internal representations to make successful category judgments in a two-alternative, forced-choice task. This is not the case if the categories are ill-defined (i.e., GC). This finding demonstrates that the nature of the category structure affects category acquisition in schizophrenia. It is also possible that schizophrenia patients could not distinguish the category-relevant information from the category-irrelevant noise (Nuechterlein and Dawson 1984; Sarter 1994). Although category-irrelevant noise was also used in the case of DCs, its characteristic was quite different (see "DC learning by successive presentation of exemplars"). However, it must be emphasized that patients required more presentations of DC exemplars to find the cue. In other words, it was more difficult for them to recognize perceptual commonness, probably because of their limited attentional resources (Braff 1993).

The differential deficit between the DC and the GC performances must be interpreted with caution. First, the DC performance may have appeared intact because the task was easier than in the case of the GCs. However, the attentional demand was higher in the DC task than in the GC task. In the testing phase of category knowledge, the exposure time for the DC exemplars was 28 ms, which is close to the critical stimulus duration measured in former studies (e.g., Braff and Saccuzzo 1985; Saccuzzo et al. 1996) and in our own pilot experiments. This brief presentation induced 80 to 81 percent performances (see table 2), although subjects knew all of the category-relevant cues. Our pilot studies also revealed that the performance displayed only a slight improvement in response to practice in both the schizophrenia and control groups, suggesting that the attentional load of the task was high. Apart from this, future studies should control the question of stimulus complexity in psychometrically matched stimulus sets in order to replicate this differential deficit. In this respect, psychometric matching is quite difficult because of the different kinetics of DC and GC learning. The performance increases rapidly to the maximum for a DC if the key features are found, while in GCs the improvement in the performance is gradual (Homma and Vosburgh 1976).

The second problem is the different reliabilities of the DC and GC tests. It is suggested that schizophrenia

patients are less impaired in tests with lower reliability (Chapman and Chapman 1978). In our case, the DC test was slightly more reliable (alpha coefficient, 0.62) than the GC test (alpha coefficient, 0.59). These psychometric data indicate that the differential deficit may not be due to external chance factors.

The most important result of our study is that, after the verbal definition, the difference between the schizophrenia subjects and the controls diminished. Human verbal and symbolic abilities are usually considered in relation to associative and meaning-based mental operations, although words can also describe structural and physical properties, with the exception of fine perceptual details. We investigated the effect of verbal description of visual appearance and found that schizophrenia patients could compensate for their impaired perceptual category acquisition in this way. Although several studies have provided evidence of verbal impairment in schizophrenia (e.g., see Andreasen 1979; Hoffman et al. 1986; Thomas and Fraser 1994), the present results indicate that patients can successfully use their linguistic aptitude when representing perceptual features of simple nonfigurative shapes.

Finally, using a feedback paradigm, participants learned small physical details of GCs, which are critical in discriminating similar exemplars near the category boundary. In this case, a significant increase in performance was found only in the control group, which shows that patients were not able to modify and refine their perceptual "hypothesis" concerning ill-defined category structures or to discriminate category exemplars with small differences. This finding is consistent with previous reports relating to impaired error-correcting behavior in schizophrenia (Malenka et al. 1982). In summary, the schizophrenia subjects had difficulties in the perceptual learning of simple categories if they are ill-defined (GCs), regardless of the type of learning (serial representation and feedback).

However, the question is still open as to whether the GC impairment is a specific deficit or is the result of the general cognitive decline in schizophrenia. Miller and colleagues (1995) showed that if the difference between the controls and the schizophrenia subjects is greatest under conditions of medium difficulty (the accuracy of performance in a two-alternative test such as categorization is around 75% in this case), then the test result is a psychometric artifact because the true-score variance is maximal in this condition. Table 2 demonstrates that in our case the difference was minimal around this preferred accuracy level and increased for both higher and lower accuracy levels. The data showed a similar pattern when the same paradigm (serial presentation of exemplars) was used throughout the whole training procedure. Thus, it is unlikely that the GC impairment is an artifact. Further studies should confirm these findings.

The categorization impairment found in the GC task correlated with the scores of the cognitive component assessed with PANSS (Lindenmayer et al. 1995). Several studies have reported evidence of different levels of perceptual dysfunction in schizophrenia (Place and Gilmore 1980; Capozzoli and Marsh 1994; Lenzenweger and Korfine 1994; O'Donnell et al. 1996). However, most of the studies attempting to build bridges between neuropsychological and clinical phenomena usually emphasize the disorder of higher-order functions such as semantic memory, executive operations and other complex cognitive functions associated with the temporal and prefrontal cortex (Goldberg et al. 1987, 1990; Liddle 1987; Weinberger 1988; Liddle and Morris 1991; Morrison-Stewart et al. 1992; Shenton et al. 1992; McKay et al. 1996; Morice and Delahunty 1996; Andreasen et al. 1997). In the Wisconsin Card Sorting Test (WCST), which is the most popular test of prefrontal functions, the stimuli have three perceptual dimensions (color, number, shape) and only one of the dimensions is correct for the categorization. During the experiment, the relevant dimension is changed and subjects have to find the new rule (Heaton 1981). The WCST is a more complex test of perceptual categorization than ours; it requires a flexible application of category knowledge. The role of the prefrontal cortex in simple category learning cannot be excluded, although in an earlier study an amnestic patient who had impaired WCST scores successfully learned perceptual categories by serial presentation (Squire and Knowlton 1995). Recent studies suggest that certain types of perceptual category learning and other related memory paradigms, which are independent of the medio-temporal structures, are mediated by neocortico-striatal circuits (Squire and Knowlton 1996; Knowlton et al. 1996; Ashby et al. 1998). This hypothesis is fairly important for schizophrenia research, suggesting a nonfrontal-nontemporal component of basic abstractional and classificational disabilities.

