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Memory impairment and auditory evoked potential gating deficit in schizophrenia

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Abstract

Impaired sensory gating and memory function were reported in a study of 10 schizophrenic patients and 10 age- and sex-matched normal subjects. The P50 component of the auditory evoked potential was used as an index of gating. Explicit memory was tested with the Wechsler Memory Scale and implicit memory by artificial grammar learning. The schizophrenic patients showed deficits in both verbal paired associate and visual reproduction tasks. They demonstrated impaired implicit learning in color patterns but not letter strings. They also showed impaired P50 sensory gating. Three-dimensional brain mapping revealed a differential distribution of brain potentials in the processing of S1 and S2 at either P50 or N100 in both groups. However, the group difference was not statistically confirmed. In the controls, both implicit letter-string learning and explicit verbal paired associates were positively correlated with N100 gating, suggesting an association of the early attentive component with lexicons. In the schizophrenic patients, color-pattern implicit learning was positively correlated with P50 gating. The modality-specific impairment of implicit learning in schizophrenia may reflect a failure of adaptive filtering on the flooding input from color patterns.

Keywords: Implicit learning; Schizophrenia; Artificial grammar; Sensory gating; Auditory evoked potentials; P50

1. Introduction

Memory deficits in patients with schizophrenia have been extensively studied (Danion et al., 1992). Research findings indicate impairments in tests of episodic memory (McKenna et al., 1990), explicit memory such as free recall and frequency monitoring (Gras-Vincendon et al., 1994), and semantic memory such as sentence verification, category judgment, and vocabulary (Clare et al., 1993). Explicit memory is assessed with recall and recognition tests in which the subject makes explicit reference to the context of a specific learning episode. In contrast, implicit memory is expressed by the extent to which previous experi-

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ences or learning episodes facilitate performance on a task at hand without conscious or intentional recollection of those experiences or the context of the learning process (Schacter, 1987). Although there are still controversies about the implicit memory deficits in schizophrenia, many studies have revealed relatively well-preserved functions in the performance of tasks such as repetition priming with stem-completion (Gras-Vincendon et al., 1994), pursuit rotor, jigsaw learning (Clare et al., 1993), and associative memory (Bazin and Perruchet, 1996). Even when schizophrenic patients reveal difficulty in some implicit tasks, it may be due to non-memory psychological influences (Gras-Vincendon et al., 1994).

However, disruption of implicit sensory processing in schizophrenic patients has been evidenced in many latent inhibition studies (Brauch et al., 1988; Guterman et al., 1996; Swerdlow et al., 1996). Inhibition can be described as adaptive learning that filters out irrelevant stimuli. In additional to the aforementioned tasks, implicit learning can also be implemented through artificial grammar acquisition. Artificial grammar learning is an implicit process, detecting the regularities in a series of stimuli generated by a finite-state-rule system. Artificial grammar acquisition is used to detect the regularities in a series of letter strings generated by a finite-state rule system (Reber, 1967, 1977) and to judge whether a new letter string adheres to the rules at a level above chance. During this process, the examinees are not able to report explicit knowledge about their judgments. In this study, we applied an implicit learning paradigm, which follows Reber's artificial grammar rules, to investigate the ability of schizophrenic patients to do implicit sensory processing with two different modes of stimuli, namely letter strings (Fig. 1a) and color patterns (Fig. 1b).

Patients with schizophrenia have an impaired ability for sensory gating that may result in the flooding of information. The sensory gating defect has been demonstrated using the decrement ratio of the P50 component of the auditory evoked potential (AEP) in a conditioning-testing paired paradigm (Boutros et al., 1991; Judd et al., 1992; Clementz et al., 1997, 1998). However, the contribution of the N100 component to sensory gating is controversial. The controversy regarding the N100 component mainly concerns its gating effect. Unlike the P50, which is relatively impervious to the manipulation of attention during the test, the S2 of N100 reflects attentional control. The attenuation of N100 to S2 may be influenced by attentional manipulations (Guterman et al., 1992). Furthermore, the gating effect of N100 suffers from significant test–retest variability (Adler et al., 1982; Freedman et al., 1983).

The P50 sensory gating reflects mainly preattentive processing (Jeger et al., 1992) whereas N100 indicates an early-attentive component. Since memory function is a multi-stage operation, we have attempted to examine both the preattentive P50 and early-attention N100 components through AEP gating.

In this study, we examine the association between memory function and sensory gating in a paired stimuli AEP paradigm. The relationship between the neurophysiology of sensory gating and the neuropsychological functions in explicit as well as implicit learning were explored.

