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## What's in a face? Effects of stimulus duration and inversion on face processing in schizophrenia\*

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### Abstract

A number of studies show deficits in early-stage visual processing in schizophrenia. Deficits are also seen at more complex levels, such as ability to discriminate faces. This study investigated the “face inversion” effect, which reflects intrinsic cortical processing within the ventral visual stream, as well as contrast sensitivity, which reflects low-level visual processing, in order to evaluate integrity of specific stages of face processing in schizophrenia. Patients with schizophrenia and controls discriminated between pairs of upright or inverted faces or houses that had been manipulated to differ in the shape of the parts or the spatial distance among parts. The duration threshold for above chance performance on upright stimuli was obtained for patients using a house discrimination task. Contrast sensitivity was assessed for gratings of three spatial frequencies ranging from 0.5 to 21 cycles/degree. Patients needed significantly longer time to obtain 70% correct for upright stimuli and showed decreased contrast sensitivity. Increased duration threshold correlated with reduced contrast sensitivity to low (magnocellular-biased) but not medium or high spatial frequency stimuli. Using increased durations, patients showed significant inversion effects that were equivalent to those of controls on the face part and spacing tasks. Like controls, patients did not show inversion effects on the house tasks. These findings show that patients have difficulty integrating visual information as shown by increased duration thresholds. However, when faces were presented at these longer duration thresholds, patients showed the same relative processing ability for upright vs. inverted faces as controls, suggesting preserved intrinsic processing within cortical face processing regions. Similar inversion effects for face part and spacing for both groups suggest that they are using the same holistic face processing mechanism.

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**Contributors:** Drs. Butler, Yovel, Kanwisher, and Javitt and Ms. Tambini designed the study, wrote the protocol, managed the literature searches, and undertook the analyses. Dr. Yovel made the stimuli and designed the original task that this study was based on. Ms. Silipo recruited participants. Ms. Tambini, Ziwich, and Jalbrzikowski collected data. Ms. Tambini, Ziwich, Jalbrzikowski and Silipo managed the data. All authors contributed to and approved the final manuscript.

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## Keywords

Schizophrenia; Face inversion effect; Visual; Magnocellular; Fusiform face area

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## 1. Introduction

Schizophrenia is associated with deficits in visual processing that represent a key feature of the disorder. Deficits are observed at both relatively basic levels of visual processing, such as the ability to discriminate gratings or detect contrast and motion (Butler et al., 2005; Chen et al., 1999; Slaghuis, 1998), as well as at more complex levels, such as the ability to discriminate faces (Addington and Addington, 1998; Kerr and Neale, 1993). The functional anatomy of such deficits remains an area of active investigation. The present study uses a phenomenon termed the “face inversion” effect to evaluate integrity of specific stages of face processing in schizophrenia.

Visual systems begin in the retina and project through lateral geniculate nucleus to cortex. At subcortical levels, visual systems are segregated into discrete magno- and parvocellular systems. Magnocellular neurons project predominantly to layers 4C $\alpha$  and 4B of primary visual cortex (V1) while parvocellular neurons project predominantly to 4C $\beta$  and superficial layers of V1. These subcortical pathways are differentiated based upon their anatomy and responsiveness to specific physical features such as contrast or spatial frequency (Kaplan, 2003). Deficits in early visual processing in patients with schizophrenia have been extensively documented over recent years (Dakin et al., 2005; Doniger et al., 2002; Krishnan et al., 2005; Spencer et al., 2003), particularly with regard to magnocellular processing (Butler et al., 2007; Butler et al., 2005; Keri et al., 2004; Slaghuis and Bishop, 2001).

At cortical levels, visual systems are segregated into dorsal and ventral visual streams. Magnocellular-recipient layers of V1 project preferentially, but not exclusively, to the dorsal visual pathway, which processes location and motion and guides visual attention. Parvocellular-recipient layers of V1 project preferentially to the ventral visual pathway (Lund, 1973; Merigan and Maunsell, 1993; Schroeder et al., 1998), which includes the fusiform face area (FFA). Ventral areas are involved with face and object identification. Significant interactions occur between these systems. In particular, information transfer through the magnocellular pathway and dorsal stream is faster than through the parvocellular pathway and ventral stream (Schroeder et al., 1998). Thus, information transmitted through the dorsal stream can enter and “prime” ventral stream areas. Significant deficits in schizophrenia have been observed on tasks that tap dorsal stream function, like motion detection (Brenner et al., 2003; Chen et al., 1999), as well as ventral stream processing, such as perceptual closure (Doniger et al., 2002). It has yet to be determined, however, whether visual cortical processing is impaired because of intrinsic dysfunction within dorsal or ventral stream cortical regions, or because of impaired input from subcortical visual systems (Butler et al., 2007).

The present study evaluates integrity of cortical visual processing using the “face inversion” effect, or the advantage for recognizing upright vs. inverted faces but not other objects (Yin, 1969). The advantage for processing upright vs. inverted faces is thought to be due to engagement of the fusiform face area (FFA), since the behavioral face inversion effect is correlated with the neural face inversion effect in the FFA only (not other face processing regions) and the FFA also shows differential sensitivity to upright vs. inverted faces (Yovel and Kanwisher, 2005). The advantage for upright vs. inverted faces thus may probe integrity of FFA functioning in individuals with schizophrenia vs. controls. Recent studies suggest that inversion effects are similar whether faces differ because of changes in specific parts or spacing between parts (Fig. 1), supporting theories that faces are processed holistically (i.e., face parts

are processed interactively instead of independently) (Farah et al., 1998; Yovel and Kanwisher, 2004). The present paradigm permits evaluation of these processes in patients. The paradigm also includes a non-face task (houses) that is psychometrically matched to the face task (Yovel and Kanwisher, 2004), permitting assessment of whether inversion effects in patients, like controls, are specific to the domain of faces.

In addition to indices of face/object processing, measures were collected that assessed integrity of visual function. These included first, the stimulus duration required for subjects to perform at threshold for object detection and second, contrast sensitivity for magnocellular-biased (low spatial frequency) and parvocellular-biased (medium/high spatial frequency) sine wave gratings. Relationships between duration threshold and contrast sensitivity were assessed to determine whether increased durations were related to deficits in visual pathway function. This study tests the hypothesis that the face inversion effect, which reflects intrinsic cortical processing within the ventral stream (Yovel and Kanwisher, 2005), will be normal in schizophrenia once visual input impairments in schizophrenia have been corrected for by increasing duration of presentation of face stimuli.