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Eredeti közlemények

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A SZENZOROS GÁTLÁSI FOLYAMATOK ZAVARA SZKIZOFRÉNIÁBAN II.:* KAPCSOLAT FIGYELMI FUNKCIÓK ELTÉRÉSEIVEL**

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Összefoglalás

Vizsgálataink célja a magnocelluláris pálya hiperaktivitásának és a magasabb szintű figyelmi mechanizmusok összefüggéseinek vizsgálata volt szkizofréniában. A magnocelluláris pálya működését a vizuális kontraszt-érzékenység, a figyelmi funkciókat a kritikus stimulus időtartam és a vonás-detekcióhoz szükséges minimális ismétlésszám mérésével határoztuk meg. A kontraszt-érzékenység és a figyelmet jellemző paraméterek közötti korrelációt vizsgáltuk. Eredményeink szerint a magnocelluláris pálya hiperfunkciója mellett károsodott figyelmi paraméterek voltak tapasztalhatók a szkizofrén csoportban, azonban ezek között korreláció nem találtunk. Ez arra utal, hogy a szenzoros gátlási folyamatok függetlenek a figyelmi mechanizmusok károsodásától szkizofréniában.

Kulcsszavak: szkizofrénia – figyelem – magnocelluláris pálya – szenzoros gátlás

Summary

This study was designed to investigate the relationship between the hyperactivity of magnocellular visual pathways and the attention deficit in schizophrenia. Magnocellular functions were evaluated with visual contrast sensitivity measurements, while attentional functions were assessed by measurements of the critical stimulus duration and the minimal number of stimulus presentation for feature extraction. The correlation between contrast sensitivity and the attentional parameters was also determined. Our results revealed the hyperactivity of magnocellular pathways and the impairment of attentional functions, but correlation was not found between them. This suggests that sensory inhibition deficit is independent of the attentional control dysfunctions in schizophrenia.

Key words: schizophrenia – attention – magnocellular pathway – sensory inhibition

Bevezetés

Számos tanulmány a korai szenzoros folyamatok gátlásának zavarát igazolta szkizofréniában [1]. A jelenség mechanizmusára vonatkozóan két hipotézis létezik. Az első a szenzoros információ-feldolgozás automatikus fázisának zavarát tételezi fel, míg a második a magasabb szintű kérgi területek „feedback" kapcsolatainak eltéréseiben keresi a jelenség alapjait. Ebben a vonatkozásban a szelektív figyelem kiemelkedő jelentőségű [2-4]. Lényege, hogy egy stimulus esetén annak nem minden elemét észleljük egyforma súllyal, hanem valamely releváns részletre összpontosítunk. A figyelmi szabályozás során a felsőbb kérgi központok hatására (prefrontális kortex és anterior cingulatum) a megfelelő szenzoros területek aktivitása fokozódik, míg az irreleváns területek gátlás alá kerülnek [5].

A vizuális információ feldolgozása két párhuzamos pályához köthető. A ventrális rendszer, amely az occipitális kéregtől az infero-temporális kéreg felé vetülő pályákat jelenti, felelős a forma és a szín észleléséért, míg a dorzális rendszer (occipito-parietális rész) végzi a mozgás és a térbeli helyzet analízisét. A dorzális rendszer afferentációja többségében (de nem kizárólagosan) a magnocelluláris, a ventrális rendszeré a parvocelluláris pályából származik [6-8]. A párhuzamos vizuális pályák szkizofréniában tapasztalt eltéréseit két pontban vázolhatjuk fel:

* Az első rész megjelent: PH 1998, 6. szám

** A munka az OTKA T025160 sz. pályázatának támogatásával készült el.

(I) amennyiben az adott feladatban jelentős figyelmi- és memóriakomponens van jelen, mindkét pálya funkciózavara megállapítható [9-11];

(II) amennyiben a feladat figyelmi- és memóriakomponense kevésbé kifejezett, a magnocelluláris (M)/dorzális rendszer szelektív zavara tapasztalható [12-14].

Ez nagy valószínűséggel annak fokozott reaktivitásaként valósul meg [15-17]. Az egyik legfontosabb idevágó kérdés a figyelmi funkciókkal való kapcsolatra vonatkozik. Vizsgálatainknak e kérdés megközelítése volt a célja. Az M pálya tesztelését a közlemény első részében leírtaknak megfelelően vizuális kontraszt-érzékenység (KÉ) mérésével végeztük [17]. A figyelmi funkciókat a kritikus stimulus időtartammal (KSI) és a vonás-detekcióhoz szükséges minimális ismétlésszámmal (VDI) írtuk le [18,19]. Amennyiben a KÉ és a figyelmi funkciók között korreláció van, feltételezhető, hogy a vizuális eltérések a magasabb szintű figyelmi kontroll zavarának következményei, míg ellenkező esetben a vizuális információ-feldolgozás alacsonyabb szintjének saját zavarát tételezhetjük fel.

