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ORIGINAL PAPER

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Contextual suppression and protection in schizophrenic patients

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Abstract *Introduction* Contextual processing is often strongly deteriorated in schizophrenic patients as found, for example, in higher cognitive as well as lower visual paradigms. In visual detection tasks, impoverished contextual facilitation was attributed to aberrant excitatory neural circuits. On the other hand, we found contextual suppression, possibly related to neural inhibition, to be fast and intact in a visual backward masking task. Here, we combine a suppressive with a "protective" paradigm to further our understanding of the contextual deficiencies of schizophrenic patients in visual information processing. *Methods* Twenty three schizophrenic patients and 18 healthy controls were asked to discriminate the offset direction of a vernier target, which was followed by one of a variety of masks for several stimulus onset asynchronies (SOAs). *Results* As in previous studies, patients needed clearly longer SOAs than controls. However, when longer SOAs were taken into account, increases as well as decreases in backward mask strength had comparable effects in patients and controls. *Conclusions* From these results, we suggest that complex spatial processing is fast and intact in schizophrenic patients.

Key words backward masking · early visual processing · vernier · schizophrenia · perceptual disorders

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Introduction

Deteriorated contextual processing is often considered a core deficit of schizophrenia occurring on many stages including sensory, semantic, cognitive, and emotional processing (for a recent review see [42]). Of particular interest are early contextual processing deficits (e.g. [14, 15, 23, 28, 30–32, 35, 36, 43]) because these deficits may cause processing deficits on higher stages.

In visual contextual modulation, perception of a target is modified by elements surrounding the target. Contextual effects can be suppressive as well as facilitative. For example, detection of a low contrast Gabor target improves when flanked by other identical Gabors at a certain distance. For other distances, detection deteriorates compared to the condition without flanks [33]. Interestingly, the facilitative effects occurred only weakly if at all in schizophrenic patients [23, 28]. These and related effects might be explained by altered neural excitatory connections in the patients [23, 36]. For example, it was proposed that the excitatory transmitter glutamate is reduced in the patients (review: [7]), possibly induced by an over expression of glutamate transporters [11].

Whereas contextual facilitation seems to be deficient, contextual suppression seems to be intact in schizophrenic patients. In a recent study, we presented a vernier target, i.e. two vertical bars that are slightly offset in the horizontal direction, followed by a masking grating comprised of 25 elements (standard

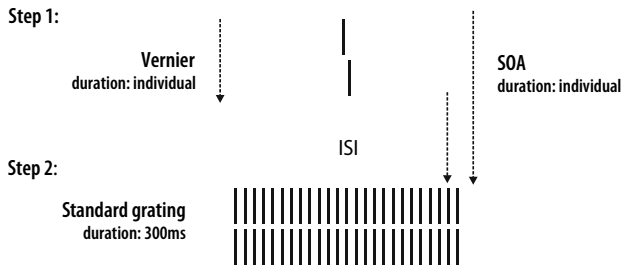

Fig. 1 Procedure. We determined the vernier duration (VD) for each observer individually without a masking grating (*step 1*). In the second step, we determined the ISI (inter-stimulus-interval) between vernier disappearance and standard grating onset individually, SOA = VD + ISI (*step 2*). These two values were used in the third step, in which the vernier was followed by the standard grating or this standard grating accompanied by additional contextual elements as shown in Fig. 2

grating, see Fig. 1). The vernier shines through the grating and masking is rather weak in healthy controls [18]. Shine-through disappears when the 25 element grating is accompanied by two single contextual lines below and above the grating (Fig. 2a) [19, 20]. Contextual suppression has occurred. This result surprises because collinear elements usually do not deteriorate performance but facilitate target processing (Gestalt law of good continuation).

Schizophrenic patients show stronger masking with the standard grating, i.e. they need longer stimulus onset asynchronies (SOAs) to yield a performance level comparable to controls. However, they show comparable collinear suppression when SOAs are adjusted properly [38]. Hence, contextual suppression seems to be intact in schizophrenia.

Because in other contextual masking paradigms [12, 23] contextual facilitation was diminished, it may be that excitatory circuits are affected in the patients but not the inhibitory ones. To further explore this fundamental question, a paradigm is needed in which suppressive and non-suppressive effects are combined.

