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Research Paper

Intact and deficient contextual processing in schizophrenia patients

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ABSTRACT

Schizophrenia patients are known to have deficits in contextual vision. However, results are often very mixed. In some paradigms, patients do not take the context into account and, hence, perform more veridically than healthy controls. In other paradigms, context deteriorates performance much more strongly in patients compared to healthy controls. These mixed results may be explained by differences in the paradigms as well as by small or biased samples, given the large heterogeneity of patients' deficits. Here, we show that mixed results may also come from idiosyncrasies of the stimuli used because in variants of the same visual paradigm, tested with the same participants, we found intact and deficient processing.

1. Introduction

Numerous studies have reported that schizophrenia patients have deficits in utilizing visual contextual information (Seymour et al., 2013; Tibber et al., 2013; review: Silverstein and Keane, 2011). For example, studies have shown diminished susceptibility to illusions in patients (e.g., depth inversion illusion: Keane et al., 2013; apparent motion: Sanders et al., 2013; Ebbinghaus illusion: Uhlhaas et al., 2006). However, Grzeczkowski et al. (2018), Kaliuzhna et al. (2019), Yang et al. (2013), and Tibber et al. (2013) found intact illusion perception, whereas Kantrowitz et al. (2009), Chen et al. (2008), and Frith and Friston (2013) found increased susceptibility. Results are clearly mixed (review: King et al., 2017; Notredame et al., 2014). Diminished dependency on contextual information can make perception even more veridical in schizophrenia patients. Dakin and colleagues (2005) presented a medium-contrast patch within a high-contrast surround. Controls perceived the contrast of the patch as largely lower than the true contrast, whereas schizophrenia patients reported a value closer to the true contrast, even though contrast discrimination itself has strongly deteriorated in schizophrenia patients (Must et al., 2004; Slaghuis, 1998). These results are usually explained in terms of weaker modulation of cortical responses in the primary visual cortex (Anderson et al., 2017; Seymour et al., 2013) or by biased expectations (or priors) in early visual areas (Frith and Friston, 2013). However, results are again mixed. Kaliuzhna et al. (2019) showed that perceptual judgments are rather biased in accordance with natural scenes' probability distributions.

Another example of visual contextual modulation is crowding. In crowding, target perception is largely impaired when presented together with flankers (review: Herzog et al., 2016; Levi, 2008; Pelli and Tillman, 2008; Strasburger, 2020). Schizophrenia patients showed less crowding (Kraehenmann et al., 2012; Robol et al., 2013). However, we found recently that crowding was intact or even stronger in the patients (Roinishvili et al., 2015). Hence, results are mixed here too.

In all of the above studies, context acted only uni-directionally, e.g., making perception less veridical. These results can be explained by many mechanisms, some of which are not necessarily visual, such as diminished attention to the target (e.g., Barch et al., 2012). We have recently used a “bidirectional” crowding paradigm where adding contextual elements first deteriorated performance, but adding further elements improved performance (Chicherov and Herzog, 2015; Chicherov et al., 2014; Doerig et al., 2019; Herzog and Manassi, 2015; Herzog et al., 2015, 2016; Malania et al., 2007; Manassi et al., 2012, 2013, 2015, 2016; Saarela et al., 2009; Sayim et al., 2008, 2010, 2011; Choung et al., 2019, 2021; Doerig et al., 2019). With this crowding and uncrowding paradigm, patients showed almost the same performance as controls, except for an unspecific target processing deficit (Roinishvili

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et al., 2015). In this paradigm, next to basic vision processing, grouping and Gestalt processing are key (Bornet et al., 2021; Choung et al., 2021, submitted; Doerig et al., 2019; Doerig et al., 2020a; Francis et al., 2017), which seem to be intact in the patients (Favrod et al., 2022).

Hence, it remains unclear whether or not there are general contextual deficits in schizophrenia. Here, we propose that there are no general impaired mechanisms but that deficits depend strongly on idiosyncrasies of the specific stimuli.