## 2. Experimental methods

### 2.1. Participants

Twenty-six patients meeting DSM-IV criteria for schizophrenia ( $n=21$ ) or schizoaffective disorder ( $n=5$ ) at inpatient and outpatient facilities associated with the Nathan Kline Institute and 32 controls participated ( $n=26$  for contrast sensitivity). Diagnoses were obtained using the Structured Clinical Interview for DSM-IV (SCID) and all available clinical information (First et al., 1977). Controls with a history of SCID-defined Axis I psychiatric disorder were excluded. Participants were excluded if they had any neurological or ophthalmologic disorders that might affect performance or met criteria for alcohol or substance dependence within the last six months or abuse within the last month. All patients were receiving antipsychotic medications at the time of testing. Clinical and demographic information are included in Table 1. The relatively high scores on symptom ratings and long duration of illness reflect patients with long-standing illness who are currently symptomatic, many of whom have negative symptoms. All patients were inpatients, with the exception of two outpatients. The patient and control groups did not differ significantly in age ( $t(56)=0.2$ ;  $p=0.87$ ) or parental socioeconomic status ( $t(48)=1.5$ ,  $p=0.13$ ), although they did differ significantly on IQ ( $t(49)=4.4$ ,  $p<0.001$ ) and gender ratio (Fisher's exact test,  $p=0.05$ ). All participants had at least 20/32 corrected visual acuity on the Logarithmic Visual Acuity Chart. After complete description of the study to the subjects, written informed consent was obtained.

### 2.2. Stimuli

Stimuli and procedure were the same as that of Yovel and Kanwisher (2004). Based on one face and one house, part and spacing sets were created resulting in four faces that differed from the original by using different eyes and mouths, four that differed in the spacing of the eyes and mouth, four houses that differed from the original by using different windows and doors, and four that differed in spacing of the windows and door (Fig. 1). Spacing among the parts was determined in pilot studies to yield similar performance levels across the faces and houses and the spacing and part tasks (4–5 pixels for faces and ~15 pixels for houses). The viewing distance was 45 cm. The faces subtended  $5.7\times 8.9^\circ$  of visual angle and the houses subtended  $7.6\times 8.9^\circ$  of visual angle.

### 2.3. Procedure

There were four separate conditions: upright face, inverted face, upright house, inverted house. Following a 500 ms fixation dot, the first and second stimuli were presented for the same

duration separated by a 1000 ms inter-stimulus interval. Participants said “same” or “different.” Each condition included a total of 80 randomized part and spacing trials, half of which contained pairs of non-matching stimuli and half contained pairs of the same repeated stimuli.

The upright house or face condition was presented before the inverted condition for all subjects. For control subjects, the order of stimuli (house/face) was counterbalanced with an exposure duration of 250 ms for all stimuli. This duration was chosen, based on previous pilot work in controls to yield performance levels that were not at ceiling or floor (about 75–80% correct) for the faces and houses. However, all patients performed the house conditions before the face conditions. Exposure duration was manipulated to increase patients' performance on either the upright house part or spacing task to at least 70% so that an inversion effect (if present) would be detected. Patients were initially shown upright houses for 250 ms. Exposure duration was increased in increments of 250 ms until 70% accuracy was achieved on one of the upright house tasks. That exposure duration was then used for all four conditions for that patient.

## 2.4. Contrast sensitivity

Spatial contrast sensitivity functions were obtained as previously described (Butler et al., 2005). Horizontal sine wave gratings were presented for 500 ms at 0.5, 7, or 21 cycles/degree on one half (either the right or left side) of a visual display, with the other side having a uniform field of equal space average luminance to the pattern field. The grating and uniform fields were presented simultaneously. The viewing distance was 160 cm and the gratings and uniform field together subtended  $5.7 \times 5.7^\circ$  of visual angle. Participants stated which side of the display contained the grating. Contrast was varied across trials using an up-and-down transformed response method to determine contrast sensitivity (the reciprocal of threshold) associated with 70.7% correct responses for each spatial frequency. Contrast was changed in 3 dB steps for each correct or incorrect response until two errors were made. Then the up-down transformed response rule began and contrast was changed in 1.5 dB steps. The mean of 10 reversals was used.

## 2.5. Statistical analysis

Percent correct performance was calculated based on 80 trials for each condition when results from part and spacing tasks were analyzed together (Sections 3.2 and 3.3 below). When part and spacing tasks were analyzed separately, percent correct performance was based on 40 trials for each task (Section 3.4). Between group differences were assessed with rmANOVAs. Gender was used as a covariate. Adding IQ as a covariate, which was also significantly different between groups, did not change the results. However, IQ scores were missing for some participants, so analyses are presented with only gender covaried so that all participants could be included. Non-parametric statistics (Mann–Whitney *U* test, Spearman's rank correlation) were used for analyses involving exposure time since this variable was not normally distributed.

## 3. Results

### 3.1. Exposure duration

Exposure duration results are shown in Fig. 2. All controls were able to perform at 70% or greater accuracy on the upright house task with a duration of 250 ms. In contrast, patients required a duration (mean $\pm$ SEM) of  $375 \pm 37.3$  ms (range: 250–750 ms) to obtain 70% correct on the upright house task leading to a significant between group difference (Mann Whitney *U*:  $Z = -3.6$ ,  $p < .001$ ).

### 3.2. Relative performance to upright houses vs. faces

Fig. 3 shows percent correct performance for house and face stimuli. A 2 Group (Patients, Controls)×2 Stimulus (Upright Face, Upright House) rmANOVA was used with percent correct as the dependent measure. There was a significant main effect of Group ( $F(1,55)=11.1$ ;  $p=0.002$ ), indicating that overall performance levels for upright faces and houses were lower in patients than controls even despite the duration titration. This indicates overall reduced accuracy in processing visual information independent of stimulus type. In the stimulus set used in this study, upright face and house stimuli had previously been matched for discrimination difficulty in controls (Yovel and Kanwisher, 2004). There was a significant main effect of Stimulus ( $F(1,56)=8.9$ ;  $p=0.004$ ), indicating that accuracy was greater for upright houses than faces across groups, although performance on upright houses and faces did not differ when only controls were considered ( $t(31)=1.6$ ;  $p=0.12$ ). Further, upright performance was in a sensitive range (i.e., not at floor or ceiling) for both groups for both stimulus types (Fig. 3). Patients showed no differential difficulty in processing faces vs. houses, as reflected in a non-significant Group×Stimulus interaction ( $F(1,56)=1.6$ ;  $p=0.2$ ).

### 3.3. Inversion effects for face and house stimuli

Fig. 4 shows inversion effects for face and house stimuli. Inversion effects (% correct upright – % correct inverted) were calculated based on data presented in Fig. 3 in order to specifically investigate the inversion effect. A 2 Group (Patients, Controls)×2 Stimulus (Inversion Effect for House, Inversion Effect for Face) rmANOVA was used with inversion effect as dependent measure. As predicted, there was no significant main effect of Group ( $F(1,55)=0.07$ ;  $p=0.8$ ), indicating that patients were as affected by inversion as controls. A between group *t*-test showed that patients were as affected by inversion as controls for face stimuli ( $t(56)=0.5$ ;  $p=0.6$ ). There was a highly significant main effect of Stimulus ( $F(1,56)=44.6$ ;  $p<0.001$ ), indicating significant inversion effects in both groups to faces but not houses. Using data from Fig. 3, within group matched pair *t*-tests showed that both patients and controls had higher accuracy for upright vs. inverted faces (controls:  $t(31)=6.5$ ;  $p<0.001$ ; patients:  $t(25)=4.07$ ;  $p<0.001$ ), whereas performance for upright vs. inverted houses was similar within each group (controls:  $t(31)=1.9$ ;  $p=0.07$ ; patients:  $t(25)=0.6$ ;  $p=0.5$ ). The Stimulus×Group interaction was also non-significant ( $F(1,56)=2.2$ ;  $p=0.14$ ), indicating similar differential face vs. house inversion effects across groups.