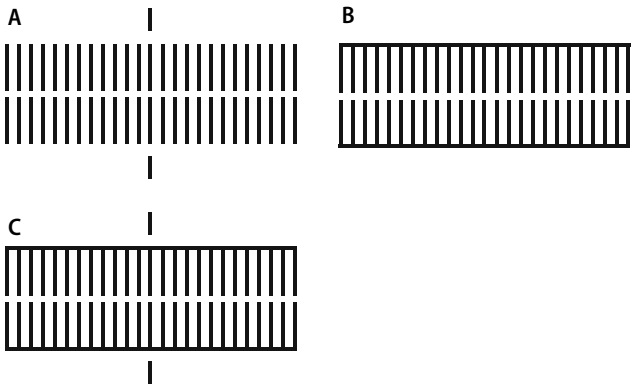

Fig. 2 Contextual conditions (the preceding vernier is not shown here). Standard grating with two collinear elements above and below (**a**), standard grating with two long horizontal lines (**b**), standard grating with long horizontal and collinear lines combined (**c**)

In healthy observers, we recently showed that the collinear suppression in the shine-through effect can be partly blocked when horizontal contextual lines are presented together with the vertical contextual lines [20]. Hence, these horizontal lines exert a "protective" effect. Here, we will repeat this experiment in schizophrenic patients to investigate whether these non-suppressive, protective mechanisms are intact in schizophrenia. Three outcomes are possible. First, as in healthy observers, adding horizontal contextual lines "undoes" the effects of vertical contextual lines. Second, adding horizontal lines leaves performance unaffected, i.e. the vertical lines still exert strong suppression. Third, performance even deteriorates when adding the horizontal lines to the vertical ones.

Methods

Diagnosis and psychopathology

We investigated 23 schizophrenic in-patients from the hospital at the Asatiani Psychiatry Research Institute and 18 control subjects without neurological or psychiatric disorders. Four patients and two control subjects had to be excluded because of low visual acuity, three patients did not pass the threshold for vernier duration. So 16 schizophrenic patients and 16 control subjects participated in experiment 1. Fourteen of these schizophrenic patients and 11 healthy observers joined experiment 2 plus 3 additional healthy observers. Diagnosis was made according to DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition) based on a clinical interview, the medical record, and interviews with the hospital staff. Exclusion criteria were age older than 50 years, diagnosis of a neurological disease, and recent substance abuse during the last 6 weeks. For the assessment of the psychopathological condition, the Scale for the Assessment of Negative Symptoms (SANS; [2]) and the Scale for the Assessment of Positive Symptoms (SAPS; [3]) were used. Diagnosis and psychopathological ratings were carried out by an experienced senior psychiatrist (E.C.) within 3 days following the day of testing. Psychopathological ratings were based on the symptoms existing in the week preceding the rating. With this method we determined symptoms with a close temporal relation to the testing.

The schizophrenic patients of this study took also part in a larger study including a neuropsychological test battery with tests such as the California Verbal Learning Test (CVLT; [13]), a computerised version of the Wisconsin Card Sorting Test (WCST; [27]), and the Continuous Performance Test (CPT; [34]).

Patients were receiving neuroleptic medication: risperidone, trifluoperazine, perazine, olanzapine, clozapine, haloperidol, and chlorpromazine. Eleven patients received two and one patient received three of these neuroleptics. Eight patients took biperiden, three patients took an additional antidepressant, two patients carbamazepine and one patient received diazepam. Chlorpromazine equivalents were calculated according to the Agency for Healthcare Research and Quality [1].

General set-up

Stimuli were generated on a Pentium-based computer and displayed on a Siemens Fujitsu P796–1 monitor (31.0 cm (H) × 23.3 cm (V), 1,024 × 768 resolution). Subjects observed the stimuli from a distance of 3.5 m in a room illuminated dimly by a background light. A pixel comprised about 18″ (sec of arc) at this distance. White stimuli were presented on a black background. Luminance of stimuli was 100 cd/m^2 approximately. Background luminance was about 0 cd/m^2, hence, contrast was 1. Refresh rate was 100 Hz.

In the *standard condition*, a vertical vernier preceded a grating comprising 25 elements (Fig. 1). A vertical vernier is composed of two bars that are slightly displaced in the horizontal direction either to the left or to the right. The length of a segment of the vernier, i.e. one bar, was 10′ (arc min). Segments were separated by a small gap of 1′. Thus, altogether a vernier was about 21′ long. In the *contextual conditions*, various contextual lines were displayed in addition to the standard grating (Fig. 2).

In each trial, the vernier offset direction was chosen randomly either to the right or to the left. In a binary task, observers were asked to indicate this offset direction. Errors and omissions were indicated by an auditory signal.

