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Multisensory Integration in Schizophrenia: A Behavioral and Event-Related Potential Study

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Abstract

Introduction—Successful processing of multisensory stimuli increases the likelihood of detection or identification of salient, biologically significant events faster and more efficiently than unisensory inputs. Schizophrenia patients (SZ) show deficits in unisensory processing, but it is unclear whether impairments are seen to multisensory stimuli, a process known as multisensory integration (MSI). We used behavioral and event-related potential (ERP) measures to examine MSI in SZ and healthy controls (HC).

Methods—Thirty-three SZ and 30 HC completed a target detection task with unisensory and multisensory stimuli. Reaction times (RT) were measured while EEG was recorded. Two auditory (N100, P200) and visual (P100, N160) ERPs were examined. MSI was analyzed in terms of violations of RT to the race model, and by comparing ERPs in the MSI condition to the sum of the unisensory ERPs.

Results—Both groups showed faster RT in MSI compared to unisensory conditions. SZ had nonsignificantly fewer violations of the race model compared to HC. SZ had significantly smaller amplitudes to unisensory visual N160 and auditory P100 relative to HC; there were no significant group differences on any ERP measure of MSI.

Conclusions—SZ showed relatively intact MSI with subtle (nonsignificant) differences at the neural and behavioral levels compared to HC. Our results suggest that neural processes associated with MSI are not an additional source of impairment in SZ.

Keywords

schizophrenia; multisensory integration; ERP; race model

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Introduction

Schizophrenia patients exhibit behavioral and EEG deficits in visual (Butler & Javitt, 2005; Chen, Levy, Sheremata, & Holzman, 2004; Green, Nuechterlein, & Mintz, 1994; Levy, Holzman, Matthysse, & Mendell, 1993) and auditory (Ford, 1999; Turetsky, Bilker, Siegel, Kohler, & Gur, 2009; Wynn, Sugar, Horan, Kern, & Green, 2010) processing. These perceptual deficits have been typically examined with stimuli presented in a single sensory modality (i.e. unisensory stimuli). However, in daily life we typically encounter stimuli from multiple sensory modalities at the same time that must be effectively integrated to adaptively guide our behavior. The process of integrating stimuli from different modalities has been termed multisensory integration (MSI) (Stein & Stanford, 2008)

Processing of spatially and/or temporally congruent stimuli across modalities results in facilitation of behavioral and neural responses compared with unisensory stimuli (Stein, London, Wilkinson, & Price, 1996; Stein, Meredith, Huneycutt, & McDade, 1989). The successful processing of multisensory stimuli increases the likelihood of detection or identification of salient, biologically significant events, and does so in a faster and more efficient manner than would be predicted by the sum of the unisensory inputs (Stein & Stanford, 2008). The facilitatory effect of multisensory cues on behavioral measures has been reflected, for example, by faster reaction times (RT) to the onset of two stimuli rather than one (Ulrich, Miller, & Schroter, 2007). In animal models, MSI has been demonstrated to decrease the amount of time between sensory encoding and formation of motor-commands (Bell, Meredith, Van Opstal, & Munoz, 2005). Moreover, MSI enhances the initial subthreshold portion of a response, resulting in a multisensory response with a shorter latency than unisensory responses (Rowland, Quessy, Stanford, & Stein, 2007). MSI is considered to be a separable neural mechanism, rather than simply the summation of neural activity from different perceptual modalities (e.g., Stein, 1998), and it involves distinct brain regions, such as the superior colliculus (Dhamala, Assisi, Jirsa, Steinberg, & Kelso, 2007) and the superior temporal sulcus (Calvert & Campbell, 2003).