2. Methods

Ten schizophrenic patients (mean age 35.1 ± 10.6 years, five women and five men) and 10 normal control subjects (mean age 33.3 ± 9.9 years, five women and five men) participated in the study with informed consent. The 10 schizophrenic patients were recruited consecutively from the psychiatric ward and diagnosed according to DSM-IV criteria (American Psychiatric Association, 1994). The patients participated after their active symptoms had subsided and standard inpatient treatment with medication had been instituted. Habits of cigarette smoking were assessed in both patients and controls. On the day of the laboratory study, subjects were restricted from smoking, coffee drinking, and alcohol use. They had no past history of epilepsy, alcoholism, or mental retardation. None had received electro-convulsive therapy within the 3 months preceding the study.

All patients and subjects completed the Wechsler Memory Scales (WMS). Verbal paired associate and visual reproduction learning tasks were used as indicators for their explicit memory capability.

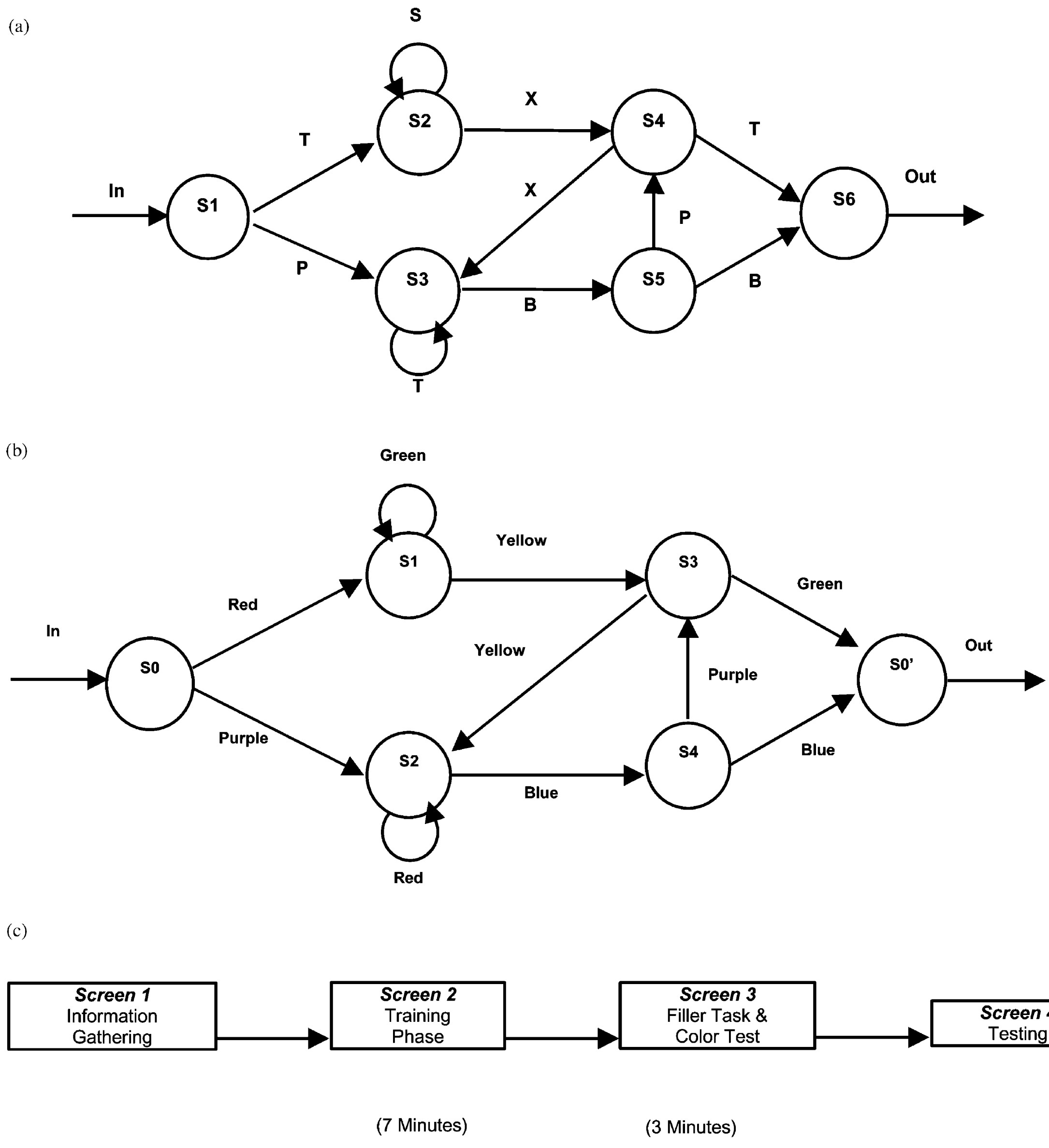

Fig. 1. (a) A finite-state-rule system, following Reber's artificial grammar, used to generate letter-string stimuli for implicit learning. (b) A finite-state-rule system, following Reber's artificial grammar, used to generate color-pattern stimuli for implicit learning. (c) Block diagrams for the training and test procedures for acquisition of artificial grammar. Two different modes of stimuli, namely letter strings and color patterns, were presented with the same procedures.

2.1. Artificial grammar learning

Implicit learning performance was assessed using letter-string (LS) and color-pattern (CP) artificial grammar learning (AGL) tasks. In each of the tasks, subjects were shown exemplars generated from a finite-state Markovian rule system (Fig. 1a–c). This rule system consisted of a finite number of legal states. It accepted predetermined input tokens and constructed sequences by concatenating the input tokens. Legal input token sequences resulted in a state change. When the END state was reached, it produced an output. If the legal input tokens were letters, the output produced would be letter strings of various lengths of alphabetic combinations (Fig. 1a). If the legal input tokens were color bars, the rule system generated color patterns consisting of various combinations of color bars (Fig. 1b). We employed both letters and color bars as input tokens. A computer program was designed to control the training and test displays (Liu, 2002). In the training phase, the computer flashed letter strings and color patterns regulated by artificial grammars at a rate of 500 ms per display for 7 min. During the test phase, displays were shown one at a time driven by the user's response.