2. Materials and methods

2.1. Participants

Seventeen schizophrenia patients and 16 age-matched unaffected participants took part in the two experiments. Patients were recruited from the Tbilisi Mental Health Center. Age and gender-matched controls were recruited from the general population in Tbilisi. Patients were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV/V), based on the Structured Clinical Interview for DSM-IV/V (Clinician Version), information from the staff, and the study of the records. Psychopathology of schizophrenia was assessed by an experienced psychiatrist (EC) by the Scales for the Assessment of Negative Symptoms and Scales for the Assessment of Positive Symptoms (SANS, SAPS; Andreasen, 1984, 1989). Two schizophrenia patients and one control participant were excluded because of poor eye fixation. Hence, we retained the data of 15 participants from each group. Group characteristics are presented in Table 1. All participants had normal or corrected to normal visual acuity in the Freiburg Visual Acuity Test (FrACT), as indicated by a binocular score >1.0 (Bach, 1996). Participants gave written consent before the experiment. All experiments were conducted following the Declaration of Helsinki except for the preregistration (World Medical Association, 2013) and were approved by the local ethics committee (Tbilisi mental Health Center, independent Ethics committee, Georgia).

2.2. Apparatus

Stimuli were displayed on an LCD screen (ASUS VG248QE, Taipei, Taiwan; screen resolution 1920 × 1080 pixels). The room was dimly illuminated (0.5 lx). The viewing distance was 75 cm, and the participant's chin and forehead were positioned on a chin-rest. Responses were collected using hand-held push buttons. Participants' eye movements were tracked with a The Eye Tribe eye tracker (60 Hz sampling frequency, The Eye Tribe, Copenhagen, Denmark), and stimuli were displayed only when participants adequately fixated.

2.3. Stimuli

Stimuli were white (100 cd/m^2) and presented on a black background with luminance below 0.3 cd/m^2. Participants were asked to fixate on a red fixation dot (diameter of 8 arcmin, 20 cd/m^2). Stimuli were presented for 150 ms in experiment 1 and 42 ms to 642 ms in experiment 2. When no response was registered within 3 s, the trial was repeated randomly within the same block. A feedback tone was given for incorrect responses (600 Hz) and omissions (300 Hz). Vernier stimuli were composed of two vertical bars. Each bar was 40 arcmin long, 1.8 arcmin wide (anti-aliased), and separated by a 4 arcmin gap. Left/right offsets of vertical verniers were balanced within a block. Flankers were either lines, combinations of squares and stars, or cuboids. In experiment 1, the target Vernier was surrounded by one square in all conditions. Flanker configurations were composed of squares and stars. Squares were composed of 96 arcmin long lines, stars were composed of seven 38.4 arcmin long lines, and the center-to-center distance between two flankers was 120 arcmin. In experiment 2, two vertical lines or two cuboids were presented to the left or the right of the Vernier target with a distance of 23.33 arcmin. Lines were 84 arcmin long; cuboids' width was 116.67 arcmin, height was 84 arcmin, and the oblique line's angle was 135° with a length of 47.14 arcmin.

Each configuration was presented at the center of the screen, and the fixation dot was presented at an eccentricity of 6° to the left, i.e., the stimulus was presented in the periphery. Psychophysics Toolbox was used to present the stimuli (Brainard, 1997; Kleiner et al., 2007; Pelli and Vision, 1997).

2.4. Procedures

2.4.1. General procedure

Two experiments were carried out on two days within a week. In both experiments, participants were asked to discriminate the Vernier offset direction of the lower bar compared to the upper bar. Different flanking configurations were tested 160 times in two sessions (80 trials per session). To reduce target-location uncertainty, only the target was presented alone for 150 ms at the beginning of each block. We used the PEST stair-case procedure (Taylor and Creelman, 1967). In PEST, test levels are changed step-wise based on the recent response history. The current test level is only changed when the percentage of correct responses for this test level lies, with some certainty, above or below the threshold criterion of 75 %. After 80 trials, we ended the procedure and derived the threshold from the psychometric function fitted to the data post-hoc (details in *Data analysis*). We randomized the order of experimental conditions across participants.

