Ego Fails to Repress: The Role of Left Frontal Lobe Hypoactivation in Associative Memory Impairment in Schizophrenia

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Based on studies of the Word Association Task (WAT), C. G. Jung stated that the associative disturbances in schizophrenia are a result of decreased attention, leading to a failure in controlling intrusive egocentric associations. The ego of the patient seems to have failed in repressing egocentric memories. Today, associative disturbances are considered a symptom of left frontotemporal disconnection. The present study investigates whether the mode of monaural presentation of verbal stimuli in a WAT results in differential effects on associative memory. A total of 30 subjects with schizophrenia from the Psychiatry Clinics of the Marmara University Hospital and 30 control subjects were divided into two subgroups of 15 each to hear the WAT via either the right ear or the left ear. The WAT consisted of three tape-recorded lists each containing five target words with different emotional valences; positive, negative, and neutral. Each subject was presented with one target word at a time and was required to repeat the target word immediately and over the next 45 seconds to say the words that came to his/her mind. Word associations were evaluated in terms of total number of responses, semantic relatedness scores, perseverations, and egocentric responses. Compared to control groups, higher rates of intrusive egocentric associations, higher perseverations, and lower semantic relatedness of associations were observed in responses of schizophrenic subjects who took the WAT via the right ear. In line with the theory of left frontotemporal disconnection, associative memory impairment in schizophrenia seemed to be more marked within the left hemisphere. Underlying the memory impairment, the conclusion that failure of appropriate inhibition over intrusive associations—due to left frontal hypoactivation—seems reasonable. Using Jung's perspective, the functional role of the left frontal lobe in the service of the repression of egocentric memories is discussed.

Keywords: psychosis, disinhibition, associative disturbances, left frontal lobe hypoactivation, word association task.

Psychoanalytic theory defines schizophrenia as a narcissistic disorder in which attention and libido are withdrawn from the outside world and invested in the self. The psychotic patient experiences a failure of repression of the unconscious and regresses to a narcissistic primitive state where primary-process thoughts dominate. In the primary-process system, the pleasure principle rules, but logic and reason do not prevail. The failure of repression leads persons with schizophrenia to express ideas and wishes that others would repress. Therefore, the loose associations observed in psychotic speech directly reflect the egocentric intrapsychic conflicts of the patient (Grotstein, 1984). In the early 1900s, associative disturbances in schizophrenia were specifically discussed by Bleuler, who observed that the speech of persons with schizophrenia was often subject to derailments due to associative distracters (Andreasen, 1984).

To examine associative disturbances (classified today as a "thought disorder") and to measure semantic information processing and retrieval from associative memory, Bleuler's assistant C. G. Jung constructed the Word Association Task (WAT). The subject was presented with a list of target words one at a time and was required to say the first word or words that came to his mind as soon as he heard the target word. The responses were analyzed according to semantic relatedness to target word (e.g., table–chair), presence of rhymes (e.g., head–bed), perseverations, and egocentric quality (Jung, 1907/1995). Jung noticed that what seemed to be a semantically unrelated response was actually related to the target word in the schizophrenic subject's

Jung 1907/1995: please give English ref, not Italian

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mind in an egocentric fashion. The normal flow of associations in the mind of the patient was interrupted by intrusive egocentric associations that reflected the current emotional concerns of the subject.

The following example from Jung's application of the WAT shows the intrusion of hypochondriacal anxiety into the associations of a subject with paranoid schizophrenia.

> Jung, "Paralysis."
>
> Patient, "Bad food . . . excess work . . . too little sleep . . . telephone, these are the natural causes . . . tuberculosis, dorsal spine . . . there comes the paralysis, only these are indicated as paralysis . . . tortured, manifested by certain pain, these are how the things are with me, the pain is not far from me . . . I belong to monopoly, to payments . . . banknote—here is stabilized the sufferings—this is a correct system . . . crutch . . . the development of dust . . .—I need immediate help!" [Jung, 1907/1995]

Elaborated within the clinical history and current concerns of that patient, the unrelated responses get connected as remote but related associations. First, he associates to the factors he thinks may be causes of paralysis. Then another illness, tuberculosis, is caught up in the network, due to his preoccupations with health. He tries to turn back to the previous network related to the target word, by retrieving "dorsal spine," but intense hypochondriac anxiety provokes the intrusive association "tortured . . . pain . . . the pain is not far from me." Then his current preoccupation with the cost of the hospital treatment (monopoly, payments, banknotes) is activated. Then he rationalizes the treatment as a "correct system, like a crutch for him." And stressed by the uncontrollable flow of associations he shouts out, "I need immediate help!"