### 3.4. Relative performance to stimuli differing in spacing vs. parts

The stimulus set used in this study was designed to yield similar performance for stimuli that differed in spacing vs. parts (Yovel and Kanwisher, 2004), permitting assessment of processes specific for parts or spacing between parts vs. holistic processes. Fig. 5 shows inversion effects for face part and face spacing tasks. A 2 Group (Patients, Controls)×2 Task (Inversion Effect for Face Part, Inversion Effect for Face Spacing) rmANOVA was used with inversion effect (% correct upright – % correct inverted) as dependent measure. There was no significant main effect of Group ( $F(1,55)=0.5$ ,  $p=0.5$ ), indicating similar face inversion effects for both groups. A one-way *t*-test of inversion effects vs. zero showed significant inversion effects for both groups on the face part (controls:  $t(31)=4.5$ ;  $p<0.001$ ; patients:  $t(25)=3.5$ ;  $p=0.002$ ) and face spacing (controls:  $t(31)=5.7$ ;  $p<0.001$ ; patients:  $t(25)=3.8$ ;  $p=0.001$ ) tasks. Further, inversion effects were similar for part and spacing tasks, as shown by a non-significant main effect of Task ( $F(1,56)=1.2$ ;  $p=0.28$ ). Within group paired *t*-tests showed that face inversion effects did not differ for part vs. spacing tasks within each group (controls:  $t(31)=0.9$ ;  $p=0.4$ ; patients:  $t(25)=0.7$ ;  $p=0.5$ ). The similar inversion effects on part and spacing tasks indicate that mechanisms of face perception are stimulus specific for faces rather than process specific for spacing or parts and that a holistic process is being used. There was also no significant interaction between Group and Task ( $F(1,56)=.03$ ;  $p=.85$ ).

### 3.5. Contrast sensitivity

Basic visual processing was assessed using contrast sensitivity to low, medium and high spatial frequency sine wave gratings (Fig. 6A). A 2 Group (Patients, Controls)×3 Spatial Frequencies (0.5, 7, 21 cycles/degree) rmANOVA was performed with contrast sensitivity as the dependent variable. There were significant main effects of Group ( $F(1/49)=19.6$ ;  $p<0.001$ ), Spatial frequency ( $F(2/49)=304.1$ ;  $p<0.001$ ), and a significant Group×Spatial frequency interaction ( $F(2/49)=6.9$ ;  $p=0.002$ ). Post-hoc analyses of the main effect of Group showed that patients had impaired contrast sensitivity compared to controls ( $n=26$ ) at 0.5 ( $t(50)=2.9$ ;  $p=0.005$ ), 7 ( $t(50)=3.4$ ;  $p=0.001$ ) and 21 ( $t(50)=3.5$ ;  $p=0.002$ ) cycles/degree.

### 3.6. Correlations

**3.6.1. Contrast sensitivity**—A significant correlation was found between exposure duration necessary to obtain 70% correct performance on one of the upright house tasks and contrast sensitivity for the magnocellular-biased low spatial frequency (0.5 cycles/degree 500 ms) condition ( $r_s=-0.51$ ,  $n=26$ ,  $p=0.008$ ) (Fig. 6B). This correlation was not found at either 7 ( $r_s=0.09$ ,  $n=26$ ,  $p=0.64$ ) or 21 ( $r_s=-0.09$ ,  $n=26$ ,  $p=0.66$ ) cycles/degree.

**3.6.2. Medication**—There were no significant correlations between medication dose and performance on any of the tasks or on the inversion effects (range of correlations:  $r=0.01$ ,  $p=0.95$  to  $r=-0.27$ ;  $p=0.2$ ).

## 4. Discussion

Deficits in face processing are a well-established feature of schizophrenia. Although such deficits have been documented most comprehensively with regard to face emotion processing (Kerr and Neale, 1993; Kohler et al., 2000), deficits have been documented as well in processing of other face characteristics — such as unfamiliarity, identity or age (Addington and Addington, 1998; Kerr and Neale, 1993; Kohler et al., 2000; Sachs et al., 2004) — as well as for processing of non-face objects (Doniger et al., 2002; Saccuzzo and Braff, 1986). An initial finding of this study is that patients, as a group, needed substantially more time than controls — 375 vs. 250 ms — to perform at 70% correct in our object discrimination task. Reduced contrast sensitivity was also found across all spatial frequencies. Within patients, increased duration threshold needed to perform at 70% correct on the object discrimination task correlated with reduced contrast sensitivity to low (magnocellular-biased), but not medium or high spatial frequency stimuli, suggesting that the increased duration thresholds may be due to magnocellular dysfunction within this group. The finding of an elevated critical duration for house discrimination in schizophrenia echoes well-established findings of elevated duration thresholds for more primitive objects (Slaghuis and Bakker, 1995) or letters (Saccuzzo and Braff, 1986). Deficits in contrast sensitivity have also been seen in other studies of schizophrenia (Butler et al., 2005; Keri et al., 2002; Slaghuis, 1998). The contrast sensitivity findings as well as prolonged duration for same/different discrimination of objects confirm earlier findings of impaired early visual processing in schizophrenia (Butler et al., 2007; Butler et al., 2005; Cadenhead et al., 1998; Green et al., 1994; Keri et al., 2004; Kim et al., 2005; O'Donnell et al., 2002; Slaghuis and Thompson, 2003).

The primary goal of this study, however, was to evaluate integrity of an intrinsic cortical process, the well-known “face inversion” effect. Individuals, in general, are more accurate in recognizing upright, than inverted, faces. In contrast, no such inversion effects are observed for non-face objects, such as houses. As opposed to significant deficits in duration threshold in object discrimination, patients showed face inversion effects that were both robust and statistically equivalent to those of controls (Figs. 3–5). Thus, once increased threshold is corrected for by using each patient's individual duration threshold, subsequent stages of

processing, at least in the ventral stream, appear intact. A previous study failed to find a face inversion effect in a face spacing task in schizophrenia, but upright performance was below chance, making it impossible to test for an inversion effect (Shin et al. in press). This highlights the importance of adjusting duration of presentation, as was done in the present study, so that upright performance is above chance.

In the present study, increased duration threshold was related to magnocellular dysfunction as seen by a significant correlation between duration threshold and contrast sensitivity to the magnocellular-biased low spatial frequency grating. Magnocellular dysfunction can affect ventral stream FFA processing via several routes. Magnocellular and parvocellular pathways interact beginning in V1 with extensive interactions thereafter (Sawatari and Callaway, 1996; Vidyasagar et al., 2002). Thus, magnocellular dysfunction can affect ventral stream processing by impaired interactions between pathways at the level of V1 or V2 leading to impaired direct input to FFA, or by aberrant cross-over input from dorsal stream areas, such as the middle temporal visual area, to FFA (e.g., the frame and fill hypothesis) (Bar, 2003; Schroeder et al., 1998). Correcting magnocellular dysfunction by increasing duration of stimulus presentation allowed investigation of intrinsic ventral stream processing.