Procedure

The design of the study was approved by the local ethic committee and was performed in accordance with the Helsinki declaration. Before the experiment proper took place, the general purpose of the experiment was explained to every observer. Moreover, subjects were told that they could quit the experiment at any time they wished.

Visual acuity

After signing a consent form, we determined visual acuity of patients and healthy controls by means of the Freiburg visual acuity test [4]. To participate in the following experiments, observers had to reach a value of 0.8 at least in one eye (equivalent to 20/25 Snellen fraction). Four patients and two control subjects did not pass this test and had to be excluded at this stage.

Vernier duration

To introduce observers to the experimental paradigm and to assess individual vernier durations, we presented verniers for various durations without a grating following (Fig. 1, step 1). For each observer, we tried to find the vernier duration for which the threshold of vernier offset discrimination was about 40″ (arc sec). Verniers were presented for 150 ms or 100 ms in the first block for all observers. In the following, we reduced the vernier duration blockwise when thresholds for offset discrimination were below the predefined value of 40″ while increasing it otherwise.

These vernier durations were used in the following experiments for each observer individually. To join the following experiments, a vernier duration shorter than 100 ms had to be reached. Three patients did not meet this predefined criterion and were excluded.

Standard condition (SOA)

Sixteen patients and 16 controls passed the two previous tests and joined the next condition: A vernier was followed by a grating comprising 25 aligned verniers, i.e. verniers without offset (standard grating). For each observer, we used the vernier duration as determined in the last condition. The horizontal distance between grating elements was about 3.33′, thus, total length of the grating was 1.3 deg. The vernier and the central element of the grating appeared always in the middle of the screen. Gratings lasted for 300 ms. We assessed adaptively the target-mask SOA to yield a performance level of 75% correct responses for a vernier with a constant offset size of about 1.19′. The SOA is defined as the difference between grating and vernier onset, i.e. vernier duration plus inter-stimulus-interval (ISI; Fig. 1). The SOA was determined by the adaptive procedure Parameter Estimation by Sequential Testing (PEST; [41]). Hence, we directly determined the masking effect in one block of 80 presentations and did not determine performance for a set of SOAs separately. Two thresholds were determined and the mean of both SOA thresholds was used in the following experiments for each observer individually.

Contextual elements

In the next step, we presented contextual elements simultaneously with the standard 25 element grating, i.e. for 300 ms. In all conditions, we determined vernier offset discrimination by means of the adaptive method PEST [41]. Thresholds were determined as the vernier offset size for which 75% correct responses were reached. Hence, in this part of the experiment spatial instead of temporal thresholds were measured.

In the first condition, we presented one collinear line below and one above the central element of the grating (Fig. 2a). Lines were 6.66′ long and separated from the grating by a gap of 3.33′. In the second condition, one horizontal line was displayed below and one above the grating (Fig. 2b). These horizontal lines were directly attached to the grating, i.e. the tips of the grating touched these lines. In the third condition, the collinear lines of the first condition were presented together with the horizontal lines of the second condition (Fig. 2c).

The first experiment took about 50 min.

No backward masking

In a second experiment, we determined the effects of single contextual lines on vernier discrimination without backward masking. In the first condition, the vernier was presented alone with the individual duration as determined before. We determined offset discrimination thresholds as in the last conditions. In the second condition, we added one single contextual line above and one below the vernier. These lines were presented simultaneously with the vernier, i.e. for the same duration. Fourteen patients and controls participated. All patients and eleven controls have joined the first experiment. Three new controls participated in addition.

The second experiment lasted 15 min.

Statistical analysis

The data were analysed by means of repeated measures analyses. The comparison of the control condition and the contextual conditions was calculated with a within-subject factor of four levels and a between-subjects factor of two levels (patients vs. controls).

Performance in experiment 2 was analysed by means of a repeated measures analysis with two within-subject levels (condition) and two groups (patients vs. controls). All repeated measures analyses were corrected by the Greenhouse-Geisser formula, if necessary. In this case, degrees of freedom were truncated to integers [5].

Pairwise comparisons of the condition factor were corrected by the Bonferroni method. The repeated measures analyses were calculated first for the total sample and afterwards within each group (controls and schizophrenic patients, respectively) separately.

In order to check the impact of neuropsychological performance and medication on the perceptual performance of the schizophrenic patients, we calculated bivariate correlations between the standard condition and the CPT (d′), CVLT (long delay free recall) and WCST (categories) within the patient group.