2.4.2. Experiment 1

7 flanker configurations were tested. The configurations were as follows: Vernier alone, Vernier surrounded by one square, Vernier with 7 horizontally aligned squares, Vernier with 35 squares (5 × 7 grid), Vernier with 3 squares and 4 stars, Vernier with 9 squares and 12 stars, and Vernier with 11 squares and 10 stars (Fig. 1). The 7 configurations were tested in a blockwise manner. Therefore, two sessions of 7 blocks each were tested, and all 7 configurations were tested in each session. The order of blocks within the session was randomized.

2.4.3. Experiment 2

Two flanker configurations (Vernier with two lines and Vernier with two cuboids) with four different stimulus durations (42 ms, 83 ms, 158 ms, and 642 ms) were tested. Each configuration was tested within a session, stimulus durations were randomized within the session. Each configuration with each stimulus duration was tested twice (80 trials each). Thus, each session was composed of 4 blocks of 80 trials, and there were 4 sessions. The experimental order was line flankers, cuboid flankers, cuboid flankers, and line flankers session.

Table 1
Group average statistics (±SD) of patients and controls. SANS stands for Scale for the Assessment of Negative Symptoms. SAPS stands for Scale for the Assessment of Positive Symptoms. CPZ stands for chlorpromazine.

	Age	Gender (F/M)	Education (years)	Handness (L/R)	Illness duration (years)	SANS	SAPS	CPZ
Patients	39.1 ± 9.5	5/10	13.5 ± 3.3	1/14	15.6 ± 8.8	7.2 ± 3.4	8.1 ± 2.4	421.9 ± 265.2
Controls	38.3 ± 8.0	5/10	14.6 ± 2.4	0/15				

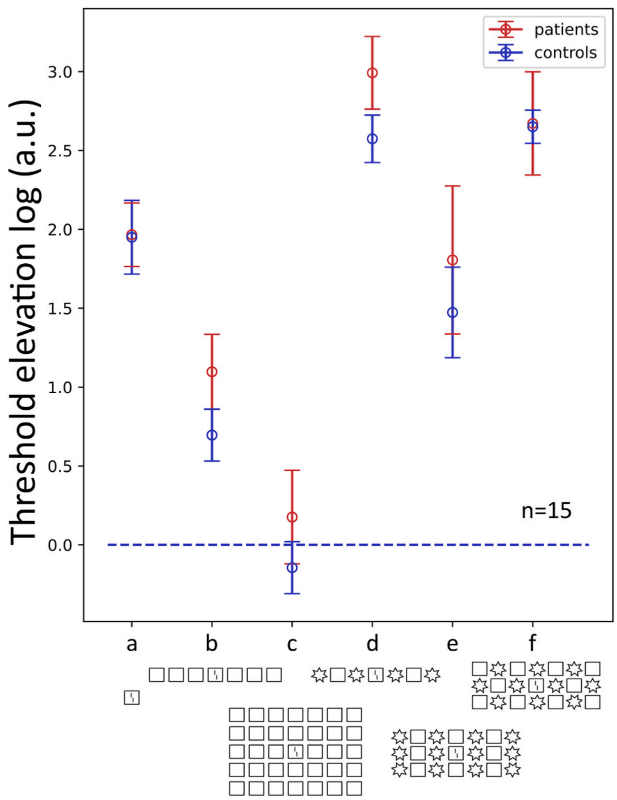

Fig. 1. Experiment 1. The y-axis shows mean of log-transformed threshold elevation (±SEM) relative to the unflanked (Vernier alone) condition (blue and red dotted lines equal to 0). Large thresholds represent poor performance (strong crowding), and low thresholds represent good performance (weak crowding). Patients and controls perform similarly. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

2.5. Data analysis

We fitted a cumulative Gaussian function (psychometric function) to the data (tested levels and hit rates) and determined the vernier offset for which 75 % correct responses were reached (threshold). Psignifit 2.5 toolbox (Fründ et al., 2011) was used for the fitting. High thresholds indicate inferior performance, and low thresholds indicate good performance. Next, we divided the threshold in each condition by the threshold in the Vernier alone condition (threshold elevation). Data were log-transformed to bring the data closer to normality. No obvious violation of normality was detected by visual inspection.