Although several brain regions are involved in general face processing, it has been suggested based upon fMRI studies that the FFA is the primary neural source of the behavioral face inversion effect (Yovel and Kanwisher, 2005). Our finding of intact face inversion effects, measured behaviorally, is consistent with a recent fMRI study showing normal activation of FFA to a face-matching task in patients with schizophrenia (Yoon et al., 2006). In that study, faces were presented at suprathreshold (600 ms) duration in a 1-back task, and similar FFA activation was observed in both groups. Performance in that study was at ceiling, suggesting that the long stimulus exposures provided both groups with adequate time for stimulus evaluation, leading to similar intact intrinsic ventral cortical processing as observed in the present study using the face inversion effect.

In contrast to our findings, several event-related potential (ERP) studies have reported decreased amplitude of the face-related N170 potential (Campanella et al., 2006; Herrmann et al., 2004; Onitsuka et al., 2006), potentially reflecting impaired cortical face processing. Although the basis for the discrepancy in findings between the different paradigms is currently unknown, one explanation may be that N170 generation involves different cortical regions than does the behavioral face inversion effect. Our finding of an intact behavioral face inversion effect is consistent with intact FFA function in schizophrenia (Yoon et al., 2006). However, generators for the N170 have been located in other face processing areas including superior temporal sulcus (Itier and Taylor, 2004b; Joyce and Rossion, 2005). Further, as compared with FFA activations, which are decreased or the same to inverted faces (Haxby et al., 1999; Yovel and Kanwisher, 2005), the N170 is consistently larger to inverted vs. upright faces (Itier and Taylor, 2004a; Rossion et al., 1999), again suggesting involvement of regions other than FFA.

Further support for intact function of FFA in schizophrenia comes from consideration of the spacing vs. part results across groups. Although somewhat controversial, most recent studies of face perception suggest that faces are processed holistically (Yovel and Kanwisher, 2004); for review see (Farah et al., 1998), rather than only by spacing between parts (Freire et al., 2000; Mondloch et al., 2002), and that FFA is responsible for this phenomenon (Schiltz and Rossion, 2006). In the paradigm used in the present study (Yovel and Kanwisher, 2004), the difficulty of spacing vs. part discriminations was matched. Patients, like controls, showed similar inversion effects whether faces differed in spacing or parts, suggesting that patients, like controls, use holistic processing for face recognition rather than a process specific for spacing. In addition, the finding that the inversion effect was largely absent for the house task

shows that patients, like controls, utilize face processing mechanisms that are domain specific for face perception (Yovel and Kanwisher, 2004).

This is the first study we are aware of to evaluate face and object processing in schizophrenia using stimuli that were manipulated to examine spacing vs. part processing along with domain- vs. process-specificity for face perception in conjunction with thresholds that produced above chance performance on upright stimuli. One prior study showed an intact face inversion effect in patients, but a face memory paradigm was used and spacing and part processing were not manipulated (Schwartz et al., 2002). Two studies looking at emotion processing showed that both patients and controls had similar inversion effects (Chambon et al., 2006; Schwartz et al., 2002), consistent with the present findings, and again suggestive of relatively intact intrinsic cortical processing. As stated above, one face processing study failed to find an inversion effect in patients in a spacing task, but upright performance was below chance (Shin et al., in press). A recent study found that while patients had a face inversion effect, it was decreased vs. controls (Chen et al., 2008). However, duration of presentation was very short (104 s or less).

A limitation is that all patients were on medication at the time of testing. However, visual processing deficits have been found in both medicated and unmedicated patients (Braff and Saccuzzo, 1982), as well as in unmedicated first-degree relatives of patients with schizophrenia (Keri et al., 2004; Yeap et al., 2006). In addition, there were no significant correlations between performance on any of the tasks including magnitude of the inversion effect and CPZ equivalents.

The lack of a between group difference in the inversion effect does not appear to result from lack of power as the sample size used here has the power to detect a large effect size. Indeed, significant differences in contrast sensitivity and duration threshold were found. The effect size for face inversion for patients and controls was 0.1, suggesting that if there is some between group difference, it is extremely small.

In summary, while a great number of cortical processes are reported to be abnormal in schizophrenia, this study reports on a well-described process, the face inversion effect, and shows that it is normal in patients. However, early stages of visual processing were impaired. Threshold prolongations correlated with reduced sensitivity to low spatial frequency stimuli, suggesting dysfunction of the magnocellular system as an underlying mechanism. The preserved face inversion effect in schizophrenia suggests relatively intact intrinsic function within cortical regions once appropriate adjustments are made for exposure duration.

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## References

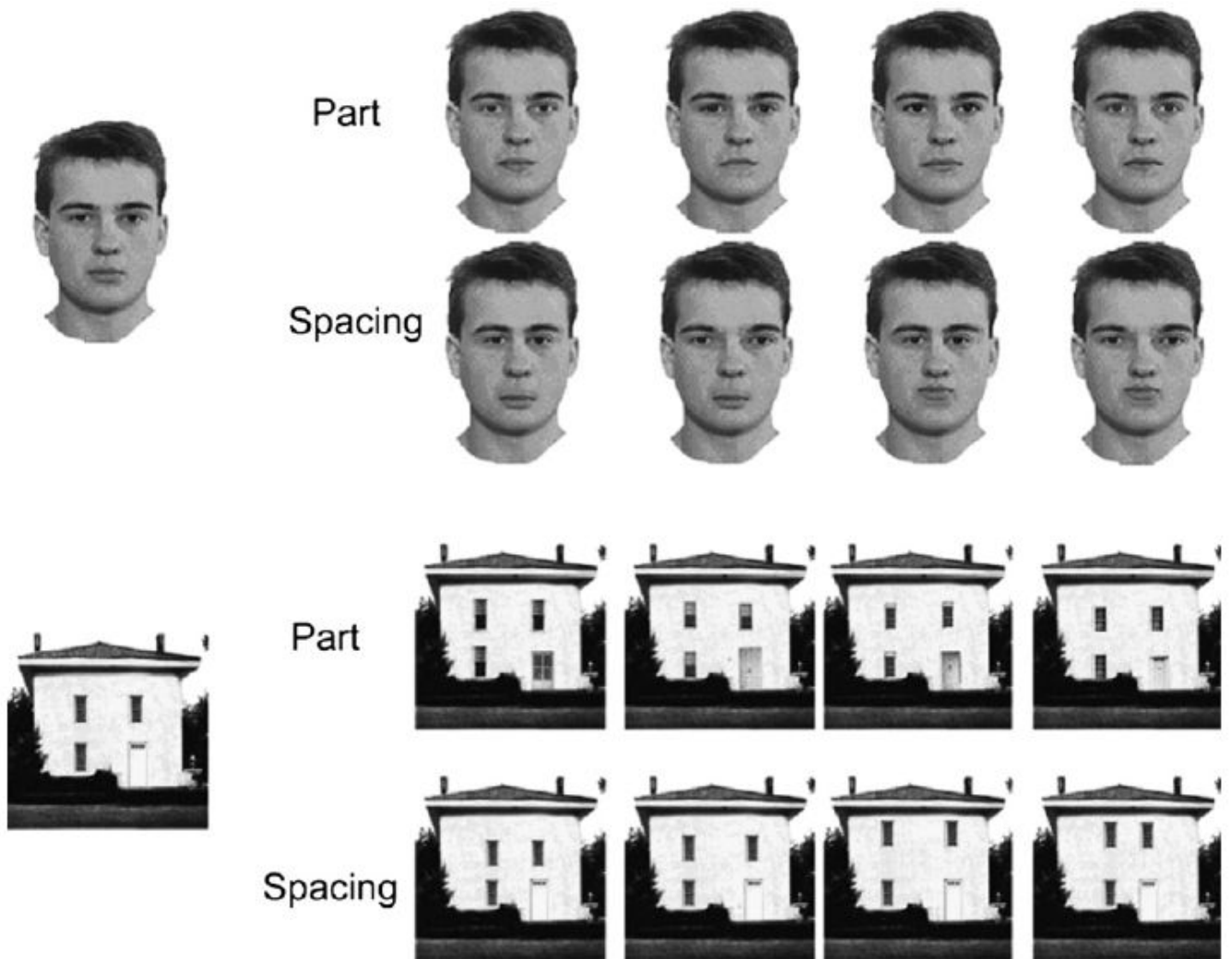
- Addington J, Addington D. Facial affect recognition and information processing in schizophrenia and bipolar disorder. *Schizophr Res* 1998;32(3):171–181. [PubMed: 9720122]
- Ammons R, Ammons C. The Quick Test (QT): provisional manual. *Psychol Rep* 1962;11:111–162.
- Andreasen, NC. The scale for the assessment of negative symptoms (SANS). The University of Iowa; Iowa City: 1984.