Módszerek

Vizsgálati személyek

A vizsgálatban résztvevő tizenkét szkizofrén beteg és tizenkét kontroll személy klinikai és demográfiai adatainak leírása a közlemény első részében található [17].

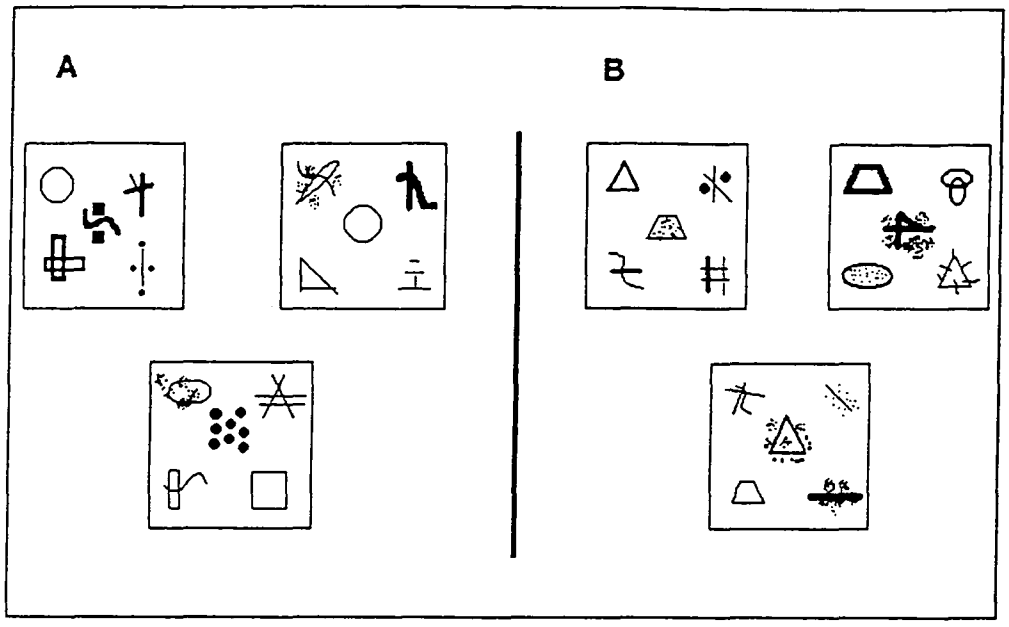
A vizuális kontraszt-érzékenység (KÉ)

A KÉ vizsgálat az eltérő luminancia-viszonyokon alapuló észlelés jelenségével áll kapcsolatban. A számítógép képernyőjén sötét vízszintes csíkok jelentek meg világos háttér előtt. A kontraszt csökkentésével a csíkok fokozatosan halványabbak lettek. A minimális észlelhető kontrasztot kontraszt-küszöbnek nevezzük, ennek reciproka a KÉ. A méréseket kis térbeli frekvenciájú („vastag") és nagy térbeli frekvenciájú („vékony") csíkok esetében is elvégeztük. Az előbbiekre az M, az utóbbiakra a P pálya mutat kifejezettebb érzékenységet (a részletes leírást lásd [17]).

Figyelmi funkciók vizsgálata

Kritikus stimulus időtartam (KSI). A KSI az a legrövidebb bemutatási idő, amely az adott kép észleléséhez szükséges. A stimulusok öt részből álló geometriai formák voltak. A méret 6.8°x6.8° volt (1. ábra). Az alanyok 1 méter távolságból látták a monitort, amely egy Pentium P54 CX személyi számítógéphez volt kapcsolva. Az öt elemből egy mindig kör vagy négyzet volt (kulcselem). Az alanyok feladata annak eldöntése volt, hogy az aktuálisan bemutatott képen melyik kulcselem volt látható. A választ a számítógép megfelelő billentyűinek lenyomásával kellett megadni. A kezdeti expozíciós idő 500 msec volt. Ez 14 msec-mal került emelésre/csökkentésre helytelen/helyes válasz esetén. A KSI az a minimális expozíciós idő, amelyen az alanyok nyolc alkalommal konzekvensen képesek a kulcselemet azonosítani [18].

A vonás-detekcióhoz szükséges minimális ismétlésszám (VDI). A VDI méréséhez hasonló stimulusokat alkalmaztunk, mint a KSI esetében. Minden kép tartalmazott két kulcselemet



1. ábra: Az ábra a kritikus stimulus időtartam (KSI) (A) és a vonás-detekcióhoz szükséges minimális ismétlésszám (VDI) (B) méréséhez használt képeket mutatja. A KSI esetén minden kép egy kört vagy egy négyzetet tartalmazott. A VDI esetében egy háromszög és egy trapéz minden stimulusban megjelent.

(trapéz és háromszög) (1. ábra). A résztvevők a feladat elején nem tudták, hogy melyek ezek. A stimulusokat egymást követően mutattuk be a KSI 20-szorosával. A résztvevőknek szóban kellett jelezniük, ha a közös kulcselemeket megtalálták. Az ehhez minimálisan szükséges képek száma a VDI [18, 19].