Using R (R Core Team, 2019) and *lme4* package (Bates et al., 2015), we computed linear mixed-effects models (LMM) to account for dependent variables and random variations due to individual differences. The fixed and random effects are specified for each experiment (see *Results* for specifications of each experiment). Significance was obtained through likelihood ratio tests (χ^2) by comparing nested models. For each fitted model, using *MuMIn* package (Barton, 2020), we computed the effect size (r^2), i.e., the explained variance, when including (conditional r_c^2) and excluding (marginal r_m^2) the random effects (Johnson, 2014; Nakagawa et al., n.d.; Nakagawa and Schielzeth, 2013).

3. Results

3.1. Experiment 1. Intact (Un)crowding in schizophrenia patients

Similar to previous findings (Roinishvili et al., 2015), schizophrenia patients showed similar crowding behavior as controls. When the Vernier target was surrounded by a simple flanker (square), the target was strongly and similarly crowded in both the patient group and control group (Fig. 1a). Patients' and controls' performance improved by adding three squares on the left and right sides of the center square (7-square; Fig. 1b). By presenting the Vernier with a grid of squares (35 squares; Fig. 1c), performance improved almost to the level of the Vernier only condition (Fig. 1 dotted lines). Crowding was strong when presenting squares and stars alternatively (Fig. 1d, e, f). Overall, performance of patients and controls were comparable in all conditions.

To analyze the relation between threshold elevation and configuration depending on the two groups, we computed an LMM with the 7 flanker configurations and the 2 groups (patients and controls) as fixed effects (Fig. 1a-f). Individual participants were considered as random intercepts. We found no significant interaction between the two fixed effects (likelihood ratio test between an additive and an interaction model: $\chi^2(5) = 2.070$, $p = 0.839$). The configurations showed clear and significant differences (configurations: $\chi^2(5) = 155.264$, $p < 0.001$), but there was no significant difference between the two groups (groups: $\chi^2(1) = 0.979$, $p = 0.322$). Although the absence of evidence is not evidence of absence, our results suggest that patients perform complex crowding tasks similarly to controls. Moreover, the difference of explained variance by the models with and without the group as a fixed effect is only 0.8 % ($r_m^2 = 0.491$, $r_m^2 = 0.483$). The detailed estimates are reported in Supp. Table 1.

3.2. Experiment 2. Deficient time-consuming processing in schizophrenia patients

As reported in previous works, grouping requires recurrent processes (Doerig et al., 2020b; Sayim et al., 2010, 2014), which may be abnormal in the patients. Hence, we tested two flanker configurations with four stimulus durations. Two configurations were two lines and two cuboids (Fig. 2 left & right). Note that both flanker configurations contained the two lines next to the target Vernier. In both the control group and patient group, performance did not improve by increasing the stimulus duration for line flankers, whereas performance improved significantly by increasing the stimulus duration for cuboid flankers. However, performance improvement for the cuboid flanker condition in the patient group required more time than in the control group.

To analyze the effects of stimulus duration and groups on Vernier threshold elevation for each condition separately, we used an LMM with stimulus duration (42, 83, 158, 642 ms) and population groups (controls and patients) as fixed effects. Individual participants were considered as random intercepts. For line the flanker condition, we found no significant interaction between the two fixed effects (likelihood ratio test between an additive and an interaction model: $\chi^2(1) = 1.553$, $p = 0.213$). Stimulation duration showed a significant effect (stimulus duration: $\chi^2(1) = 43.784$, $p < 0.001$), whereas the population group only showed marginal significance (groups: $\chi^2(1) = 4.479$, $p = 0.034$). For the cuboid flanker condition, we found a significant interaction between the two fixed effects (likelihood ratio test between an additive and an interaction model: $\chi^2(1) = 8.559$, $p < 0.01$). Therefore, the effect of stimulus duration should be considered per group. The detailed estimates are reported in Supp. Tables 2 and 3.