These intrusive associations, which sounded bizarre to the listener, were considered to be so out of mental control that even the patients were unable to follow and explain the connections underlying their own responses. When distracted, normal subjects produced responses similar to the responses of schizophrenic subjects, with more rhyming responses and perseverations. Jung theorized that attentional reduction in schizophrenia decreased control over semantic memory and facilitated automatic processing of associations, causing the intrusion of egocentric associations.

Consistent with Jung's thinking of a century ago, modern studies of semantic priming tasks and cued-word recall tasks also detect increased activation in semantic association networks in subjects with schizophrenia (Nestor et al., 1998; Spitzer et al., 1994). The overactivation of semantic memory in subjects with schizophrenia is considered to be the reason for intrusive associations leading to loosening of associations (Aloia et al., 1998). This overactivation of semantic memory with loose associations is found to be more frequent in patients with severe formal thought disorder (TD), than in low TD and non-TD patients (Aloia et al., 1998; Spitzer et al., 1994). The findings of semantic priming, semantic fluency, word recall, and WAT studies (Levine, Caspi, & Laufer, 1997; Levine, Schild, Kimhi, & Schreiber, 1996) all point to the possibility that semantic association networks of subjects with schizophrenia are overactivated with egocentric associations due to failure of inhibition.

Regarding the underlying neurobiology of associative disturbances, several studies of a semantic fluency task report a neural circuitry impairment along the semantic association networks of subjects with schizophrenia (Baaré et al., 1999; Chen, Lam, Chen, Nguyen, & Chan, 1996; Feinstein, Goldberg, Nowlin, & Weinberger, 1998; Kerns, Berenbaum, Barch, Banich, & Stolar, 1999; Rossell, Rabe-Hesketh, Shapleske, & David, 1999). This neural impairment is thought to lead to disorganization in semantic memory, which in turn prepares the ground for the production of loose associations. Functional neuroimaging techniques during cognitive tasks, which require the activation of the frontal lobe, repeatedly detect hypofrontality in subjects with schizophrenia (Hazlett et al., 2000; Higashima et al., 2000; Nohara et al., 2000). There are studies pointing to left temporal lobe dysfunction in schizophrenia (Bruder, 1994; Flor-Henry, 1969). It is known that both left frontal and left temporal lobe damage can impair associative memory of normal individuals (Dimitrov et al., 1999). Therefore, the finding that subjects with schizophrenia display a left frontotemporal dysfunction (Rushe, Woodruff, Murray, & Morris, 1999) points to the role of left frontotemporal dysfunction in associative memory impairment in schizophrenia. Supporting this finding is a CT finding of enlargement in the left sylvian fissure, separating the temporal and frontal lobes in subjects with schizophrenia (McCarley et al., 1989). This enlargement is correlated with positive symptoms of schizophrenia, especially thought disorder. Reduced interaction between frontal and temporal lobes in the left hemisphere of schizophrenic subjects is also detected by neuroimaging analysis (e.g., Bullmore et al., 1998) and during verbal associative learning tasks (e.g., Rushe et al., 1999).

Consistent with left frontotemporal dysfunction, during auditory discrimination tasks schizophrenic—compared to control—subjects show greater activation in the left temporal lobe and reduced activation in the left frontal lobe (Higashima et al., 2000) and phonological fluency tasks (Yurgelun-Todd et al., 1996).

There are other studies reporting reduced activation in the left frontal lobe of schizophrenic subjects during verbal associative learning tasks, semantic fluency tasks, and the Wisconsin Card Sorting Test (Chen et al., 1996; Morice, 1990; Nohara et al., 2000). Impairment in information processing in the left prefrontal cortex of neuroleptic-free schizophrenic subjects was also demonstrated by findings of low EEG coherence in left prefrontal regions. Interestingly, this impairment was correlated with positive symptoms of schizophrenia, such as the loose associations observed in formal thought disorder (Tauscher, Fischer, Neumeister, Rappelsberger, & Kasper, 1998).

On the other hand, while several studies indicate a frontotemporal dysfunction in the left hemisphere, there are also studies demonstrating such a dysfunction in both hemispheres. Using functional MRI during a verbal recall task, it was detected that while frontal activation was higher than temporal activation in control subjects, the reverse was true in schizophrenic subjects (Yurgelun-Todd, Baird, Gruber, Cohen, & Renshaw, 1997). This increased temporal and reduced frontal activity in schizophrenic subjects was suggested as the cause of frontotemporal network dysfunction leading to semantic memory deficits. However, the detected dysfunction was reported as a bilateral problem, rather than a problem specific to the left hemisphere. Also, Hazlett et al. (2000) observed a bilateral pattern of activation during a recent study of word recall and proposed this to be the reason for frontotemporal disconnectivity

Although a disconnection based on an overactivated left temporal and an underactivated left frontal lobe was repeatedly reported in studies discussed above, the inconsistent results of monaural (Galin, Rodgers, & Merrin, 1990; Kwapil, Chapman, & Chapman, 1992) and dichotic listening studies (Bruder, 1994; Grosh, Dochetry, & Wexler, 1995) have not provided a clear picture of whether the left or the right temporal lobe shows more overactivation in memory networks. In addition, it remains uncertain whether bilateral hypofrontality (e.g., Weinberger, Berman & Daniel, 1991), or left frontal hypoactivation (e.g., Higashima et al., 2000; Nohara et al., 2000) is the case. The existence of more severe hypofrontality in one hemisphere suggests lateralization of associative memory impairment.