Eredmények

Vizuális kontraszt érzékenység

Amint az a tanulmány első részében leírásra került, a szkizofrén csoport szignifikánsan emelkedett KÉ-t mutatott a legalacsonyabb térbeli frekvencia esetén (1.19 cpf) [17].

Figyelmi funkciók

Az egyutas variancia-analízis (ANOVA) szignifikánsan emelkedett KSI-t mutatott a szkizofrén csoportban ($F(1,22)=7.76$, $p<0.02$). A kontrollok esetében a KSI átlaga 22.95 (SD=9.22) ms, míg a szkizofrén csoportban 35.01 (SD=12.02) ms volt. Ezek szerint a betegeknek hosszabb bemutatási időre volt szükségük a kulcselemek észleléséhez. Ehhez hasonlóan a VDI is magasabb volt a betegcsoportban (szkizofrén átlag: 20.82 (SD=5.38), kontroll átlag: 8.84 (SD=3.39), ANOVA: $F(1,22)=43.97$, $p<0.0001$), vagyis a közös elemek felismeréséhez több ismétlésre volt szükség.

A KSI és a VDI értékek, valamint a legalacsonyabb térbeli frekvencián mért KÉ között számított korrelációs koefficiensek nem mutattak szignifikáns összefüggést ($r<0.3$). Amennyiben a KÉ értékeket vizsgáló ANOVA-ban a KSI, illetve a VDI értékek kovariánsként szerepeltek (kovariancia-analízis, ANCOVA), hasonló eredményekhez jutottunk.

Megbeszélés

Eredményeink két fontos jelenséget világítottak meg: (I) szkizofrén személyek esetében a figyelmi funkciók károsodottak. A betegeknek hosszabb időre van szükségük egy kép észleléséhez, valamint több ismétlés kell a képek közös vonásainak felismeréséhez. (II) Az M pálya hiperaktivitása nem függ a figyelem-deficittől, vagyis a szenzoros folyamatok alacsonyabb szintű zavarát tükrözi. Ez utóbbi következtetés azonban óvatosan kezelendő. A VDI esetén a figyelmet formákra kellett összpontosítani, nem pedig a térbeli lokalizációra vagy mozgásra. Az emelkedett KÉ ugyanakkor az M pálya zavarára utal, amely elsősorban az utóbbi információ-feldolgozási folyamatokra specializálódott [6-8], vagyis a kis térbeli frekvencián mért KÉ, és az alkalmazott figyelmi feladat nem ugyanarra a vizuális almodalitásra vonatkozott. Megjegyzendő azonban, hogy a kulcselemek helyzete véletlenszerűen változott a stimuluson belül, vagyis a detekcióhoz az elhelyezkedés észlelésére is szükség volt.

Számos tanulmány vizsgálta a vizuális rendszer figyelmi modulációját [2-4]. A prefrontális kortex és az anterior cingulatum az aktuális kognitív folyamatoknak megfelelően képes a V2-V5 vizuális kérgi területek, valamint a V5 és a poszterior parietális „area" közötti kapcsolatot szabályozni [20]. Valószínű, hogy a V1 (primer vizuális „area") már nem áll intenzív „feedback" szabályozás alatt. Elképzelhető, hogy az igen alacsony szintű kontraszt-észlelés e terület funkciói közé tartozik, bár egyes tanulmányok a magasabb szintű, specializált „areák" szerepét hangsúlyozzák [21].

Bár a prefrontális kortex sajátosságait széles körben tanulmányozták szkizofréniában [10], a poszterior kéreg szabályozásban betöltött szerepe kevésbé ismert. A fronto-temporális kapcsolatok tekintetében hipofrontalitáshoz kapcsolódó bal temporális hiperaktivitást írtak le [22]. Közvetlenül a szenzoros kéreg szabályozásának vonatkozásában az Andreasen-csoport rendelkezik előzetes eredményekkel [23]. A résztvevők fejhallgatón keresztül lejátszott hangingerekre összpontosítottak, miközben a párhuzamosan bemutatott vizuális ingereket figyelmen kívül kellett hagyniuk. A feladat közben pozitron emissziós tomográffal (PET) mérték a regionális agyi vérátáramlást. A kontroll személyekhez viszonyítva a szkizofrén betegek csökkent perfúziót mutattak a prefrontális, jobb parietális és az auditoros kortex területén. Ezzel ellentétben az occipitális kéregnél hiperperfúziót észleltek. Ezek az eredmények a figyelem kettős zavarát bizonyítják. Egyrészt a betegek esetében a releváns szenzoros kéreg aktivitása nem fokozódott, másrészt az irreleváns „areák" nem kerültek megfelelő gátlás alá. Egy másik vizsgálatban egy kereszt alakú stimulusra kellett fixálni [24]. Szkizofrén személyeknél a prefrontális hipoaktivitást abnormálisan emelkedett vérátáramlás kísérte a kétoldali gyrus fusiformis és a bal hippocampus területén. A betegcsoportban tehát olyan vizuális és memória-folyamatokkal kapcsolatos kérgi területek aktivációját figyelték meg, amelyek az egyszerű feladathoz egyáltalán nem szükségesek.