To closely dissect the effect of stimulus duration per participant, we fitted individual participants' threshold elevation levels against the stimulus duration with a regression line. Then, we compared the fitted slope values between the groups. For the control group in the line flanker condition, the fitted slope values' 25th, 50th, and 75th quantiles were −0.296, −0.201, and −0.165, respectively (r^2=0.677 ± 0.065). For the patient group in the line flanker condition, the fitted slope values' 25th, 50th, and 75th quantiles were −0.344, −0.107, and 0.000, respectively (r^2=0.790 ± 0.068). There was no significant difference between the two groups ($t(28) = 0.848$, $p = 0.404$, $d = 0.310$). With line flankers, the performance was bad in both groups, regardless of the stimulus presentation time.

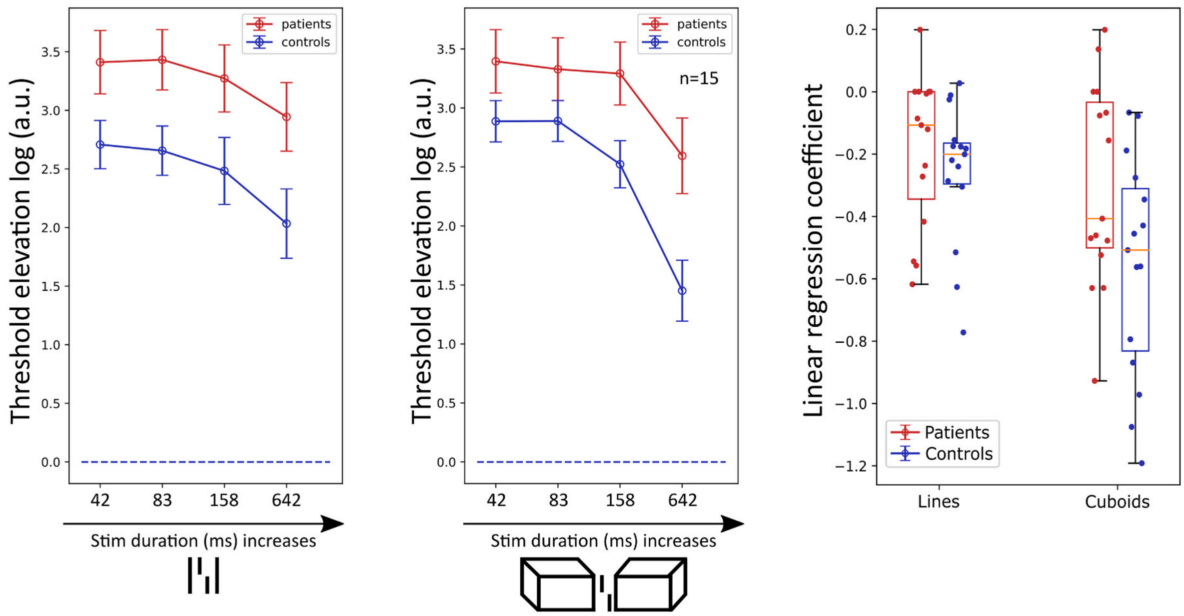

Fig. 2. Experiment 2. Left & middle, the y-axis shows mean of log-transformed threshold elevation (±SEM) relative to the unflanked (Vernier alone) condition (blue and red dotted lines equal to 0). Larger thresholds represent poor performance (strong crowding), and smaller thresholds represent good performance (weak crowding). Right, beta coefficients for linear regression of each participant. The y-axis shows the linear regression coefficient. Close-to-zero coefficient (gray dotted line) means the performance did not change by increasing the stimulus duration. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

In the cuboid flanker condition, we found a group difference. For the control group, the fitted slope values' 25th, 50th, and 75th quantiles were −0.831, −0.508, and −0.311, respectively ($r^2 = 0.789 \pm 0.041$). For the patient group, the fitted slope values' 25th, 50th, and 75th quantiles were −0.501, −0.407, and −0.034, respectively ($r^2=0.733 \pm 0.070$). There was a significant difference between fitted slope values ($t(28) = 2.077$, $p = 0.047$, $d = 0.758$). The significant difference shows that performance improves significantly more in the control than patient group by increasing the stimulus time.