To our knowledge, only one group of researchers focused on the lateralization of associative disturbances in schizophrenia. Kiefer, Weisbrod, Kern, Maier, and Spitzer (1998), measuring the event-related potentials during indirect semantic priming tasks, found that in normal individuals left-hemisphere semantic processing focused on close associations (e.g. "pencil–wood") and inhibited remote associations (e.g., "pencil–ecosystem"), whereas right-hemisphere semantic processing facilitated both close and remote associations (e.g. "pencil–wood–tree–forest–flora–ecosystem"). Observing the lateralized semantic and indirect semantic priming effects in people with schizophrenia, Weisbrod, Maier, Harig, Himmelsbach, and Spitzer (1998) found that remote associations were facilitated by both hemispheres of schizophrenic subjects. This was interpreted as a failure of inhibition, related to semantic processing in the left hemisphere. According to Weisbrod, Kiefer, Marzinzik, and Spitzer (2000), deficient processing in left frontal areas is the reason for failure of response inhibition in schizophrenic individuals.

The neuroscientific studies summarized above mostly state that left frontal hypoactivation leads to a disinhibition of semantic associations encoded in the temporal memory system. This disinhibition causes an overflow of egocentric semantic associations. The explanation can be stated in psychoanalytic terms as: Due to the ego's failure of repression (probably with left frontal hypoactivation underlying it), disinhibited egocentric memories intrude into the consciousness of schizophrenic individuals. The invaded consciousness can be observed by the presence of egocentric associations that sound bizarre and meaningless to the listener. However, these remote associations are subjectively meaningful and semantically connected in the primary-process system. Self-focused associations, free of left frontal inhibition, reflect the primitive nature of primary-process thoughts, which are probably encoded in the right-hemisphere semantic system. Combining the neurology of left frontal hypoactivation with the psychological construct of invasion into consciousness of egocentric associations is a neuropsychoanalytic conceptualization.

The aims of the present study

Although most studies point to the role of left-hemisphere dysfunctions in associative impairments—consistent with a neuropsychoanalytic perspective—some other studies consider the impairment as an outcome of bilateral dysfunction. Therefore, to observe whether associative memory impairment in schizophrenia varies depending on the hemispheric network (left frontotemporal vs. right frontotemporal networks), we decided to construct a WAT consisting of emotionally positive, negative, and neutral target words to be applied monaurally. During monaural stimulation, the temporal cortex contralateral to the stimulated ear is activated initially, prior to the stimulation of the ipsilateral cortex (Connolly, 1985). Monaural application of the revised WAT was expected to reveal whether associative memory performance varies depending on which hemispheric network (left vs. right) was initially activated. Based on the accumulated evidence in the literature, inhibition of the network in the left hemisphere was predicted to be more impaired.

In addition, the mnemonic difficulties experienced by subjects with schizophrenia seem to vary according to the emotional valence of the stimuli (Bell, Bryson, & Lysaker, 1997; Mueser et al., 1996). For instance, schizophrenic subjects' immediate recall and delayed recall for negative-affect materials were reported to be superior to those for positive-affect materials (cf. Calev, 1996). Considering that in intact brains the right frontal lobe is specialized for negative-affect processing, whereas the left frontal lobe is specialized for positive-affect processing (Davidson, 1994), lateralization of associative disturbances would need to be investigated in connection with the lateralization of affect processing. Therefore, the second aim of the present study was to observe whether associative memory performance varies depending on the emotional valence (positive, negative, or neutral) of the target word.

Method

Subjects

Participants were 30 schizophrenic subjects on medication and 30 control subjects, all right handed and without a history of previous neurological or auditory deficit. Each group was divided into two subgroups (*n* = 15), one receiving the WAT from the right ear and the other from the left ear.

Schizophrenic subjects were diagnosed by the second author at the Hospital of Marmara University Psychiatry Outpatients and Inpatients Departments, based on DSM-IV criteria. Control subjects were selected from the security staff and interns of the same hospital. Age, completed years of education, and gender were matched among the groups. A one-way analysis of variance revealed no significant difference between groups in terms of age and years of education. The patient subgroups were equal in terms of numbers of outpatients and inpatients (Table 1).