Results

Psychopathology and neuropsychological tests

Demographical and psychopathological data (SANS and SAPS) as well as chlorpromazine equivalents are shown in Table 1. Positive (SAPS) and negative (SANS) symptoms were similar within the schizophrenic patients (8.94 ± 3.3 vs. 9.06 ± 5.01, respectively).

Table 1 Demographic and clinical data of schizophrenic patients and controls

	Schizophrenic patients	Healthy controls	*P*-value
N	16	16	
Gender (F/M)	4/12	8/8	
Age (years)	31.75 ± 7.29	31.06 ± 10.87	ns
Education (years)	12.13 ± 2.6	15.5 ± 3.98	0.008
Duration of illness (years)	8.34 ± 6.57		
CPZ (mg)	366.69 ± 346.14		
SANS	9.06 ± 5.01		
SAPS	8.94 ± 3.3		
CPT (d′)	2.9 ± 0.9		
CVLT (LDFR)	13.8 ± 2.7		
WCST (categories)	3.8 ± 1.4		

Vernier duration and SOA

In the unmasked condition, an ANOVA showed that the critical vernier duration for the patients was slightly longer than for the controls (Fig. 3; 31.9 ± 4.8 and 22.5 ± 1.9, respectively) with a tendency to significance ($F[1,30] = 3.9$, $P = 0.06$).

In the masked condition with the standard grating, threshold SOAs of the schizophrenic patients were substantially longer than those of healthy controls (Fig. 3; 106.9 ± 12.4 and 35.6 ± 4.2, respectively; $F[1,30] = 31.1$, $P \leq 0.0001$).

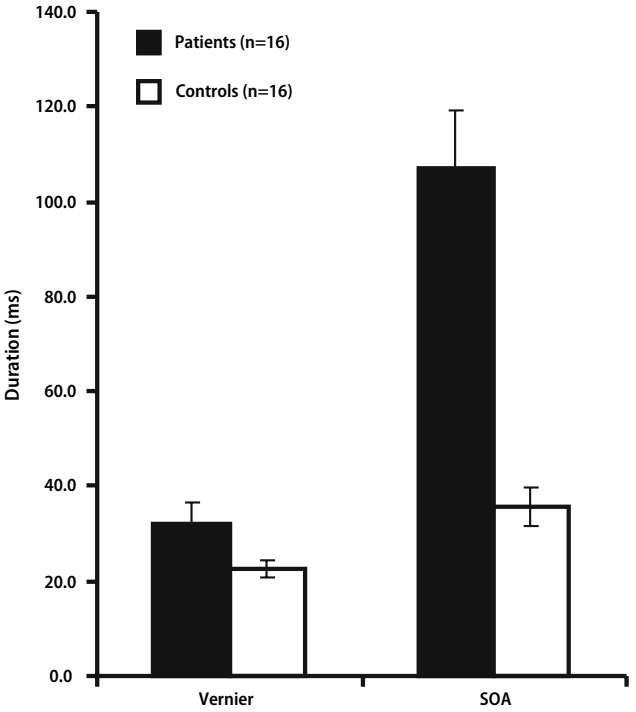

Fig. 3 Mean vernier duration and SOA (± std. err) for patients and controls. Patients need only slightly longer vernier durations in the unmasked, vernier only, condition and much longer SOAs than controls in the masked condition with the standard grating

Contextual elements

In the contextual conditions, we determined spatial vernier discrimination thresholds, i.e. we determined the offset size for which 75% correct responses were reached. We computed a repeated measures analysis with a within-subjects factor (four conditions) and a between-subjects group factor (patients vs. controls). We found a highly significant condition factor ($F[1,53] = 89.0$; $P < 0.0001$) and a significant group factor ($F[1,30] = 11.9$; $P = 0.002$) but no significant interaction. Also within each single group (patients and controls), the condition factor was highly significant ($F[2,30] = 53.3$; $P < 0.0001$ and $F[1,21] = 36.2$; $P < 0.0001$, respectively).

Adding vertical contextual lines to the 25 element grating yielded a strong threshold elevation in both groups [Fig. 4b; Bonferroni corrected pairwise comparison $P < 0.0001$ (patients) and $P < 0.0001$ (controls)]. If long horizontal lines were added to the standard grating no or only a slight threshold elevation occurred (Fig. 4c). If vertical and horizontal lines were combined, performance was within that of the two former conditions with significant differences to condition B and C (Fig. 4d; condition B vs. D: $P = 0.007$ (patients), $P = 0.01$ (controls); condition C vs. D: $P < 0.0001$ (patients), $P < 0.0001$ (controls)). This is the major result of this investigation showing that horizontal lines can diminish the suppression exerted by contextual vertical lines (Fig. 4d).