Two filler tasks, for the lexical-string and color-pattern AGL test, lasting 3 min each, were used to reduce the short-term memory effect. The filler tasks were inserted between the training and testing phases. We adopted the procedure that was used in earlier studies on statistical learning (Reber, 1967, 1977). We asked subjects to passively observe the displays. They were only told that the experiment was a type of memory test. Subjects were seated approximately 60 cm away from the computer monitor. At the end of the filler tasks, the subjects were given a test in which they were asked to report if any given letter strings or color patterns looked 'familiar' (an instant *déjà vu*). Fifty letters strings or color patterns were shown twice for a total of 100 displays. Half of the displays appeared in the training phase and the other half were new. The duration of the experiment was approximately 45 min. The responses were recorded by the computer program as correct choice, correct reject, false choice and false reject. The subject's final score of modality-specific implicit learning was computed by combining scores of correct choice and correct reject, which entered the final analysis.

2.2. Sensory gating of AEPs

Eighteen Ag/AgCl cup scalp electrodes (F4, C4, P4, O2, Fp2, F8, T4, T6, F3, C3, P3, O1, Fp1, F7, T3, T5, Cz, and Pz) were placed according to the international 10–20 system. Reference was linked earlobes. The sampling rate was at 1 KHz and the band pass 0.15–100 Hz. Interstimulus intervals were 500 ms for S1–S2 and 10 s for S1–S1 10 s (Nagamoto et al., 1989). Auditory stimuli were bursts of 2000 Hz with 1-ms duration and an intensity of 80–90 dB SPL delivered to both ears. Subjects were tested for their auditory acuity and to adjust the sound intensity for stimulation before the examination started. Evoked potentials were obtained from averages of 66 study blocks. Blocks contaminated by artifacts were removed from further analysis. The software automatically rejected those blocks greater than ± 50 μV at Fp1 and Fp2. There were, on average, 60 blocks for controls and 55 blocks for schizophrenic patients after removal of artifact-contaminated ones. Visual recognition of waveforms at Cz was performed on -5 to $+200$ ms epochs. Baseline adjustments were to the mean amplitude at -50 ms to 200 ms, and digital filtering between 1 Hz and 30 Hz was performed before the measurement. Identification of the AEP waveform began with the recognition of N100 and then proceeded backward. The most positive peak was identified between 40 ms and 80 ms after the S1 as the first P50. Peak-to-peak amplitudes were measured for P50 and N100. Latencies of both P50 and N100 components were also measured. Percentages of sensory gating were computed as $[1-(S2/S1)]\times 100\%$ for all the aforementioned components. To avoid skewing the data by a single (or a few) extreme ratios, the P50 suppression ratios were truncated between -100 and 100% (Nagamoto et al., 1991; McCallin et al., 1997; Erwin et al., 1998). Brain mapping with the grand averaged EP from the normal control and schizophrenic subjects for S1 and S2 was also performed using double spline interpolation (ANT A/S, The Netherlands).