The two patient groups were matched in terms of duration of illness, the number of hospitalizations, total duration of hospitalization, and duration of medication (Table 2).

Hemispheric asymmetry has been shown to vary according to symptomatology (Bruder, 1994; Gruzelier et al., 1999; Gruzelier, Wilson, & Richardson, 1999; Galderisi, Mucci, Mignone, Bucci, & Maj, 1999); thus differences between patient groups in terms of symptoms could lead to misleading results. In the present study, there was no difference between the patient groups in terms of positive- and negative-scale and subscale scores (as shown in Table 2).

Materials

The Word Association Task (WAT): The WAT included three tape-recorded lists of target words (each list with 5 words), consisting of emotionally positive, negative, or neutral content. All words were recorded with the same pitch and neutral tone to equalize the arousability of the lists. The selection of emotionally laden target words was based on a preliminary study carried out with 45 normal subjects (30 females, 14 should 45 be 44?

Table 1. Sample characteristics of each group

"Group sizes" added: ok?

	Schizophrenics				*Controls*			
	Left ear		***Right ear***		*Left ear*		*Right ear*	
	M	***SEM***	***M***	***SEM***	*M*	*SEM*	*M*	*SEM*
Age	**32.5**	**2.15**	**36.0**	**3.18**	28.9	1.22	33.3	2.71
Education	**11.9**	**0.78**	**12.5**	**0.78**	12.1	0.98	11.6	1.24
Group sizes (*N*)								
Male	12		11		11		11	
Female	3		4		4		4	
Outpatient	14				14			
Inpatient	1				1			

Table 2. Characteristics of the course of illness of the patient groups and their symptom scores

	Schizophrenics			
	Left ear		*Right ear*	
	M	*SEM*	*M*	*SEM*
Duration of illness (years)	11.5	1.55	12.7	2.56
Number of hospitalizations (hosp)	2.9	0.72	3.7	0.36
Total duration of hospitalizations (days)	93.3	28.01	85.4	11.27
Duration of medication (years)	10.3	1.42	11.5	2.69
Negative-scale score	41.5	5.66	38.7	5.22
Positive-scale score	30.3	4.08	35.1	4.21
Thought disorder subscale score	9.3	1.60	10.8	2.38

males) and 20 schizophrenic subjects (5 females, 15 males), selected from members of the Schizophrenia Friends Association, medicated outpatients from the Hospital of Istanbul University, and medicated inpatients from the Hospital of Marmara University. In the preliminary study, subjects were asked to write down separately words that evoked negative and positive emotions for them. The responses were than tabulated in a frequency list, and the 5 most frequently used responses for each question were selected as target words to be included in the WAT. If the percentage of usage of a response was not similar in the patient and the control groups, it was not selected as a target word, even if it was in the highest 5 of the frequency list. In addition, when the same word was written as evoking negative emotions by one subject and as evoking positive emotions by another, it was discarded from the frequency list. The neutral target words were selected from words belonging to the categories of household, clothes, and stationery.

The Scale for the Assessment of Positive Symptoms (SAPS) and Negative Symptoms (SANS): The Turkish versions (Erkoç, Arkonaç, Ataklı, & Özmen, 1991a, 1991b) of SAPS and SANS (Andreasen, 1990) were used in the study. SAPS and SANS were filled out based on a 1-hour assessment interview conducted by the first author. The behavioral observations during the interview and the clinical history of the patients was reported by their psychiatrists, who had been following them since admission to the hospital. Only complaints present within the month prior to the interview were scored. Scores consisted of a positive-scale score and four subscale scores for SAPS, and a negative-scale score and five subscale scores for SANS.

Procedure

Subjects in each group were randomly assigned to the left- or right-ear subgroups and tested individually. Prior to the experiment, each subject read and signed a written consent form, including a statement of confidentiality. After the experimenter read the instructions, a sample trial for a neutral target word was given prior to the application of the WAT. Only after it was established that the subject totally understood what he/she had to do was the WAT begun. The procedure was the same for all four groups, except that two groups heard the WAT in the right ear while the other two groups heard the WAT in the left ear. In each group, subjects were presented the words successively with a break of 1 minute between words, which they listened to monaurally via an earphone. Each subject was required to repeat the target word as soon as it was presented and then to say the words that came to his/her mind immediately after hearing the target word. After 45 seconds the subject heard the warning of “Stop” via the earphone and, following a pause of 15 seconds, the next target word was presented. Responses for each target word were recorded. To avoid a possible order effect, the presentation of the lists was counterbalanced for each subgroup. The 1-hour interview for SAPS and SANS was carried out with the schizophrenic subjects after the completion of the WAT.