By adjusting individual vernier durations and SOAs, we aimed to reach a comparable performance level across all participants in the basic 25 element grating condition (Fig. 4a). However, schizophrenic patients performed worse than the controls; this result

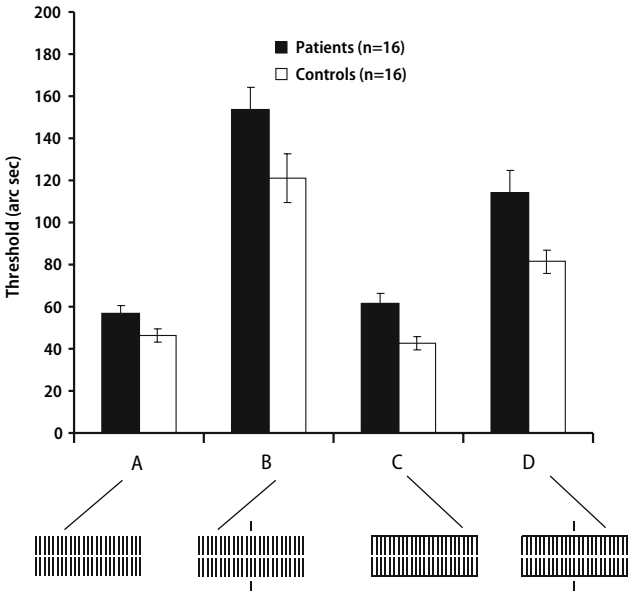

Fig. 4 Results of patients and controls for different contextual gratings. (**a**) Standard condition. As aimed, performance between groups is roughly comparable reflecting the individually adjusted SOAs. (**b**) Performance strongly deteriorates by adding single collinear lines. (**c**) Horizontal contextual lines yield a performance level comparable to the standard condition (**a**). (**d**) Combining vertical and horizontal lines from the conditions (**b**) and (**c**) leads to an improvement of performance compared to (**b**)

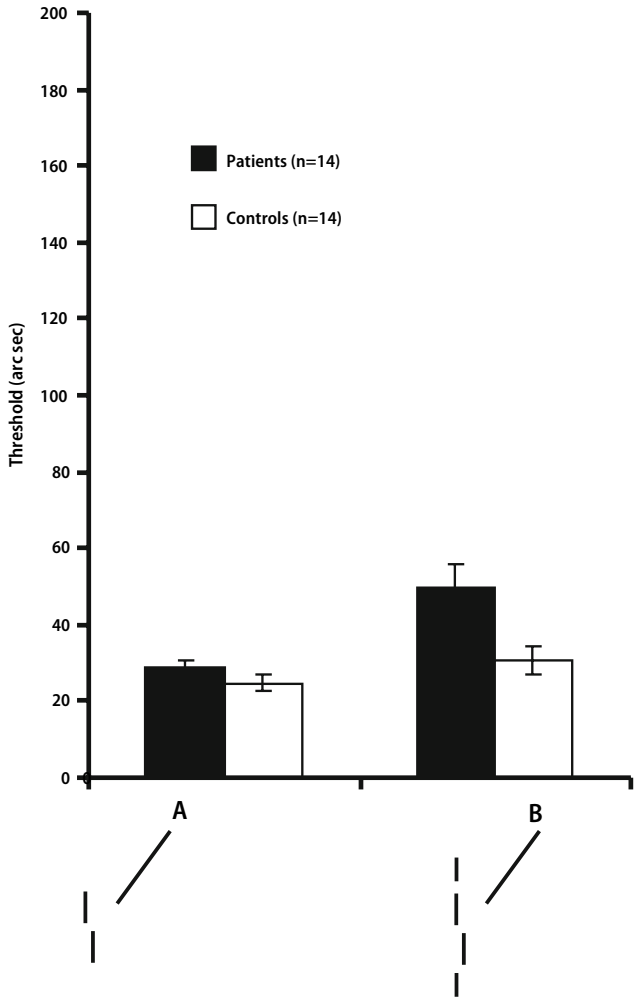

Fig. 5 (**a**) We determined vernier offset discrimination thresholds without a masking grating (the individual vernier duration of each observer was determined in the previous experiment). Patients and controls perform roughly comparable. This result is not surprising because vernier durations were adjusted individually. (**b**) We added single collinear lines to the vernier. Whereas performance for controls is virtually not affected by this manipulation, patients show a threshold elevation

can possibly be explained with the highly variant performance in schizophrenic patients yielding often unstable results; indeed, with the very same procedure, patients performed slightly *better* than controls in a previous study [38]).