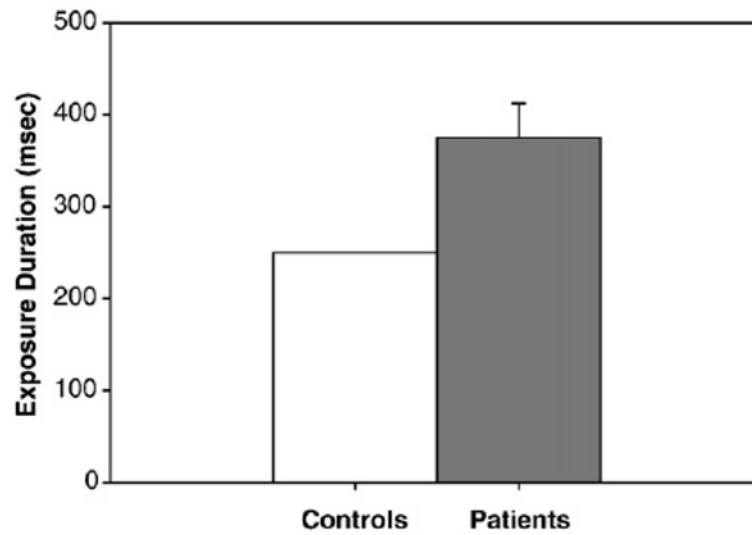
- Bar M. A cortical mechanism for triggering top-down facilitation in visual object recognition. *J Cogn Neurosci* 2003;15:600–609. [PubMed: 12803970]
- Braff DL, Saccuzzo DP. Effect of antipsychotic medication on speed of information processing in schizophrenic patients. *Am J Psychiatry* 1982;139(9):1127–1130. [PubMed: 6126128]
- Brenner CA, Wilt MA, Lysaker PH, Koyfman A, O'Donnell BF. Psychometrically matched visual-processing tasks in schizophrenia spectrum disorders. *J Abnorm Psychology* 2003;112(1):28–37.
- Butler PD, Zemon V, Schechter I, Saperstein AM, Hoptman MJ, Lim KO, Revheim N, Silipo G, Javitt DC. Early-stage visual processing and cortical amplification deficits in schizophrenia. *Arch Gen Psychiatry* 2005;62(5):495–504. [PubMed: 15867102]
- Butler PD, Martinez A, Foxe JJ, Kim D, Zemon V, Silipo G, Mahoney J, Shpaner M, Jalbrzikowski M, Javitt DC. Subcortical visual dysfunction in schizophrenia drives secondary cortical impairments. *Brain* 2007;130(Pt 2):417–430. [PubMed: 16984902]
- Cadenhead KS, Serper Y, Braff DL. Transient versus sustained visual channels in the visual backward masking deficits of schizophrenia patients. *Biol Psychiatry* 1998;43(2):132–138. [PubMed: 9474445]
- Campanella S, Montedoro C, Strel E, Verbanck P, Rosier V. Early visual components (P100, N170) are disrupted in chronic schizophrenic patients: an event-related potentials study. *Neurophysiol Clin* 2006;36(2):71–78. [PubMed: 16844545]
- Chambon V, Baudouin JY, Franck N. The role of configural information in facial emotion recognition in schizophrenia. *Neuropsychologia* 2006;44(12):2437–2444. [PubMed: 16806310]
- Chen Y, Palafox GP, Nakayama K, Levy DL, Matthyse S, Holzman PS. Motion perception in schizophrenia. *Arch Gen Psychiatry* 1999;56(2):149–154. [PubMed: 10025439]
- Chen Y, Norton D, Ongur D, Heckers S. Inefficient face detection in schizophrenia. *Schizophr Bull* 2008;34(2):367–374. [PubMed: 17631619]
- Dakin S, Carlin P, Hemsley D. Weak suppression of visual context in chronic schizophrenia. *Curr Biol* 2005;15:R822–R824. [PubMed: 16243017]
- Doniger GM, Foxe JJ, Murrar MM, Higgins BA, Javitt DC. Impaired visual object recognition and dorsal/ventral stream interaction in schizophrenia. *Arch Gen Psychiatry* 2002;59:1011–1020. [PubMed: 12418934]
- Farah MJ, Wilson KD, Drain M, Tanaka JN. What is “special” about face perception? *Psychol Rev* 1998;105(3):482–498. [PubMed: 9697428]
- First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. *Structured Clinical Interview for DSM-IV Axis I Disorders—Patient Edition*. New York State Psychiatric Institute; 1977.
- Freire A, Lee K, Symons LA. The face-inversion effect as a deficit in the encoding of configural information: direct evidence. *Perception* 2000;29(2):159–170. [PubMed: 10820599]
- Green MF, Neuchterlein KH, Mintz J. Backward masking and mania. II. Specifying the visual channels. *Arch Gen Psychiatry* 1994;51:945–951. [PubMed: 7979882]
- Haxby JV, Ungerleider LG, Clark VP, Schouten JL, Hoffman EA, Martin A. The effect of face inversion on activity in human neural systems for face and object perception. *Neuron* 1999;22:189–199. [PubMed: 10027301]
- Herrmann MJ, Ellgring H, Fallgatter AJ. Early-stage face processing dysfunction in patients with schizophrenia. *Am J Psychiatry* 2004;161(5):915–917. [PubMed: 15121660]
- Hollingshead, AB. *Four factor index of social status*. Yale University Department of Sociology; New Haven, CT: 1975.
- Itier RJ, Taylor MA. N170 or N1? Spatiotemporal differences between object and face processing using ERPs. *Cereb Cortex* 2004a;14:132–142. [PubMed: 14704210]
- Itier RJ, Taylor MJ. Source analysis of the N170 to faces and objects. *NeuroReport* 2004b;15(8):1261–2165. [PubMed: 15167545]
- Joyce C, Rossion B. The face-sensitive N170 and VPP components manifest the same brain processes: the effect of reference electrode site. *Clin Neurophysiol* 2005;116:2613–2631. [PubMed: 16214404]
- Kaplan, E. The M, P, and K pathways of the primate visual system. In: Chalupa, LM.; Werner, JS., editors. *The Visual Neurosciences*. MIT Press; Cambridge, Mass: 2003. p. 481–493.
- Keri S, Antal A, Szekeres G, Benedek G, Janka Z. Spatiotemporal visual processing in schizophrenia. *J Neuropsychiatry Clin Neurosci* 2002;14(2):190–196. [PubMed: 11983794]