The non-parametric Mann–Whitney *U*-test was used to examine differences between groups on both scores of the memory tests and parameters of the AEPs. Spearman's rho correlation coefficients were computed to explore the relation between scores of the memory tests (implicit as well as explicit learning tasks) and AEP gating (P50 and N100 suppression). The effects of task (pair stim-

Table 1
Results of memory tests, AEP gating and Mann–Whitney *U*-test

	P50SUP	N100SUP	LS	CP	VPA	VR
Schizophrenia	30.5 ± 44.2	66.2 ± 22.3	56.4 ± 8.3	48.8 ± 6.4	23.8 ± 5.5	56.9 ± 9.7
Control	63.3 ± 32.8	54.7 ± 37.4	61.7 ± 5.3	58.6 ± 5.0	28.3 ± 2.4	72.9 ± 6.9
Mann–Whitney *U*	27.5*	43.0	31.0	8.5**	24.0*	10.5*

Mean ± S.D.; P50SUP, % of P50 suppression; N100SUP, % of N100 suppression; LS, letter string; CP, color pattern; VPA, verbal-pair associate; VR, visual reproduction; $*P<0.05$, $**P<0.01$ (one-tailed).

Table 2
Results of AEP in conditioning-testing paradigm and Mann–Whitney *U*-test

	P50S1L	P50S1A	N100S1L	N100S1A	P50S2L	P50S2A	N100S2L	N100S2A
Schizophrenia	53.2 ± 44.2	4.2 ± 2.4	111.6 ± 19.4	15.0 ± 12.8	51.0 ± 10.4	2.8 ± 2.0	89.8 ± 24.4	3.7 ± 1.6
Control	55.8 ± 10.7	3.7 ± 2.9	115.1 ± 13.2	14.8 ± 9.2	54.9 ± 12.0	1.3 ± 1.9	101.6 ± 18.1	5.6 ± 4.3
Mann–Whitney *U*	41.5	43.5	49.0	47.5	35.5	27.0	39.0	39.0

P50S1L, Mean ± S.D. of the latency of P50 from the conditioning stimulus (S1) in milliseconds; N100S2A, Mean ± S.D. of the amplitude of N100 from the testing stimulus (S2) in microvolts; none of the differences between the groups reached statistical significance.

Table 3
Spearman's rho correlation coefficients of memory tests and AEP gating in normal controls

	VR	LS	CP	P50SUP	N100SUP
VPA	0.618*	0.701*	0.544	0.165	0.793**
VR	–	0.009	0.500	0.426	0.353
LS		–	0.163	0.061	0.755**
CP			–	0.036	0.517
P50				–	0.127

P50SUP, % of P50 suppression; N100SUP, % of N100 suppression; LS, letter string; CP, color pattern; VPA, verbal-pair associate; VR, visual reproduction; $*P<0.05$, $**P<0.01$.

ulus paradigm) related asymmetries on different brain-topographic sites (electrode positions) of interest were separately analyzed by multivariate analysis of variance (MANOVA) with repeated measures (Merrin and Floyd, 1997). The probability values for within-subject factors and interactions were derived from the Wilks Lambda *F*-statistic. The within-subject repeated measure factors included condition (S1, S2), side (left, right), AP (anterior, posterior), PT (parasagittal, temporal) and vertex leads (C3, C4, Cz, Pz). The between-subject factor was diagnosis (control, schizophrenic). The statistical analysis was performed with SPSS for Windows, Release 8.0.1C (Chicago, IL).

3. Results

In the WMS test, schizophrenic patients scored low for both verbal paired associate (schizophrenia/control: 23.8 ± 5.5/28.3 ± 2.4, $P<0.05$) and visual reproduction learning tasks (schizophrenia/control: 56.9 ± 9.7/72.9 ± 6.9, $P<0.05$) (Table 1). Schizophrenic patients performed as well as normal subjects when using letter strings in implicit learning but were unable to process color patterns (schizophrenia/control: 48.8 ± 6.4/58.6 ± 5.0, $P<0.01$) as well as controls (Table 1).