Összefoglalva, a szkizofréniában a figyelmi funkciók számos aspektusa károsodott. Funk-

cionális képalkotó eljárásokkal az anterior kortex hipofunkciója és a poszterior területek abnormális mintázatot mutató aktivációja figyelhető meg. További vizsgálatok szükségesek annak tisztázására, hogy a szenzoros kapuzás zavarai miként függnek a magasabb szintű figyelmi funkciók eltéréseitől.

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SCHIZOPHRENICS KNOW MORE THAN THEY CAN TELL

Probabilistic classification learning in schizophrenia

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ABSTRACT

Background. Previous studies have demonstrated impaired explicit and preserved implicit memory functions in schizophrenia. However, it is less known whether schizophrenics can learn complex information (e.g. probabilistic stimulus-response associations) with or without access for conscious recollection. In this study we applied a classification learning task to assess explicit and implicit processes concurrently.

Methods. Two test procedures were administered to 40 schizophrenic subjects and 20 healthy volunteers: (1) A probabilistic classification learning (PCL) task to evaluate implicit memory functions, (2) category cue recognition to investigate the explicit memory system. The PCL task included feedback guided category learning of geometrical shapes. These shapes were called category cues, predicting class membership with certain probabilities. The gradual increase of categorisation performance during the feedback learning is a potentially implicit process, whereas the subsequent recognition of category cues requires explicit memory functions.

Results. The schizophrenic patients improved their categorisation performance to a similar extent as the controls did, but they failed to recognise the category cues. Memory performances were independent of the positive and negative symptoms.

Conclusions. Patients with schizophrenia were able to establish representations of complex categories, but they remained unconscious. This is consistent with earlier reports, suggesting damaged explicit and spared implicit memory in schizophrenia.

INTRODUCTION

Several lines of research provided evidence that memory is not a unitary cognitive function. The most widespread distinction is made between explicit and implicit memory (Squire & Zola-Morgan, 1996; Gabrieli, 1998). Explicit (overt) memory refers to conscious recollection of facts and events, whereas the contents of implicit (covert) memory are inaccessible for conscious information processing. Most of the studies, investigating memory processes in schizophrenia, have demonstrated impaired explicit and preserved implicit functions such as repetition priming and procedural skill learning (McKenna *et al.* 1990; Tamlyn *et al.* 1992; Clare *et al.* 1993; Goldberg *et al.* 1993; Gras-Vincedon *et al.* 1994; Dominey & Georgieff, 1997; Brébion et al. 1997). In a typical repetition priming experiment, subjects are given a list of words. Explicit memory can be tested by asking the subject to recall the words, whereas implicit memory can be assessed, for example, with a word-stem or a word-fragment completion task. It has been demonstrated that schizophrenics fail to recall the words, but show intact priming effect in completion tasks. Skill learning, including various "tower-type" tests, mirror drawing and pursuit rotor tasks, is also relatively spared in schizophrenia. However, these tests are different from the priming procedure. Skill learning is dependent upon basal ganglia structures, while perceptual repetition priming is believed to be mediated by the sensory neocortex (Gabrieli, 1998). As the aforementioned examples demonstrated, there is a dissociation between explicit and implicit knowledge of word lists in schizophrenia. However, it is less known whether information, acquired during skill learning, is available for conscious recollection in this disorder. An additional issue is that a few studies have challenged the theory of selective explicit memory deficit in schizophrenia (Heinrichs & Bury, 1991; Schroder *et al.* 1996). In this respect, an increasing amount of information is available on the dysfunction of basal ganglia, often related to skill learning and to the control of central cognitive pattern generators (Robbins, 1990; Graybiel, 1997).

This study targeted three issues. First, we intended to replicate the results of previous studies, reporting intact cognitive skill learning in schizophrenic subjects (for review, see Elliott & Sahakian, 1995). Second, we investigated whether patients can

gain conscious access into the information acquired during skill learning. Finally, we examined the relationship between memory performance and the clinical-demographical characteristics. To answer these questions, probabilistic classification learning (PCL) and cue recognition tasks were applied, which assess the formation of visual stimulus-response associations and their conscious representations (Knowlton *et al.* 1994; Knowlton *et al.* 1996; Reber *et al.* 1996). This task, representing a type of rule learning, is not an obvious memory test. However, together with other somewhat similar procedures (e.g. artificial grammar learning, category learning and prototype abstraction), PCL has been extensively used in different patients populations to examine the nature of parallel memory systems (Squire & Zola-Morgan, 1996). Therefore, PCL appeared a suitable tool to gain more insight into the characteristics of this problem area in schizophrenia.

METHODS

Subjects

The patient group comprised 40 schizophrenic patients (29 male, 11 female) who were recruited from the Department of Psychiatry, Albert Szent-Györgyi Medical University, Szeged and the Psychiatry Centre, Bács-Kiskun Country Hospital, Kecskemét. The diagnosis was based on the DSM-IV criteria (American Psychiatric Association, 1994). None of the patients had a history of drug abuse, head trauma, or any neurological disorder. The 20 comparison subjects (15 male, 5 female) were university employees or their relatives. Control subjects were excluded if they had a history of psychiatric or neurological disorder. Participants were evaluated with the Scale for the Assessment of Positive Symptoms (SAPS) (Andreasen, 1983a), the Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1983b), the Mini-Mental Status Examination (MMSE) (Folstein *et al.* 1975), and the Global Assessment of Functioning Scale (GAF) of DSM-IV. A low score in the MMSE (<25) was a general exclusion criterion (Table 1).