Verbal responses measured. Total number of responses, perseverations, egocentric responses, and relatedness scores were measured as dependent variables, for the three lists. Perseverations and egocentric responses scores were computed as percentage scores over total number of responses. Repetition of a certain response during the period of 45 seconds was considered as a perseveration. The egocentric responses were those that included subjective comments about the target word (e.g., love: "The only thing important in this world") or responses including "I" or "my" (e.g., pencil: "my pencil was lost").

The level of semantic relatedness between the target word and the responses were scored based on a relatedness analysis. The relatedness analysis was carried out after the study by the usage of Likert-type relatedness ratings (from 0: not related at all; to 5: totally related) of 5 rater groups, each including 3 raters, unaware of the aim and sample of the study. Prior to rating the actual responses, all raters received a 1-hour training session about how to score semantic relatedness and filled an example relatedness scale. Based on the Pearson correlation coefficients, the intragroup reliabilities of the five rater groups were $r = .735$, $r = .718$, $r = .687$, $r = .717$, $r = .806$, all significant at the 0.01 level. The intergroup reliability was $r = .887$, significant at the 0.01 level. Given the significant intra- and intergroup reliabilities, the sample of actual responses of the 60 subjects were equally divided among the five rater groups, each rater group rating the responses of 3 subjects from each group. The relatedness score of a single target word was calculated as the mean of scores given by the three raters for that target word. Final relatedness scores for the positive, negative, and neutral lists were calculated as the mean of relatedness scores of target words within each list.

Results

The four dependent variables (total number of responses, relatedness scores, perseveration scores, egocentric responses) were submitted to separate 4 × 3 mixed-design repeated-measures ANOVAs, with groups (schizophrenic subjects tested via left ear, schizophrenic subjects tested via right ear, control subjects tested via left ear, and control subjects tested via right ear) and word lists (emotionally positive, negative, and neutral list) as the factors. Since the number of groups exceeded 3, post-hoc comparisons were made by using Fisher's LSD (Least Significant Difference).

Fischer's changed to Fischer's: ok? (Least Significant Difference) added: ok?

Total number of responses

The means and standard error of means (*SEM*) of the total number of responses produced are summarized in Figure 1. ANOVA results indicated that the main effect of group, $F(3, 56) = 1.71$, $MSE = 55.46$, $p > .05$, and the main effect of list types, $F(2, 112) = 2.25$, $MSE = 4.01$, $p > .05$, did not attain significance. However, a significant Group × List interaction was obtained, $F(6, 112) = 2.22$, $MSE = 3.95$, $p < .05$. The cell means revealed that control subjects receiving the WAT from the right ear produced strikingly more responses on the neutral words list compared to the other three groups.

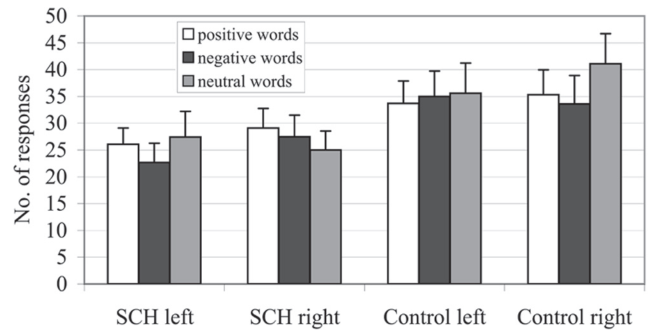

Figure 1. Means and standard error of means of the total number of responses produced.

Relatedness scores

The means and SEMs for the relatedness scores are shown in Figure 2. An ANOVA revealed a significant main effect for groups, $F(3, 56) = 8.28$, $MSE = 8.64$, $p < .001$, but not for lists, $F(2, 112) = 2.23$, $MSE = 0.70$, $p > .05$, or for the Group × List interaction, $F(6, 112) = 1.52$, $MSE = 0.48$, $p > .05$. Post-hoc comparisons showed that relatedness scores of the schizophrenic subjects' right-ear group were lower than the scores of both control groups ($p < .0001$).

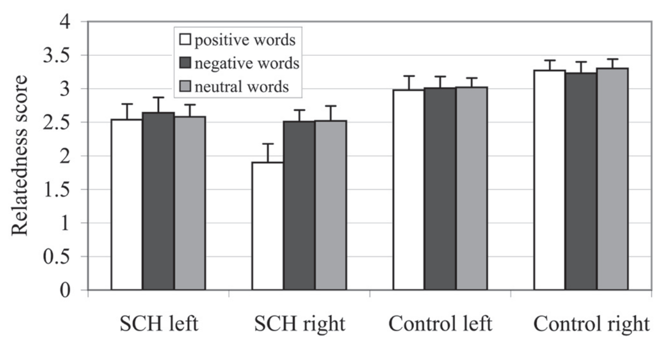

Figure 2. Means and standard error of means of the relatedness scores.