- Keri S, Kelemen O, Benedek G, Janka Z. Vernier threshold in patients with schizophrenia and in their unaffected siblings. *Neuropsychology* 2004;18(3):537–542. [PubMed: 15291731]
- Kerr SL, Neale JM. Emotion perception in schizophrenia: specific deficit or further evidence of generalized poor performance? *J Abnorm Psychology* 1993;102(2):312–318.
- Kim D, Zemon V, Saperstein A, Butler PD, Javitt DC. Dysfunction of early-stage visual processing in schizophrenia: harmonic analysis. *Schizophr Res* 2005;76(1):55–65. [PubMed: 15927798]
- Kohler CG, Bilker W, Hagendoorn M, Gur RE, Gur RC. Emotion recognition deficit in schizophrenia: association with symptomatology and cognition. *Biol Psychiatry* 2000;48(2):127–136. [PubMed: 10903409]
- Krishnan GP, Vohs JL, Hetrick WP, Carroll CA, Shekhar A, Bockbrader MA, O'Donnell BF. Steady state visual evoked potential abnormalities in schizophrenia. *Clin Neurophysiol* 2005;116(3):614–624. [PubMed: 15721075]
- Lund JS. Organization of neurons in the visual cortex, area 17, of the monkey (*Macaca mulatta*). *J Comp Neurol* 1973;147(4):455–496. [PubMed: 4122705]
- Merigan, WH.; Maunsell, JHR. How parallel are the primate visual pathways?. In: Cowan, WM.; Shooter, EM.; Stevens, CF.; Thompson, RF., editors. *Ann Rev Neuroscience*. Annual Reviews, Inc.; Palo Alto, CA: 1993. p. 369-402.
- Mondloch CJ, Le Grand R, Maurer D. Configural face processing develops more slowly than featural face processing. *Perception* 2002;31(5):553–566. [PubMed: 12044096]
- O'Donnell BF, Potts GF, Nestor PG, Stylianopoulos KC, Shenton ME, McCarley RW. Spatial frequency discrimination in schizophrenia. *J Abnorm Psychology* 2002;111(4):620–625.
- Onitsuka T, Niznikiewicz MA, Spencer KM, Frumin M, Kuroki N, Lucia LC, Shenton ME, McCarley RW. Functional and structural deficits in brain regions subserving face perception in schizophrenia. *Am J Psychiatry* 2006;163(3):455–462. [PubMed: 16513867]
- Overall JE, Gorham DR. The brief psychiatric rating scale. *Psychol Rep* 1962;10:799–812.
- Rossion B, Delvenne JF, Debatisse D, Goffaux V, Bruyer R, Crommelinck M, Guerit JM. Spatio-temporal localization of the face inversion effect: an event-related potentials study. *Biol Psychiatry* 1999;50:173–189.
- Saccuzzo DP, Braff DL. Information-processing abnormalities: trait- and state-dependent components. *Schizophr Bull* 1986;12(3):447–459. [PubMed: 3764361]
- Sachs G, Steger-Wuchse D, Kryspin-Exner I, Gur RC, Katschnig H. Facial recognition deficits and cognition in schizophrenia. *Schizophr Res* 2004;68(1):27–35. [PubMed: 15037337]
- Sawatari A, Callaway EM. Convergence of magno- and parvocellular pathways in layer 4B of macaque primary visual cortex. *Nature* 1996;380:442–446. [PubMed: 8602243]
- Schiltz C, Rossion B. Faces are represented holistically in the human occipito-temporal cortex. *Neuroimage* 2006;32:1385–1394. [PubMed: 16870475]
- Schroeder CE, Mehta AD, Givre SJ. A spatiotemporal profile of visual system activation revealed by current source density analysis in the awake macaque. *Cereb Cortex* 1998;8(7):575–592. [PubMed: 9823479]
- Schwartz BL, Marvel CL, Drapalski A, Rosse RB, Deutsch SI. Configural processing in face recognition in schizophrenia. *Cogn Neuropsychiatry* 2002;7(1):15–39. [PubMed: 16528403]
- Shin YW, Na MH, Ha TH, Kang DH, Yoo SY, Kwon JS. Dysfunction in configural face processing in patients with schizophrenia. *Schizophr Bull*. in press
- Slaghuis WL. Contrast sensitivity for stationary and drifting spatial frequency gratings in positive- and negative-symptom schizophrenia. *J Abnorm Psychology* 1998;107(1):49–62.
- Slaghuis WL, Bakker VJ. Forward and backward visual masking of contour by light in positive- and negative-symptom schizophrenia. *J Abnorm Psychology* 1995;104(1):41–54.
- Slaghuis WL, Bishop AM. Luminance flicker sensitivity in positive- and negative-symptom schizophrenia. *Exp Brain Res* 2001;138(1):88–99. [PubMed: 11374087]
- Slaghuis WL, Thompson AK. The effect of peripheral visual motion on focal contrast sensitivity in positive- and negative-symptom schizophrenia. *Neuropsychologia* 2003;41(8):968–980. [PubMed: 12667532]