Probabilistic classification learning (PCL)

To assess implicit memory functions, the PCL paradigm was used. In the weather prediction task, which was a pen-and-paper version of the original test (Knowlton *et al.* 1994; Knowlton *et al.* 1996; Reber *et al.* 1996), subjects were requested to decide whether a pattern of cues predicted rain (category 1) or sunshine (category 2). Four cues were used (A, B, C, and D), each comprising simple geometrical forms. Each cue was associated with a particular weather outcome with a certain probability. For instance, cue A predicted sunshine with a high probability and rain with a low probability, whereas cue D had the inverse meaning. In a trial, the experimenter presented 1, 2, or 3 cues (Table 2). The cues were presented on separate cards and their left-to-right sequence was randomised in each trial. Subjects were asked to respond by deciding whether the cue(s) indicated rain or sunshine. After each trial, the experimenter provided a verbal feedback. If no response was made within 5 s, subjects were asked again to predict the weather outcome. All participants were able to make decisions in this forced-choice paradigm. Altogether 50 trials were included (5 blocks of 10 trials). Performance was defined as the percentage of correct responses, that is, selection of the weather outcome that was most probably associated with the presented cue(s). Cue patterns associated with rain and sunshine with equal probabilities were excluded from the data analysis (Table 2).

Explicit knowledge of category cues

The explicit knowledge relating to cue probability was evaluated after the 50 trials had been completed. In this phase, all cues were presented together in a randomised sequence. Subjects were asked 2 questions: "What if you knew it was going to be rainy (sunny) and one card was showing? Which card would be most likely to be showing?" Such questions were repeated, the subjects being asked which 2 and then which 3 cues were most probably visible. The sequence of questions about a rainy or a sunny outcome was counterbalanced across participants. Performance was graded on a 1-to-4 scoring system. In the single-cue selection task, a score of 1 was given if the subject was able to select the most probable cue (e.g. cue A for sunny weather), a score

of 4 was given for the selection of the least probable cue (e.g. cue D for sunny weather), and scores of 2 and 3 for the intermediate cues (cues B and C for sunny weather, respectively). In the two-cue selection task, the selected cards were scored separately (e.g. for cues A and D the scores of 1 and 4 were assigned, respectively), and the sum of the scores was calculated. The sum of the scores was then recalculated from the obtained 3-to-7 range to a 1-to-4 range ([0.75 x sum] - 1.25). In the three-cue selection task, a score of 1 was assigned to the best pattern (e.g. ABC for sunny weather), 2 and 3 for the intermediates (ABD and ACD for the sunny weather, respectively), and 4 for the worst alternative (e.g. BCD for sunny weather) (Table 2). In these tests, lower scores were associated with better explicit memory function (for methodological details, see Knowlton *et al.* 1994; Knowlton *et al.* 1996; Reber *et al.* 1996).

RESULTS

Probabilistic classification learning

A 2 (groups) x 5 (trial blocks) analysis of variance (ANOVA) conducted on the classification performance revealed a significant main effect of trial blocks ($F(4,232)=10.96$, $p<0.0001$) (analysis of linear trend: $F(1,58)=36.39$, $p<0.0001$). The effect of group and the group by block interaction remained non-significant ($p=0.22$ and $p=0.49$, respectively). Newman-Keuls tests confirmed the ANOVA results, demonstrating no significant difference between the schizophrenic patients and the control subjects for any blocks ($p>0.2$) (Figure 1).

The effect of training was additionally investigated by comparison of the performances in the first and last (fifth) blocks. This within-group analysis, together with the main effect of trial blocks in the two-way ANOVA, indicated significant training effects in the control group ($p<0.0001$) and in the schizophrenic group ($p<0.005$) (Figure 1).

Explicit knowledge of category cues

A 2 (groups) x 3 (number of cues presented) ANOVA performed on the cue selection scores demonstrated a main effect of group ($F(1,58)=13.25$, $p<0.001$). The effect of cue and the group by cue interaction did not reach the level of statistical significance ($p=0.10$ and $p=0.23$, respectively). Newman-Keuls tests yielded that the schizophrenic patients had significantly higher scores (i.e. lower recall performances) when 2 and 3 cues had to be selected ($p<0.005$ and $p<0.0005$, respectively) (Figure 2).

Effects of clinical and demographical parameters on test performances

In the above-described ANOVAs, age, duration of illness, SAPS/SANS scores, and the chlorpromazine-equivalent neuroleptic dose were included as covariates. These separate analyses revealed negative results, suggesting that PCL and cue recognition performances were independent of the clinical and demographical parameters tested. In addition, Pearson's correlation coefficients were calculated between the test results (including PCL performance in each block and the recognition scores for 1, 2, and 3 cues) and the aforementioned clinical and demographical parameters. These analyses indicated no significant correlations ($r<0.2$). Separate ANOVAs were also conducted to compare the performances of female and male patients. These ANOVAs demonstrated no significant differences ($p>0.6$).