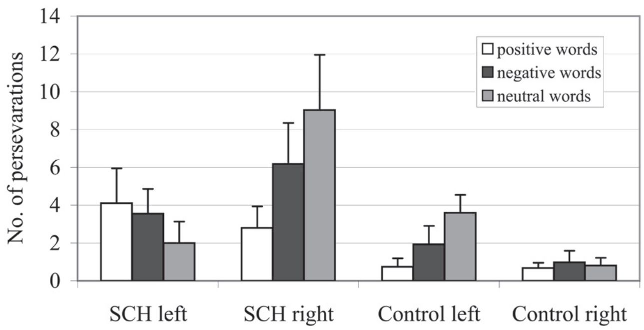

Figure 3. Means and standard error of means of perseverations.

Perseverations

The means and *SEM*s for perseverations are shown in Figure 3. An ANOVA for perseverations revealed a significant main effect for group, $F(3, 56) = 3.63$, $MSE = 219.58$, $p < .05$, and for list types, $F(2, 112) = 3.46$, $MSE = 47.81$, $p < .05$, as well as a significant Group × List interaction, $F(6, 112) = 3.54$, $MSE = 49.04$, $p < .005$. Post-hoc comparisons showed that schizophrenic subjects receiving the WAT from the right ear perseverated more than the controls receiving it via the right ($p < .005$) or the left ear ($p < .05$). The Group × List interaction revealed that schizophrenic subjects receiving the WAT from the right ear perseverated significantly more on the neutral list.

Egocentric responses

figure 4 uses "idiosyncratic responses": changed figure, or text, so that they match?

The means and *SEM*s of egocentric responses are displayed in Figure 4. An ANOVA revealed a significant main effect for word lists, $F(2, 112) = 18.22$, $MSE = 3{,}852.46$, $p < .0001$. There was a trend toward a significant main effect for groups, $F(3, 56) = 2.36$, $MSE = 3{,}312.98$, $p = .081$, while no Group × List interaction was observed, $F(6, 112) = .98$, $MSE = 207.40$, $p > .05$. Tests of within-subjects contrasts showed that all subjects produced more egocentric responses for the positive and the negative words lists than for the neutral words list ($p < .0001$). The trend toward a significant main effect of groups showed that schizophrenics receiving the WAT from the right ear produced more egocentric responses than did the control subjects receiving the WAT from the right ear, whereas schizophrenic subjects receiving the WAT from the left ear and the two control groups did not differ from each other.

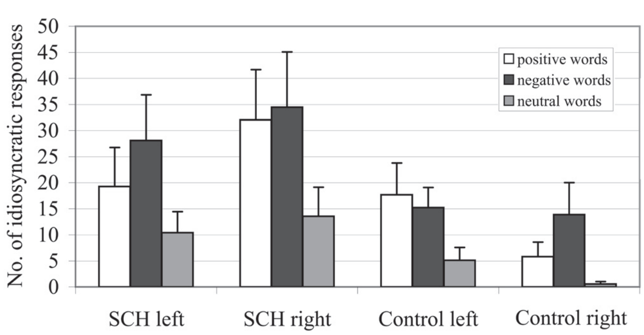

Figure 4. Means and standard error of means of the egocentric responses.

Discussion

The relation of WAT performances with the associative memory network that is initially activated

With respect to the primary aim of the study—examining whether associative memory impairment in schizophrenia varied depending on which hemispheric network (left vs. right) is initially activated—findings supporting our prediction were obtained. While the results related to the total number of responses showed no difference between the groups, analysis of the relatedness scores revealed that schizophrenic subjects who received the WAT in the right ear produced associations less related to the target word compared to the controls who received the WAT in the right or the left ear.

As predicted, these findings suggest that when the WAT was heard in the right ear, and the associative network in the left hemisphere was initially activated, the associations of the schizophrenic subjects became semantically more unrelated to the target word and more remote associations appeared. The detection of a more marked associative memory impairment in the left hemisphere is in agreement with findings in the literature reporting more severe frontotemporal disconnection in the left hemisphere of schizophrenic subjects (Bullmore et al., 1998; McCarley et al., 1989; Rushe et al., 1999). In contrast to the studies stating equal levels of frontotemporal impairment in both hemispheres of schizophrenic subjects (Hazlett et al., 2000; Yurgelun-Todd et al., 1997), the present findings suggest that the left frontotemporal disconnection in schizophrenic subjects is more severe.