In addition the patients showed less gating of the P50 component (schizophrenia/control: 30.5 ± 44.2/58.6 ± 5.0, $P<0.01$) of the AEP (Table 1) compared with control subjects. Although N100 gating in the patients was higher than in the controls, the difference did not reach statistical significance (schizophrenia/control: 66.2 ± 22.3/54.7 ± 37.4, $P>0.05$). Comparison of the AEP parameters between groups showed no significant differences for amplitudes and latencies of either the P50 or the N100 component (Table 2). Table 3 provides the Spearman correlation coefficients between scores of memory tests and AEP gating of the normal controls. The control group had a positive correlation between the explicit verbal paired associate (VPA) and implicit

Table 4
Spearman's rho correlation coefficients of memory tests and AEP gating in schizophrenia

	VR	LS	CP	P50SUP	N100SUP
VPA	0.170	−0.275	−0.170	−0.154	−0.302
VR	–	−0.207	−0.442	−0.365	−0.304
LS		–	−0.091	−0.328	−0.255
CP			–	0.638*	−0.012
P50				–	0.491

P50SUP, % of P50 suppression; N100SUP, % of N100 suppression; LS, letter string; CP, color pattern; VPA, verbal-pair associate; VR, visual reproduction; $*P<0.05$.

letter string (LS) learning ($r=0.701$, $P<0.05$). Both VPA ($r=0.793$, $P<0.01$) and LS ($r=0.755$, $P<0.01$) learning were positively correlated with N100 suppression. Table 4 presents the results of the Spearman correlation analysis of the schizophrenic group. The only significant finding was the positive correlation between implicit color learning and P50 suppression ($r=0.683$, $P<0.05$).

Fig. 2 illustrates the three-dimensional topography for P50 and N100 in S1 and S2 for both the controls and schizophrenic patients. In S1, the controls exhibited bilateral temporal spread, while the patients showed a clear vertex maximum for P50. Repeated measures MANOVA supported this