To assess the facilitatory effects of MSI on behavioral responses, one can use a statistical model known as the “race model,” (Raab, 1962). According to the race model, when processing multisensory stimuli, facilitation of behavioral responding occurs as a result of having two cues instead of one. However, this facilitation could be explained by either integration of responses or simple additive effects. The race model enables one to determine if integration of responses has occurred by comparing the observed distribution of the RT values to the expected distribution of the RTs from additive effects (Miller, 1982). Violations of the race model (i.e., when RTs in the multisensory condition are significantly faster than the summed probabilities of the unisensory conditions) are thought to reflect MSI (Diederich & Colonius, 1987; Ulrich, et al., 2007). Figure 1 depicts a hypothetical race model analysis. Cumulative density functions (CDFs) of reaction time data for auditory-alone, visual-alone, multisensory, and race model data are plotted at 20 different percentiles. If the data for the multisensory stimuli are faster (i.e., lower) than the data for the race model, the model is violated and MSI is thought to have occurred (left panel, Figure 1). If the data for the multisensory stimuli are slower (i.e., higher) than the data for the race model then the model is not violated and no MSI occurred (right panel, Figure 1). While the studies

in this area assume neural integration occurs it may not be necessarily required to produce facilitatory effects. Rather simple multisensory processing could account for these facilitatory effects. However, we will keep to the existing literature in using the term multisensory integration (MSI).

At the neural level, event-related potentials (ERPs), with their millisecond precision, have been used to examine how and when MSI occurs in the brain. In a typical ERP MSI paradigm, stimuli are presented either in the auditory modality alone (A), visual modality alone (V), or combined audio-visually (AV). If neural activity in the AV condition is greater than the sum of activity in the unisensory conditions (A+V), then it reflects unique activity associated with integration (Molholm et al., 2002). However, if activity in the AV condition is equal to the sum of the unisensory conditions, then it reflects a simple additive effect. Studies in healthy individuals frequently find greater ERP activity to AV vs. A+V stimuli (Giard & Peronnet, 1999; Molholm, et al., 2002; Senkowski, Saint-Amour, Höfle, & Foxe, 2011), indicating unique neural activation associated with MSI. However, some studies find the opposite pattern of activity in controls where ERP activity to A+V stimuli is greater than that to AV (e.g., Stone et al., 2011).

Despite considerable interest in MSI from the experimental literature, there are few published reports of MSI in schizophrenia, and the findings are somewhat mixed. Some studies have found MSI deficits in patients when using complex stimuli, such as speech (de Gelder, Vroomen, Annen, Masthof, & Hodiament, 2003; Pearl et al., 2009; Szyck et al., 2009) or socially relevant stimuli (e.g., facial expression and prosody) (de Gelder et al., 2005; de Jong, Hodiament, Van den Stock, & de Gelder, 2009; Fiszdon & Bell, 2010). Other studies have shown that when multisensory stimuli are synchronous, MSI is intact in patients; however, when there is asynchrony between multisensory stimuli patients show deficits (e.g., Foucher, Lacambre, Pham, Giersch, & Elliott, 2007; Martin, Giersch, Huron, & van Wassenhove, 2013). Tschacher and Bergomi (2011) and Surguladze et al. (2001) found evidence of intact MSI in schizophrenia patients, though these patterns were affected by levels of psychotic symptoms. A more recent study examined behavioral facilitation effects of MSI using the race model and very simple stimuli (a letter and a tone) (Williams, Light, Braff, & Ramachandran, 2010). While patients showed some facilitatory MSI effects on reaction times, they had significantly fewer deviations from the race model than healthy controls, indicating that patients did not integrate multisensory stimuli as well as controls.

To date only two studies have explored MSI with EEG and behavior in patients with schizophrenia (Stekelenburg, Maes, Van Gool, Sitskoorn, & Vroomen, 2013; Stone, et al., 2011). Using complex stimuli (a picture and sound of a soccer ball near or far from the observer), Stone et al. (2011) showed a greater facilitatory effect on both RT and EEG measures in patients. Specifically, the patients showed faster RT to AV vs. unisensory stimuli, and greater EEG activity to AV vs. A+V conditions, compared to controls. The authors interpret their findings as showing intact MSI in schizophrenia patients. Stekelenburg et al. (2013) examined MSI by determining the effects on ERPs of visual stimuli that shortly preceded auditory stimuli; in this case integration has been associated with dampened auditory N100 responses. Stekelenburg et al. found that controls showed

evidence of N100 dampening whereas patients did not, suggesting that patients did not sufficiently integrate the multisensory stimuli.