DISCUSSION

Results revealed that the schizophrenic patients were able to improve their performance in the PCL task as indicated by the percentage of correct category decisions, while they showed a severe impairment in the recognition of category cues. This was unrelated to the clinical and demographical characteristics. Since IQ was not assessed in this study, one can suppose that the failure of schizophrenic patients in the explicit recognition test was due to their general intellectual disabilities. However, three facts are against this possibility. Firstly, MMSE scores did not reveal clinically significant dementia. Secondly, the patients were able to improve their categorisation performance, which placed a heavy burden on several cognitive functions (e.g.

understanding test instructions, focusing and maintaining attention, and decision-making). Third, the level of social functioning, as indexed by the GAF scores (Table 1), was relatively high in this schizophrenic population. These suggest sufficient general intellectual abilities.

In the implicit condition (PCL), the learning effect can be observed as a potentially covert increase of performance, while in the explicit condition (cue selection) participants are requested to report their knowledge overtly. In the schizophrenic group, there was a dissociation between these functions: the successfully established category knowledge remained unconscious. Interestingly, the schizophrenic patients showed impairments only for 2 and 3 cues in the selection task. This may suggest a failure to store associations of stimuli rather than a single item. In the case of more generalised dysfunction, conscious representation of a single cue without extended associations may also be disrupted. Altogether, these results confirm the findings of earlier studies, using a wild variety of tests for the evaluation of memory functions (McKenna *et al.* 1990; Tamlyn *et al.* 1992; Clare *et al.* 1993; Goldberg *et al.* 1993; Duffy & O'Carroll, 1994; Gras-Vincedon *et al.* 1994; Saykin *et al.* 1991; Dominey & Georgieff, 1997; Brébion *et al.* 1997; Rushe *et al.* 1999). It is notable that in classification procedures with greater attentional load (in the presence of distracting features), schizophrenic patients benefit well from the explicit verbal description of the categorisation rules (Kéri *et al.* 1998; Kéri *et al.* 1999). This suggests that, in spite of their inability to establish conscious representations, schizophrenics can use explicit information to improve their performance.

The schizophrenic patients in this study displayed an amnesic-like deficit as a mirror image situation for the basal ganglia disorders. This is consistent with recent data from letter sequence learning procedures, demonstrating disturbed explicit learning of an abstract structure and spared implicit learning of surface characteristics in schizophrenia (Dominey & Georgieff, 1997). This pattern of performance is exactly the inverse that seen in Parkinson's disease (Dominey & Jeannerod, 1997). Moreover, schizophrenic patients show preserved learning rate in several other skill learning procedures that are damaged in basal ganglia diseases (Clare *et al.* 1993; Gras-Vincedon

et al. 1996). It is important to emphasise, however, that the global neuropsychological profile of schizophrenia is not equivalent to that of the amnesic or even prefrontal patients, sharing many features with basal ganglia disorders (Pantelis *et al.* 1997).

It must be noted that PCL is somewhat different from conventional memory tests. Stimulus-response associations, which are striatally mediated (caudate nucleus and putamen), can gain consciousness if the explicit memory system is working. In other words, normal controls might solve this problem using conscious representations, although the probabilistic structure of the task may defeat them to intentionally memorise specific stimuli and associated responses. Subjects with explicit memory impairments can also perform correctly in the PCL task using implicit striatally mediated habits. However, experimental data partially contradicts these assumptions. Previous reports have demonstrated a double dissociation between the PCL performance and the explicit knowledge of category cues. Amnesic patients with temporo-hippocampal and diencephalic lesions performed similarly to the schizophrenic patients: they were able to increase their performance in the implicit PCL task, but failed to establish an explicit knowledge of category cues (Knowlton *et al.* 1994; Reber *et al.* 1996). As the other aspect of double dissociation, Parkinson's disease patients with a neostriatal dysfunction exhibited impaired PCL and spared explicit memory functions (Knowlton *et al.* 1996). Thus, in some cases spared explicit memory can not fully compensate striatal deficits in PCL tasks.

A number studies have examined probabilistic reasoning in schizophrenic patients, using different experimental procedures. Although it was initially hypothesised that abnormal reasoning and decision biases are specifically related to delusion formation, subsequent studies failed to demonstrate evidence for these assumptions (Garety *et al.* 1991; Young & Bentall 1997; Simpson *et al.* 1998). Unfortunately, the heterogeneity and complexity of these tasks rarely allow us to draw inferences about the underlying neuronal mechanisms. A recent exceptional investigation used a gambling task to assess probabilistic stimulus-reward associations. The schizophrenic patients in that study, similarly to the normal control participants, selected from groups of stimulus cards in which there were frequent rewards and infrequent penalties (Wilder *et al.*

1998). This pattern of performance is the reverse to that of the subjects with ventromedial prefrontal lesions (Bechara *et al.* 1994). These data are consistent with our present results, demonstrating intact probabilistic stimulus-response habit learning in schizophrenia.