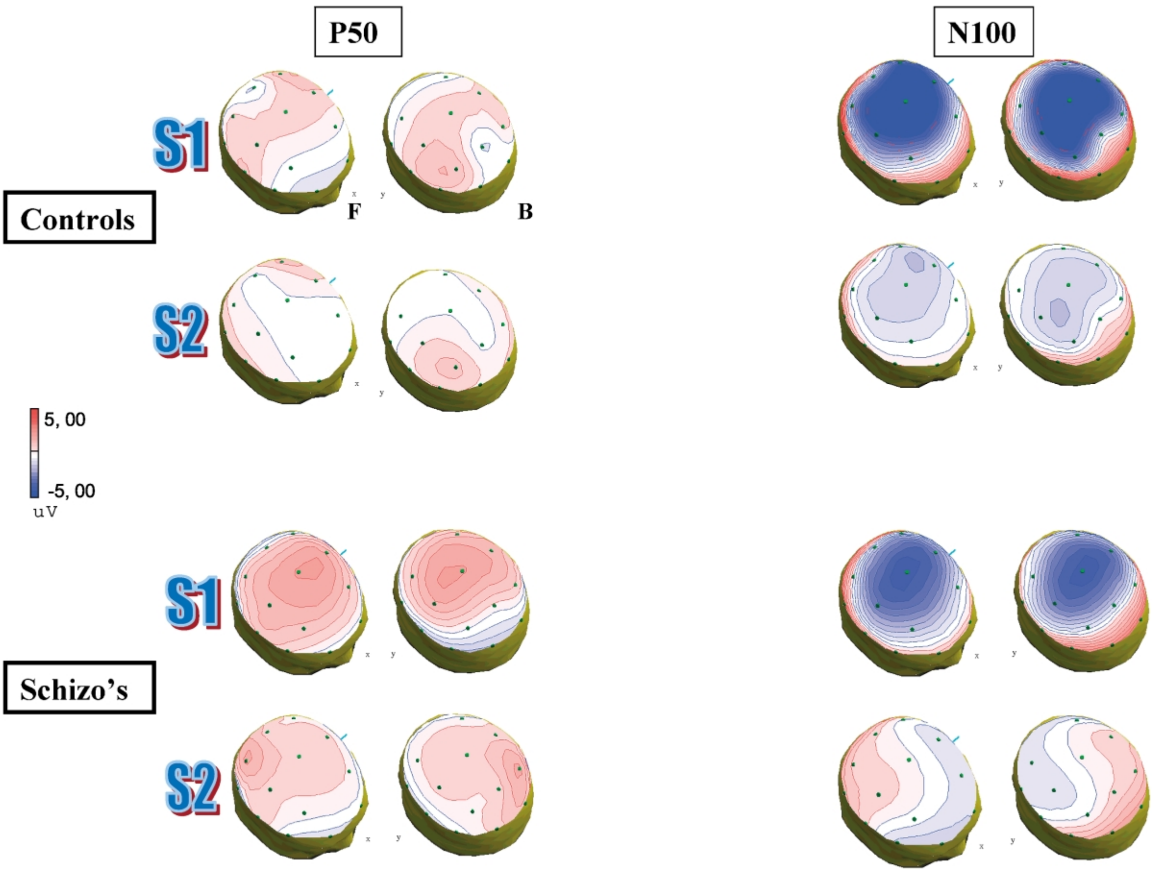

Fig. 2. Three-dimensional topographic mapping of peak maxima at P50 and N100 obtained from the grand mean AEPs of either the controls or schizophrenics for S1 and S2. The topographic maps are examined from both the anterior–superior view of the right hemisphere and posterior–superior view of the left hemisphere. 'F' indicates the front (nose) and 'B' back of the head (occiput). Please see text for description and the results of MANOVA with repeated measures.

positional effect (parasagittal–temporal: $F_{3,16}$= 4.5, P=0.018) but not the between-group difference (diagnosis×parasagittal–temporal interaction: $F_{3,16}$=1.78, P=0.192) for P50. In S2, the controls exhibited a left parietal prominence, while the schizophrenic patients had a right parietal prominence for P50. However, both the effect of side ($F_{1,18}$=0.676, P=0.422) and the diagnosis×side interaction ($F_{1,18}$=2.06, P=0.168) in repeated measures MANOVA did not reach statistical significance for P50. The topographic difference between S1 and S2 for P50 was further confirmed by the statistically significant condition×anterior–posterior×parasagittal-temporal interaction ($F_{3,16}$=5.27, P=0.01). In S1, both groups showed vertex N100 maxima with less activity in the schizophrenic patients. Again, the inter-group difference did not reach statistical significance among vertex electrodes for N100 in MANOVA (diagnosis×vertex×condition: $F_{3,16}$= 0.213, P=0.886). In comparison, the controls showed a left centroparietal prominence, while the schizophrenic patients showed a prefrontal prominence in N100 for S2. Both anterior–posterior ($F_{1,18}$=29.08, $P<0.001$) and parasagittal–temporal ($F_{3,16}$=17.88, $P<0.001$) position effects were statistically significant. The condition×anterior–posterior×parasagittal–temporal interaction also reached statistical significance ($F_{3,16}$=9.88, P= 0.001). In summary, the repeated measures MANOVA supported the position effect related to condition (S1 vs. S2) in both P50 and N100 but did not confirm the intergroup difference on the topographic display.

4. Discussion

The impaired performance of the verbal paired associate (VPA) and visual reproduction (VR) learning tasks, both representing explicit memory function, in our schizophrenic patients is compatible with many previous studies (McKenna et al., 1990; Clare et al., 1993; Stirling et al., 1997; Rushe et al., 1999). In the control group, we found positive correlations between the VPA and VR learning tasks. This suggests that both aspects of the explicit memory function, i.e. verbal (VPA) and non-verbal (VR), are somewhat parallel in normal subjects. Therefore, the two-way impairment may further suggest, at least to a certain degree, that the schizophrenic patients suffered from common deficit in memory system such as temporal lobe dysfunction.

Also, in the control group, the implicit letter strings were well correlated with the explicit VPA. This might reflect that both of these tasks, i.e. letter strings (LS) vs. words, involve a common mechanism, probably related to the lexical gateway. This interpretation is further supported by the fact that N100 gating was markedly correlated with both explicit VPA and implicit LS. These correlations suggest that N100 gating may be involved in lexicon processing. In that sense, although artificial grammar learning is implicit, the implicit LS task may still require some verbal (lexical) ability, which is also essential for explicit verbal memory to be carried out. Nevertheless, the relation of N100 lexicon processing is a possible interpretation of the correlation study, but it does not show a causal relation. It was not associated with any disease mechanism of schizophrenia. Therefore, the precise role of N100 gating in lexical processing remains unsettled, awaiting future study.

The results of implicit learning showed a selective deficit in color-pattern (CP) learning in schizophrenic patients, compatible with a previous study (Liu et al., 2000). The modality-specific impairment of implicit learning is an interesting finding worthy of further discussion, together with the findings of AEP gating. The Spearman correlation analysis showed a positive correlation between P50 gating and CP learning. This may imply that the patients' implicit learning of the CP is in some degree parallel to their ability to suppress the second P50. Since a positive correlation was not observed in normal control subjects, we may propose that only in the disease state does the parallelism exist. In normal controls, the parallelism may be obscured by a ceiling effect of either the performance on P50 suppression or CP implicit learning. Thus, it is possible inadequate gating function may impair the implicit learning of CP.