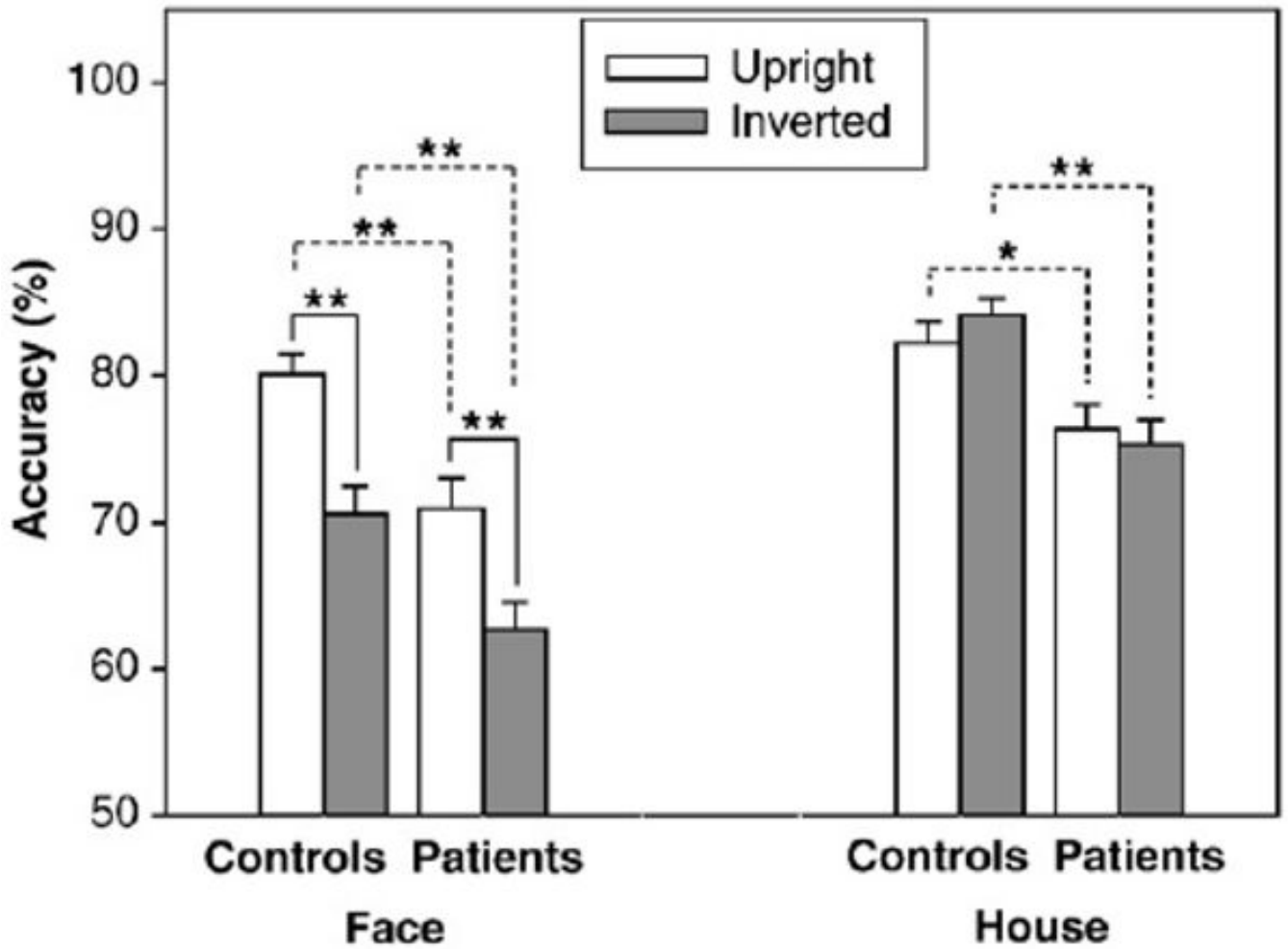
- Spencer KM, Nestor PG, Niznikiewicz MA, Salisbury DF, Shenton ME, McCarley RW. Abnormal neural synchrony in schizophrenia. *J Neurosci* 2003;23(19):7407–7411. [PubMed: 12917376]
- Vidyasagar TR, Kulikowski JJ, Lipnicki DM, Dreher B. Convergence of parvocellular and magnocellular information channels in the primary visual cortex of the macaque. *Eur J Neurosci* 2002;16:945–956. [PubMed: 12372031]
- Yeap S, Kelly SP, Sehatpour P, Magno E, Javitt DC, Garavan H, Thakore JH, Foxe JJ. Early visual sensory deficits as endophenotypes for schizophrenia: high-density electrical mapping in clinically unaffected first-degree relatives. *Arch Gen Psychiatry* 2006;63:1180–1188. [PubMed: 17088498]
- Yin RK. Looking at upside-down faces. *J Exp Psychol* 1969;81:141–145.
- Yoon JH, D'Esposito M, Carter CS. Preserved function of the fusiform face area in schizophrenia as revealed by fMRI. *Psychiatry Res* 2006;148(2–3):205–216. [PubMed: 17095198]
- Yovel G, Kanwisher N. Face perception: domain specific, not process specific. *Neuron* 2004;44(5):889–898. [PubMed: 15572118]
- Yovel G, Kanwisher N. The neural basis of the behavioral face-inversion effect. *Curr Biol* 2005;15(24):2256–2262. [PubMed: 16360687]



**Fig. 1.** Face and house stimuli that were used. Face and house stimuli were closely matched for difficulty. An image of a face or a house was manipulated so that the shapes of the parts (eyes and mouth for faces, windows and doors for houses) differed but the spacing between parts remained the same or the spacing between parts was changed but the shape of the parts remained the same.



**Fig. 2.** Exposure durations necessary to obtain at least 70% correct performance on either the upright house part or spacing task so that an inversion effect (if present) could be detected.



**Fig. 3.**

Percent correct performance for upright and inverted face and house stimuli. *T* tests showed that patients performed significantly worse than controls on the face upright ( $t(56) = 3.9, p < 0.001$ ), face inverted ( $t(56) = 3.0, p = 0.004$ ), house upright ( $t(56) = 2.6, p = 0.01$ ), and house inverted ( $t(56) = 4.5, p < 0.001$ ) conditions. \* $p = 0.01$ ; \*\* $p < 0.005$ .