In summary, we found that, in the uncrowding condition (cuboid flanker condition), patients' performance improves less than that of control participants when increasing the stimulation duration. Thus, the data shows that patients have mainly a quantitative but not a qualitative deficit in processing the line flankers and a quantitative and qualitative deficit with the cuboid flankers.

4. Discussion

Contextual processing is often seriously impaired, and various mechanisms were proposed to explain these effects in schizophrenia; such as reduced surround suppression (Anderson et al., 2017; Seymour et al., 2013), or abnormal expectations (or priors) (Friston, 2005; Frith and Friston, 2013; Sterzer et al., 2018). However, the results are mixed. Hence, it is unclear whether or not the proposed mechanism is, indeed, at work and whether it is impaired in schizophrenia patients. Mixed results may come from biased sampling, and unspecific non-visual aspects, among others. Alternatively, there may not be *one* abnormal mechanism for contextual vision in general. Here, we have shown evidence for this latter hypothesis. We found that the same patients can have intact processing in one paradigm (Exp. 1, Fig. 1) but deficient processing in a variant of the very same paradigm (Exp. 2, Fig. 2). This result rules out unspecific aspects, such as diminished attention and biased sampling since the very same observers participated in all the experiments. It may well be that the small changes in the spatial layout of the crowding stimuli lead to the involvement of different mechanisms, of which only some are abnormal. Hence, claims about abnormal mechanisms should be verified with more than one paradigm. On the other hand, our results offer the opportunity to pit intact and deficient processing against each other within one paradigm and, thus, unearth specific abnormal mechanisms.

We like to mention that it is important to publish null results, such as the ones of intact processing in Fig. 1. Since patients usually perform worse than controls, a significant group difference always indicates a deficit, which may lead to the impression that patients are deficient in most paradigms. However, this is not the case.

Interestingly, patients show strong crowding (Fig. 1, a, d, f, and Fig. 2 left: line flanker) and uncrowding (Fig. 1, b, c, e, and Fig. 2 middle: cuboid flanker), similar to the control group, suggesting that complex grouping and Gestalt processing are intact. However, in Exp. 2, we found a significant difference in the time-consuming recurrent processing. Indeed, for the cuboid condition, where control participants have uncrowding with longer stimulus duration, schizophrenia patients needed longer stimulus duration to have uncrowding (cuboid condition, Fig. 2 middle). Importantly, uncrowding in patients was intact. However, the sample size is small (15 per group). Our results point to the possibility that some configurations of the stimuli might reveal clear-cut group effects, which might provide a ground for investigating putative underlying mechanisms. However, we suggest that group effects on certain configurations of stimuli might be driven by idiosyncratic aspects of the paradigm rather than by a common disease-related mechanism. We need to mention that also in Exp. 1 processing is most likely not feedforward and relies on grouping.

The results of Exp. 2 are in accordance with previous results, where specific complex processing is intact, but there is a main deficit (Brand et al., 2005; Lauffs et al., 2016; Roinishvili et al., 2015; Schütze et al., 2007). Importantly, this deficit cannot come from target processing per se because the performance in the vernier alone condition was only slightly deteriorated. What causes this general deficit remains an enigma.

CRediT authorship contribution statement

Oh-Hyeon Choung: idea and conceptualization, methodology, software, data curation, formal analysis, writing original draft and revision, visualization.

Dario Gordillo: formal analysis, writing original draft and revision, visualization.

Maya Roinishvili: idea and conceptualization, resources, data curation and collection, writing original draft.

Andreas Brand: conceptualization, writing original draft and revision.

Michael H. Herzog: idea and conceptualization, writing original draft and revision, supervision, project administration, funding acquisition.

Eka Chkonia: resources, data curation, writing original draft and revision, project administration, funding acquisition.

Declaration of competing interest

The authors (OHC, DG, MR, AB, MHH, and EC) declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scog.2022.100265.

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