Recent development in cognitive neuropsychology, functional imaging and animal models provides us an opportunity to speculate about the neuronal correlates of schizophrenic cognitive dysfunctions. It has been shown that different fronto-striatal functions are anatomically dissociable. Data from animal studies revealed that lateral prefrontal lesions led to the impairment of shift learning (i.e. shifting cognitive sets), whereas reversal learning (i.e. forming cognitive sets) remained spared. Lesion to the ventral prefrontal areas resulted in the opposite pattern of functional disturbances (Dias *et al.* 1996). Anatomically, the lateral prefrontal cortex is connected with dorsal neostriatal regions, while the ventral prefrontal cortex projects to ventral portions of the neostriatum (for a review and conceptualisation, see Lawrence *et al.* 1998). In PCL, subjects need to update the actual representations of stimulus-reward associations according to new experiences in order to establish appropriate stimulus-response habits. According to an interesting theoretical approach, stimulus-response habit learning can be viewed as a form of reversal learning mediated by ventral fronto-striatal pathways (Lawrence *et al.* 1998). Therefore, our results, together with findings from earlier studies using the attentional set-shifting test of the CANTAB (Cambridge Automated Neuropsychological Test Battery) and the gambling paradigm, suggest that the ventral fronto-striatal system is relatively spared in some schizophrenic patients (Elliott *et al.* 1995, 1998; Wilder *et al.* 1998).

On the other hand, a significant amount of neuropsychological and functional imaging data suggests a characteristic impairment of the dorsal fronto-striatal circuits. The well-known dorsolateral prefrontal deficit of schizophrenic patients has been demonstrated in the form of impaired Wisconsin Card Sorting Task (WCST) performance (perseverative extradimensional shifting deficit in the CANTAB) accompanied by disturbed brain activation (Weinberger *et al.* 1994; Elliott & Sahakian, 1995; Goldman-Rakic & Selemon, 1997). In accordance with these considerations, a

PET (positron-emission tomography) study found a prominent dysfunction in the dorsal and lateral neostriatum of schizophrenic patients performing a serial verbal learning test (Shihabuddin *et al.* 1998). Interestingly, prefrontal patients with poor WCST performances displayed normal PCL effect, similarly to the schizophrenic patients tested in the present study (Knowlton *et al.* 1996). Although cognitive set-shifting in the WCST and related paradigms is traditionally interpreted as a function of dorsolateral prefrontal areas, recent event-related fMRI (functional magnetic resonance imaging) studies demonstrated transient activation in the posterior part of the inferior frontal sulci during the inhibition of habituated responses, which is as an important condition for strategy shifting (Konishi *et al.* 1998; Konishi *et al.* 1999). Therefore, further studies are necessary to understand the exact role of fronto-striatal systems in forming and shifting cognitive strategies and their significance in neuropsychiatric diseases.

A few authors reported deficient procedural learning in negative and delusional schizophrenic subsyndromes, suggesting a marked heterogeneity and syndrome specificity (Schroder *et al.* 1996). It is possible that in these patients more profound striatal impairments can be found. However, in this study there was no significant correlation regarding the positive and negative syndromes and the test performances. Nevertheless, further studies are warranted to investigate the functioning of parallel memory systems in distinct schizophrenic subsyndromes. In conclusion, we found a dissociation between the implicit learning and explicit knowledge of probabilistic category structures. Patients with schizophrenia established representations of categories without awareness: they knew more than they could tell.

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Table 1. *Clinical and demographical characteristics of the participants*

	Schizophrenics (N=40)	**Controls (N=20)**
Age (years)	33.9 (9.6)	35.6 (10.4)
Education (years)	12.2 (3.1)	12.6 (6.9)
MMSE	27.8 (1.9)	28.7 (1.4)
Duration of illness (years)	6.5 (4.2)	-
SAPS	11.1 (5.5)	-
SANS	12.6 (5.4)	-
GAF	64.9 (8.3)	-
Mean atipsychotic dose	251.3 (249.9)	-

The Table depicts mean values (SD). The schizophrenic and control groups were matched for age, duration of education, and the MMSE (t-test, $p>0.2$). The dose of antipsychotics (mg/day) is given in terms of chlorpromazine-equivalents.

Table 2. *Probabilistic structure of category cue(s)*

Cue(s) representing test stimuli	Frequency	Sunshine	Rain	$P_{sunshine}$
AB	4	4	0	1.00
ABC	1	1	0	1.00
A	7	6	1	0.86
AC	4	3	1	0.75
B	5	3	2	0.60
AD	2	1	1	0.50
BC	2	1	1	0.50
ACD	2	1	1	0.50
ABD	2	1	1	0.50
C	5	2	3	0.40
BD	4	1	3	0.25
D	7	1	6	0.14
BCD	1	0	1	0.00
CD	4	0	4	0.00
Total	50	25	25	

A, B, C, and D symbolise different geometrical forms. Frequency refers to how many times a certain stimulus occurred during the test. Sunshine and Rain refer to how many times a stimulus indicated sunshine/rain during the test. $P_{sunshine}$ is the probability that the weather outcome was sunny for a particular stimulus ($P_{rain} = 1 - P_{sunshine}$). As an example, stimulus AC (row 4) consisted of 2 cues (2 geometrical forms) and was presented 4 times during the test (3 times sunshine, 1 time rain). Thus, AC predicted sunshine with 75% probability.

FIGURE LEGENDS

Figure 1. Mean classification performances as a function of trial blocks for the normal controls and the schizophrenic patients. Error bars indicate standard deviations.

Figure 2. Selection of category cues for the normal controls and the schizophrenic patients. A higher score represents a lower performance. The chance level is 2.5 for each task. The performances of schizophrenic patients for 2 and 3 cues did not differ from the chance level ($p>0.1$, t-test). Error bars indicate standard deviations.