Since P50 gating is an early pre-attentive component, the impaired gating at P50 in those schizophrenic patients with impaired CP may indicate that defective filtering function is important in the impaired performance on the implicit learning task for color patterns.

Basically, both LS and CP stimuli reach the brain via the visual system and probably arrive at the associate visual cortex. Both implicit learning tasks are within the finite-state-rule system, which follows Reber's artificial-grammar rule. Psychophysically, the only difference is whether letter strings or color bars are used in the tasks. Furthermore, both learning processes are modulated, in quantitative terms, by the sensory gating system, which helps filter out irrelevant or excessive stimuli. The specific impairment of implicit learning may indicate failure of sensory gating for the flooding of inputs during the CP learning task. Since color bars carry many more information components, such as hue, saturation, and value, than the plain letter strings, they may overwhelm the impaired ability for sensory gating of the patients with schizophrenia and may result in the flooding of information (Weiss et al., 1988).

Although it is premature to draw definitive conclusions from the results of the topographical analysis, the three-dimensional display of the multiple-channel evoked potentials shows different distributions of the potentials at both P50 and N100 in the S1 and S2 for both the controls and patients. The bilateral temporal distribution in the control group for S1 may suggest a more differentiated function than those from the schizophrenic group with a vertex maximum. However, the difference did not reach statistical significance, so whether this interpretation can account for the less effective P50 suppression at S2 awaits further exploration. Nevertheless, a temporal lobe dysfunction in the schizophrenic patients may be reasonably speculated. At this moment, only the condition (S1, S2) related position effect can be confirmed by repeated measures MANOVA, which might offer clues for the participation of a brain area other than the subcortical source for vertex projection with consequent vertex maximum, specifically in the poststimulus inhibition, i.e. S2 processing.

Finally, schizophrenia is a syndrome. Therefore, the patient group data may have the problem of heterogeneity, i.e. some schizophrenic patients may still have the capability of sensory gating while others do not. The relatively small sample size of this study prevents further stratification of the patients by clinical subtypes, positive vs. negative symptomatology, or conventional vs. atypical antipsychotic medication. The delineation and clarification of these confounding factors are nevertheless important.

In conclusion, explicit memory functions, both verbal and non-verbal, are impaired in schizophrenic patients. However, color-pattern learning shows a modality-specific impairment in schizophrenia in the domain of implicit memory function. Impaired sensory gating may be responsible for such impairment as a result of an adaptive filtering failure during the learning process. Further correlation studies of the memory function with latent inhibition (Guterman et al., 1996) and mismatch negativity (Kreitschmann-Andermahr et al., 1999) are necessary to explore the full spectrum of impairment of sensory-information processing in schizophrenic patients.

Acknowledgments

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References

Adler, L.E., Pachtman, E., Franks, R.D., Recevich, M., Waldo, M.C., Freedman, R., 1982. Neuro-physiological evidence for a defect in neuronal mechanism involved in sensory gating in schizophrenia. Biological Psychiatry 17, 639–654.

American Psychiatric Association, 1994. Diagnostic and Statistical Manual of Mental Disorders, 4th ed., Washington, DC.

Bazin, N., Perruchet, P., 1996. Implicit and explicit associative memory in patients with schizophrenia. Schizophrenia Research 22, 241–248.

Boutros, N.N., Zouridakis, G., Overall, J., 1991. Replication and extension of P50 findings in schizophrenia. Clinical Encephalography 22, 40–45.

Brauch, I., Hemsley, D.R., Gray, J.A., 1988. Differential performance of acute and chronic schizophrenics on a latent inhibition task. Journal of Nervous and Mental Disease 176, 598–606.

Clare, L., McKenna, P.J., Mortimer, A.M., Baddeley, A.D., 1993. Memory in schizophrenia: what is impaired and what is preserved? Neuropsychologia 31, 1225–1241.

Clementz, B.A., Geyer, M.A., Braff, D.L., 1997. P50 suppression among schizophrenia and normal comparison subjects: a methodological study. Biological Psychiatry 41, 1035–1044.

Clementz, B.A., Geyer, M.A., Braff, D.L., 1998. Poor P50 suppression among schizophrenia patients and their first-degree biological relatives. American Journal of Psychiatry 155, 1691–1694.

Danion, J.M., Peretti, S., Gras-Vincendon, A., Singer, I., 1992. Les troubles de la mémorie dans la schizophrénie. L'Encéphale 18, 315–328.