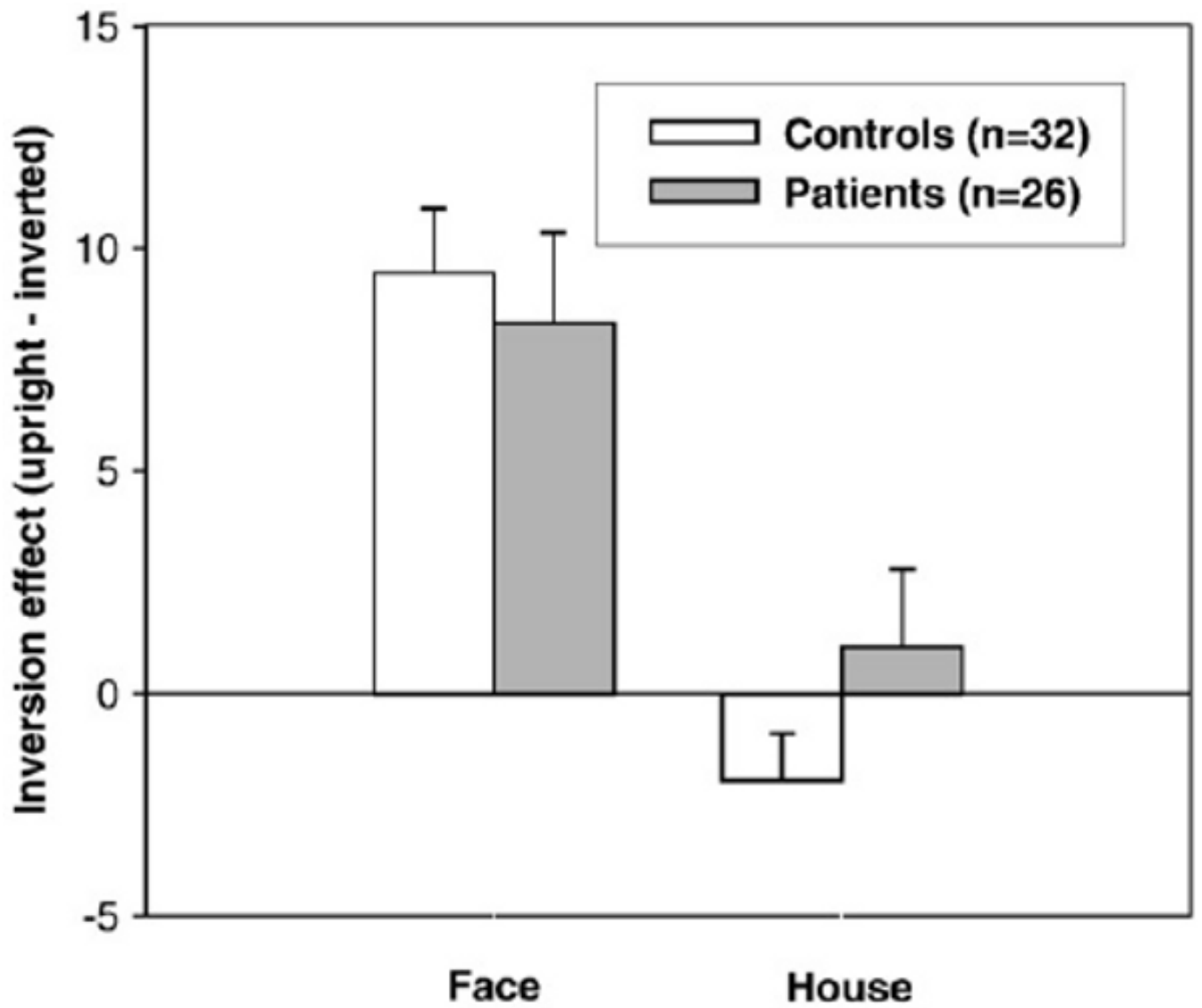
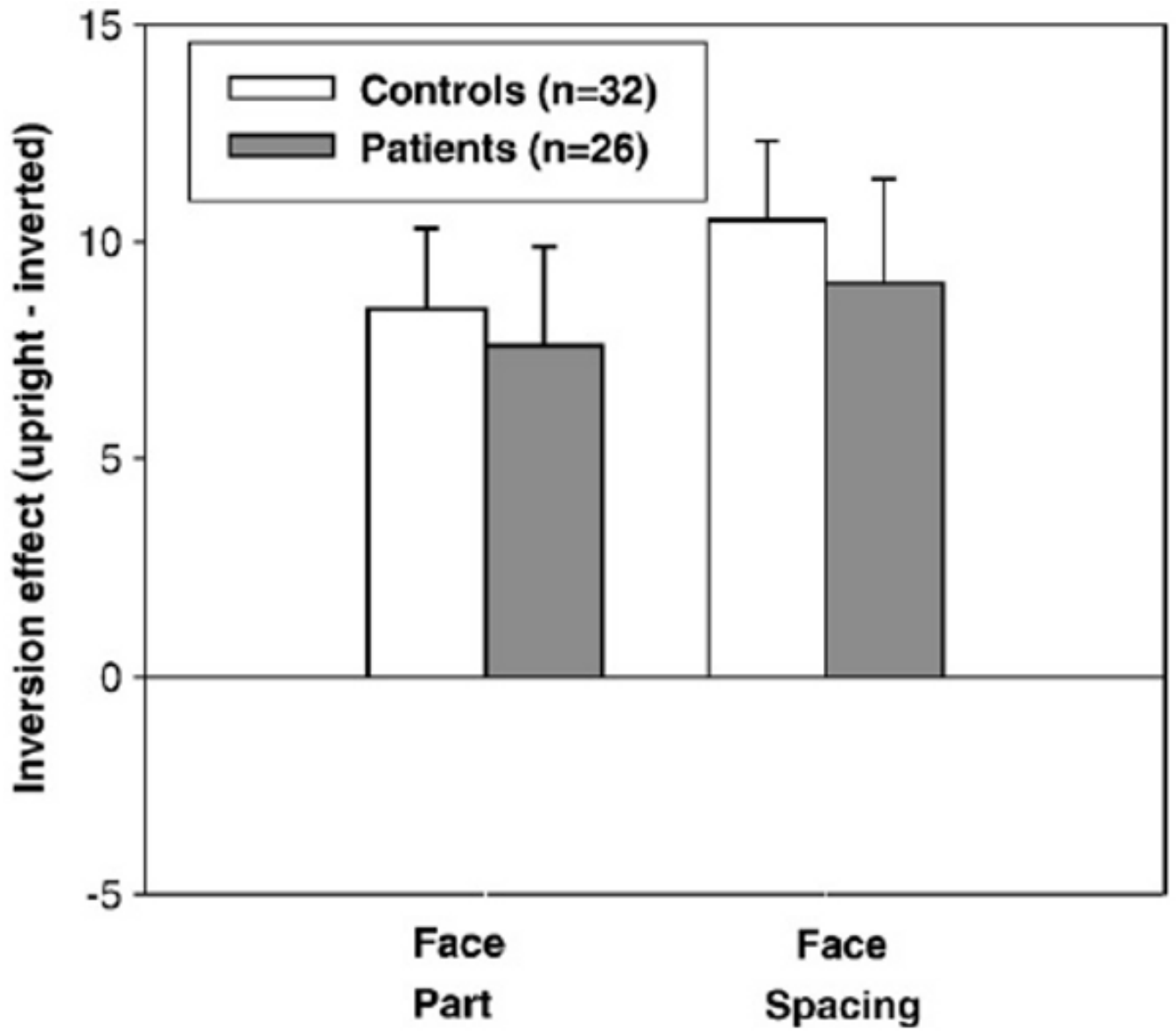


Fig. 4.  
Inversion effects (upright–inverted) for face and house stimuli.



**Fig. 5.** Inversion effects (upright–inverted) for face part and face spacing tasks.





**Table 1**

Demographic and clinical characteristics of healthy control and patient populations

| Demographic/clinical criteria              | Controls (n=32)    | Patients (n=26) |
|--|--------------------|-----------------|
| Age  | 36.6±1.7           | 36.2±1.9        |
| Gender (M/F)                               | 22/10*             | 24/2            |
| Chlorpromazine daily equivalent, mg        |                    | 1170±102.3      |
| Antipsychotics                             |                    |                 |
| Atypical                                   |                    | 22              |
| Typical                                    |                    | 0               |
| Both                                       |                    | 4               |
| Parental socioeconomic status              | 44.5±2.2 (n=31)    | 38.4±3.7 (n=19) |
| IQ (Quick test) score                      | 111.4±1.9** (n=27) | 99.7±1.9 (n=24) |
| BPRS total score                           |                    | 42.1±2.5        |
| SANS total score (including global scores) |                    | 38.5±2.6        |
| Duration of illness (years)                |                    | 17.0±1.8        |

Values are mean±SEM. Numbers of subjects per group are noted when there is missing data. Socioeconomic status was measured by the 4-factor Hollingshead Scale (Hollingshead, 1975); IQ was measured with the Quick test (Ammons and Ammons, 1962).

Abbreviations: M, male; F, female; BPRS, Brief Psychiatric Rating Scale (Overall and Gorham, 1962); SANS, Scale for the Assessment of Negative Symptoms (Andreasen, 1984).

Atypical antipsychotics included risperidone, clozapine, olanzapine, quetiapine, and aripiprazole. Typical antipsychotics included haloperidol, haloperidol decanoate, and fluphenazine.

\*  $p < 0.05$ ;

\*\*  $p < 0.001$ .