In the second experiment, we compared performance with a vernier only and this vernier accompanied by two collinear lines (both without grating) in 14 patients and 14 controls. With the vernier only, performance of both groups was comparable ($F[1,26] = 1.7$, $P = 0.2$) whereas with additional collinear lines, schizophrenic patients needed a larger offset (Fig. 5; $F[1,26] = 6.7$, $P = 0.02$; indicated by a significant interaction of group by condition: $F[1,26] = 4.7$, $P = 0.04$). Moreover, there was a significant condition effect ($F[1,26] = 14.7$, $P = 0.001$) and a significant group effect ($F[1,26] = 6.9$, $P = 0.02$). Both effects were caused by the differences in the condition with the collinear lines.

Within the schizophrenia group, there were no significant correlations between the standard condition and the WCST and the CVLT, the degraded CPT showed a tendency to statistical significance (d′: $r = -0.51$; $P = 0.06$). Neither there was a significant correlation between the standard condition and medication (CPZ).

Discussion

In accordance with previous studies, backward masking performance is seriously deteriorated in schizophrenic patients (e.g. [6, 8, 16, 17, 26, 29, 37, 39, 40, 44, 45]). Patients need clearly longer SOAs to reach a performance level comparable to healthy controls in the standard condition (Fig. 3) [21].

As shown previously [38], if these longer SOAs are adjusted individually, patients show a comparable deterioration of performance when vertical contextual lines are presented indicating strong contextual suppression. This conclusion is further supported by the second experiment in which collinear lines accompanied the vernier without a masking grating (Fig. 5 b). With these collinear lines, a threshold elevation occurred for the patients but not for the controls indicating an even more pronounced effect in the patients (Figs. 4, 5) whereas contextual facilitation was found to be weakened in schizophrenic patients (e.g. [12, 23, 36]). A straightforward explanation is that neural excitation is affected by schizophrenia whereas neural inhibition is not.

The goal of the present study was to further explore this hypothesis by testing whether contextual suppression can be counteracted by "protective" means, hence, to pit, presumably, inhibitory against non-inhibitory neural mechanisms.

For this, we presented horizontal contextual lines above and below the standard grating (Fig. 4c). These lines do virtually not change performance in both patients and controls. In this respect, the lines can be considered as "neutral", i.e. neither suppressive nor facilitative. Interestingly, when these horizontal lines are combined with the vertical lines, they significantly weaken contextual suppression as reflected by the lower thresholds in both populations (Fig. 4b, d). Hence, not only contextual suppression is intact but also these protective, non-inhibitory mechanisms indicating a rather complex intact spatial processing (see also [9, 10]).

One limitation of our study is the small sample size. Studies with larger samples are needed to investigate the complex spatial interactions involved in our paradigm and compare the results, with psychopathological and demographic parameters.

It is important to note that comparable performance in contextual processing between patients and

controls relies on highly different SOAs between groups. Patients need about three times longer SOAs than controls (Fig. 3). It is surprising that, even after such a long duration, the standard grating can make an impact on performance. It is even more surprising that contextual elements can potentiate this effect and "protective" elements in turn, can counteract it. If the masks of Fig. 2 would be presented to the controls using the SOAs of the patients, performance would not differ across conditions. For example, thresholds in the standard condition and the condition with collinear lines would be on a comparable, low performance level.

Contextual interactions, with comparable paradigms, as used here, were found to have a neural base in the primary visual cortex in the awake behaving monkey (e.g. 22, 24, 25]. Hence, it may be that our investigations open a window to understand how schizophrenia alters the circuits of early visual processing. Exactly characterizing these aberrancies is of fundamental importance since early processing defects may affect later, for example, cognitive processing.

However, at the current stage, we can only speculate about the underlying mechanisms. We suggest that all kinds of suppressive mechanisms, possibly related to neural inhibition, are intact. However, also more complex processing seems to be spared, for example, related to the spatial interactions between vertical and horizontal contextual lines, which possibly are not be based on inhibition only (see also [21]). On the other hand, there is clear evidence that contextual facilitation is deteriorated [12, 23] and patients need clearly longer SOAs in our paradigm. Therefore, the deficits of schizophrenic patients may, possibly, be too complex to be described with the deficits related to one system such as inhibition or excitation only. However, as mentioned, these considerations remain speculation at the current stage.

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