Erwin, R.J., Turetsky, B.I., Moberg, P., Gur, P.E., 1998. P50 abnormalities in schizoprenia: relationship to clinical and neurpsychological indices of attention. Schizophrenia Research 33, 157–167.

Freedman, R., Adler, L.E., Waldo, M.C., Franks, R.D., 1983. Neurophysiological evidence for a deficit in the inhibitory pathways of schizophrenics: comparison of medicated and drug-free patients. Biological Psychiatry 18, 537–551.

Gras-Vincendon, A., Danion, J.M., Grangé, D., Bilik, M., Willard-Schroeder, D., Sichel, J.P., Singer, L., 1994. Explicit memory, repetition priming and cognitive skill learning in schizophrenia. Schizophrenia Research 13, 117–126.

Guterman, Y., Josiassen, R.C., Bashore, T.R., 1992. Antentional influence on the P50 component of the auditory event-related brain potentials. International Journal of Psychophysiology 12, 197–209.

Guterman, Y., Josiassen, R.C., Bashore, T.E., Johnson, M., Lubow, R.E., 1996. Latent inhibition effects reflected in event-related brain potentials in healthy controls and schizophrenics. Schizophrenia Research 20, 315–326.

Jeger, K., Biggins, C., Fein, G., 1992. P50 suppression is not affected by attentional manipulation. Biological Psychiatry 31, 365–377.

Judd, L.L., McAdams, L., Budnick, B., Braff, D.L., 1992. Sensory gating deficits in schizophrenia: new results. American Journal of Psychiatry 149, 488–493.

Kreitschmann-Andermahr, I., Rosburg, T., Meier, T., Volz, H.P., Nowak, H., Sauer, H., 1999. Impaired sensory processing in male patients with schizophrenia: a magnetoencephalographic study of auditory mismatch detection. Schizophrenia Research 35, 121–129.

Liu, K., 2002. Evidence for Color Patterns and Letter Strings Implicit Learning from an Artificial Grammar Study. Doctoral Dissertation, University of Washington, Seattle.

Liu, K., Hsieh, M.H., Liu, S.K., Hwu, H.G., Chiu, M.J., 2000. Dissociation of lexical and color pattern implicit learning in schizophrenic patients. Consciousness and Cognition 9, S91–92.

McCallin, K., Kardenas, V.A., Fein, G., 1997. P50 event-related brain potential amplitude and suppression measurements recorded with subjects seated vs. supine. Biological Psychiatry 41, 902–905.

McKenna, P.J., Tamlyn, D., Lund, C.E., Mortimer, A.M., Hammond, S., Baddeley, A.D., 1990. Amnesic syndrome in schizophrenia. Psychological Medicine 20, 967–972.

Merrin, E.L., Floyd, C.F., 1997. Clinical symptoms of schizophrenia affect reference-independent measures of task-induced EEG alpha asymmetry. Psychiatry Research: Neuroimaging 74, 47–62.

Nagamoto, H.T., Adler, L.E., Waldo, M.C., Freedman, R., 1989. Sensory gating in schizophrenics and normal controls: effects of changing stimulation interval. Biological Psychiatry 25, 549–561.

Nagamoto, H.T., Adler, L.E., Waldo, M.C., Griffith, J., Freedman, R., 1991. Gating of auditory response in schizophrenics and normal controls: effects of recording site and stimulation interval on the P50 wave. Schizophrenia Research 4, 31–40.

Reber, A.S., 1967. Implicit learning of artificial grammars. Journal of Verbal Learning and Verbal Behavior 77, 317–327.

Reber, A.S., 1977. Toward the theory of implicit learning: the analysis of the form and structure of a body of tacit knowledge. Cognition 5, 333–361.

Rushe, T.M., Woodruff, P.W., Murray, R.M., Morris, R.G., 1999. Episodic memory and learning in patients with chronic schizophrenia. Schizophrenia Research 35, 85–96.

Schacter, D.L., 1987. Implicit memory: history and current status. Journal of Experimental Psychology: Learning, Memory and Cognition 13, 501–518.

Stirling, J.D., Hellewell, J.S., Hewitt, J., 1997. Verbal memory impairment in schizophrenia: no sparing of short-term recall. Schizophrenia Research 25, 85–95.

Swerdlow, N.R., Braff, D.L., Hartston, H., Perry, W., Geyer, M.A., 1996. Latent inhibition in schizophrenia. Schizophrenia Research 20, 91–103.

Weiss, K.M., Vrtunski, P.B., Simpson, D.M., 1988. Information overload disrupts digit recall performance in schizophrenics. Schizophrenia Research 1, 299–303.