The present results can be evaluated in the light of findings that the neural breakdown in communication between the frontal and the temporal lobes, a possible reason for schizophrenic patients' loose associations (Hoffman, 1987), seems to be more severe in the left hemisphere. In other words, the associative memory network in schizophrenic patients' left hemisphere is interrupted by remote associations more than is the network in right hemisphere (Hoffman, 1987; Hoffman & McGlashan, 1993; cf. Crow, 1998).

Hoffman & McGlashan, 1993: not in Refs

Analysis of perseverations during the WAT revealed supporting evidence for studies reporting left frontal lobe hypoactivation of persons with schizophrenia as the crucial determinant of the left frontotemporal disconnection (Chen et al., 1996; Higashima et al., 2000; Morice, 1990; Nohara et al., 2000; Tauscher et al., 1998; Yurgelun-Todd et al., 1996). The present results showed that schizophrenic subjects receiving the WAT via the right ear perseverated significantly more than the control subjects receiving the WAT via the right or the left ear, whereas schizophrenic subjects receiving the WAT via the left ear did not differ from either control group in terms of perseverations. Considering perseverations as the outcome of the frontal dysfunction (Shimamura, Janowsky, & Squire, 1991), the lateralized findings about perseverations imply that during the WAT a frontal hypoactivation may have occurred in the schizophrenic subjects' left hemisphere, while their right frontal activation remained intact. This finding provides support for left frontal hypoactivation during the WAT and suggests that the presence of frontal hypoactivation in both hemispheres of the schizophrenic subjects during neuropsychological tasks (Hazlett et al., 2000) has to be reinterpreted as depending on the administered task. The present finding also provides additional evidence for the underlying reasons for the left frontotemporal disconnection. Given the importance of the inhibitory functions of the frontal lobes and the hypofrontality detected in the left hemisphere of schizophrenic subjects, the disorganization of memory networks in the left hemisphere may be more understandable in terms of the failure of left frontal inhibition (Weisbrod et al., 2000). The present findings are also in line with the previous study indicating that left frontal deficiencies in schizophrenia lead to the failure of left hemisphere semantic processing characterized by the inhibition of remote associations (Weisbrod, 1998).

Weisbrod, 1998: not in Refs, or Weisbrod et al.?

Additional support for the left-hemisphere semantic processing deficit underlying the associative memory impairment comes from the analysis of egocentric responses produced during the WAT. Although it was not statistically significant, schizophrenic subjects receiving the WAT from the right, but not the left, ear produced more egocentric responses than did their controls. Therefore, the egocentric associations interrupting the associative network seem to occur more frequently when the left hemisphere of schizophrenic subjects is initially activated. The production of egocentric responses by persons with schizophrenia is considered to be one of the reasons leading to deviations from the normal flow of associations (Jung, 1995; Kerns et al., 1999; Levine, Caspi, & Laufer, 1997; Rossell et al., 1999). Thus, the trend of more egocentric responses during activation of the left hemisphere is in line with the higher amounts of deviation in the associative tracks within the left hemisphere, shown by lower relatedness scores for the schizophrenia–right-ear group.

Jung 1995: as per earlier query

The relation of WAT performances with the emotional valence of target words

The second aim of the study was to examine whether associative memory performance varied with the emotional valence of the target word. Subjects in all treatment groups produced similar numbers of responses on each list, suggesting that the level of activation of the associative memory networks did not vary according to the affective content of the words in the WAT. In addition, analysis of relatedness scores showed no significant difference due to the emotional valence of the target-word lists. Therefore, stimuli with varying affective content did not seem to influence the associative memory tracks. These findings were obtained for all the groups, suggesting that the associative memory impairment in schizophrenia did not vary according to the emotional valence of the target word. In the literature, word-recall studies that examined the variance of recall performances according to emotionally laden words found an inferior recall of positive-affect materials in schizophrenics (cf. Calev, 1996). However, there are no comparable studies examining the effects of differential affective processing on the associative memory performances.

The results of the present study also indicate that both schizophrenic and control subjects produced significantly more egocentric responses to the negative and the positive lists than to the neutral list. Using a version of the WAT that included only negative and neutral words, Levine, Caspi, and Laufer (1997) found that schizophrenic subjects produced more egocentric responses to negative target words than to neutral words. While Levine, Caspi, and Laufer (1997) explained their findings in terms of the greater attractiveness of negative-affect materials for subjects with schizophrenia, the present study revealed that this effect is valid not only for material with negative affect, but also for words with positive affect. In addition, it was seen that this effect is important not only for the schizophrenic subjects, but also for the control subjects. Therefore, it can be stated that the issue is not the attractiveness of negative-affect materials on persons with schizophrenia, but the general attractiveness of emotionally laden stimuli for all subjects. During the WAT, stimuli with emotional valence provoke more egocentric responses because when a subject is faced with an emotional reminder, egocentric associations within personal memory are activated. In contrast, neutral stimuli do not have direct influences on personal associations.

Schizophrenic subjects receiving the WAT from the right ear perseverated strikingly more on the neutral words list. This higher number of perseverations may be interpreted in terms of the left hemisphere's role in functional/action related knowledge, which is relevant for representing artifacts/man-made categories (Kiefer, 2001; Tranel, Damasio, & Damasio, 1997). It is generally accepted that the left hemisphere encodes and stores concrete categories better than the right hemisphere does (reviewed in Brown & Kosslyn, 1993). Therefore, the storage and retrieval of information related to concrete objects, like artifacts, are the specializations of the left hemisphere. Since, the neutral words used in the WAT in the present study were selected from artifacts (e.g., plate, coat), the associations related to these neutral words required the activation of the left hemisphere. Given the left-hemisphere impairment observed in schizophrenia, the higher perseverations in response to neutral target words received via the right ear may be a meaningful result in terms of the functional failure of the left hemisphere for concrete stimuli. More response production on the neutral words list by control subjects receiving the WAT from the right ear also confirms the general assumption that in intact brains the left hemisphere is better in retrieving information about visual—thus concrete—categories.

Conclusion and recommendations

Performances on the WAT demonstrated that the associative memory impairment in schizophrenia was, as predicted, more marked when the right ear was stimulated. Although the monaural application of word-generation tasks involves mostly contralateral and some ipsilateral projections, the performance abnormalities of the schizophrenic subjects were higher for right-ear presentation. As WAT is a task of word generation, the left hemisphere could be assumed to be primarily involved, and poorer performance for both schizophrenic groups—regardless of stimulation side—could have been expected. But the performances of the schizophrenic group receiving the WAT via the left ear were not significantly different from the performance of the control groups. Thus, the monaural application of WAT seemed to provide a lateralized investigation of the associative memory impairment. The higher rate of intrusive egocentric associations and the lower semantic relatedness of associations observed in responses of schizophrenic subjects who took the WAT via the right ear supported the left frontotemporal disconnection hypothesis. The higher rate of perseverations while the WAT was administered via the right ear pointed to left frontal hypoactivation, which seems to be related to the lack of inhibition over associative memory networks in the left hemisphere. Disinhibition of egocentric associations, which may be interpreted as a failure of repression, causes an intrusion of the unconscious into the consciousness of the patients. Supporting the study of Weisbrod (1998), the present findings may also indicate that *while right-hemisphere semantic processing, responsible for both remote and close associations, seems more intact in schizophrenia, left-hemisphere semantic processing, responsible for the inhibition of remote associations, is disturbed.*

Weisbrod (1998: not in Refs, or Weisbrod et al.?

The interpretations above are also in line with psychoanalytic theorization that schizophrenia is a narcissistic disorder, in which libido is withdrawn from the outside world and invested in the self (Grotstein, 1984). Due to the failure of repression of the unconscious processes related to the self, the patient regresses to a narcissistic primitive state, presumably with right-hemisphere processes underlying it. In narcissistic primitive states, where primary-process thoughts dominate, schizophrenic patients express ideas and wishes that other people repress. Therefore, loose associations observed in psychotic speech reflect the egocentric intrapsychic conflicts of the patient. In conclusion, the psychoanalytic suggestion that, in schizophrenia, "*Ego fails to repress the unconscious*" is parallel to the findings of the present study stating that "*The left frontal lobe fails to inhibit remote associations processed by right-hemisphere semantic networks*." This brings out the question of whether underlying the psychic phenomenon there are impairments of these neural mechanisms. The "failure of repression by the ego" may have a neural substrate linked with the "failure of the inhibitory functions of the left frontal lobe." According to the dual-aspect theory, these two similar explanations seem to reflect a unique quality of mind–body interactions in schizophrenia. However, it is highly important not to equate the psychodynamic and neuroscientific terminologies stated above, since only their integration explains the whole phenomenon. Neither the psychodynamics nor the neural mechanics can explain the whole picture alone.

Regarding the limitations of the present study, these relate to monaural application and the effect of medication. As monaural stimulation leads to mostly contralateral and some ipsilateral projections, the study of monaural tasks—as in the present study—is intended to observe the processing of the initially activated cortex, which is the contralateral one. Considering the interhemispheric transmission deficit suggested for schizophrenia (Mohr, Pulvermüller, Cohen, & Rockstroh, 2000; Endras, Mohr, & Rockstroh, 2002), a future study comparing the monaural and dichotic application of the WAT is required. In addition, the present study investigated the associative disturbances of schizophrenic subjects who were on medication. Since medications lead to neurochemical changes, it would be useful to repeat this research with a sample of schizophrenic subjects who are not on medication.

Endras, Mohr, & Rockstroh, 2002: spelling Endrass in Refs: which is correct?

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