The goal of the current study was to conduct a careful multi-method examination of multisensory processing in patients with schizophrenia and healthy controls. In particular, we were interested in examining the facilitatory effects of multisensory stimuli on behavioral and neural responses. We used both behavioral and ERP measures and a target detection task with very simple stimuli. We examined deviations from the race model, as well as two auditory (N100 and P200), and two visual (P100 and N160¹) ERPs reflecting early sensory processing in each modality.

Methods

Participants

Thirty-three patients with schizophrenia and 30 healthy comparison subjects participated in the study. All participants were between the ages of 18 and 60, had an IQ over 70, and were sufficiently fluent in English to understand the procedures. Subjects were excluded if they had substance dependence in the last 6 months, substance abuse in the last month, neurological illness (e.g., seizures, stroke), or significant head injury with loss of consciousness for greater than 60 minutes.

Patients with schizophrenia were recruited from outpatient treatment clinics at the Veterans Affairs Greater Los Angeles Healthcare System (VAGLAHS) and from board-and-care residences in the community. Diagnosis was based on the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I; First et al., 1997). Patients were considered to be clinically stable, defined as no psychiatric medication changes in the past six weeks, no inpatient hospitalization in the past three months, and no changes in housing in the past two months. All patients were taking antipsychotic medication at the time of testing; 24 were receiving second-generation medications, 2 were taking a first-generation medication, 1 was taking both a first and second-generation medication, and 6 were missing medication information.

Healthy controls were recruited through newspaper and internet advertisements and were screened with the SCID-I and SCID-II (First et al., 1996). Exclusion criteria included any lifetime psychotic disorder, bipolar disorder, recurrent depression, substance dependence, paranoid, schizotypal, or schizoid personality disorder, or a history of psychotic disorder among their first-degree relatives. All SCID interviewers were trained through the Treatment Unit of the Department of Veterans Affairs VISN 22 Mental Illness Research, Education, and Clinical Center (MIRECC) to a minimum k of 0.75 for key psychotic and mood items (Ventura, Liberman, Green, & Shaner, 1998). All participants had the capacity to give informed consent and provided written informed consent after all procedures were explained in accordance with procedures approved by the Institutional Review Boards at the University of California, Los Angeles and VAGLAHS.

¹We use the term visual N160, instead of the more commonly used visual N100, so as not to confuse it with the auditory N100.

Measures

Clinical Ratings—Psychiatric symptoms were rated using the Scale for the Assessment of Negative Symptoms (SANS; Andreasen, 1984a), and the 24-item Brief Psychiatric Rating Scale (BPRS; Ventura et al., 1993). We report the positive symptoms and depression/anxiety factors as well as the total score for the BPRS (Kopelowicz, Ventura, Liberman, & Mintz, 2008); for the SANS we report the global scores for affective flattening, alogia, anhedonia, and avolition in Table 1.

MSI Paradigm—Participants performed a MSI behavioral task while EEG was recorded. All stimuli were presented with E-Prime 2.0 (Psychology Software Tools, Inc., Sharpsburg, PA). Participants were seated approximately 1 m from a 17" cathode ray tube monitor. Auditory stimuli were delivered binaurally through foam ear inserts. Trials began with a fixation cross presented for 1500 ms, followed by a blank screen for 500 to 1500 ms, then by either a 100 ms visual (V) stimulus (black letter "X"), a 100 ms auditory (A) stimulus (1000 Hz tone, 10 ms rise/fall time, 75 dB), or both stimuli simultaneously (AV) in the bimodal condition. Thirty blank catch trials, with no stimuli presented, were inserted randomly to help prevent anticipation of responses. The letter X subtended 1.15×1.43 degrees of visual angle. Subjects were instructed to push the mouse button as quickly as possible whenever they heard or saw any stimulus and reaction times were recorded. The inter-trial interval was 1800 to 2200 ms. Stimuli were presented in random order with 60 trials in each stimulus condition (total of 180 trials), plus 30 catch trials. The task took approximately 20 min to complete.

EEG Recording and Analysis

EEG recordings were acquired with a 64-channel BioSemi ActiveTwo amplifier (Biosemi B. V., Amsterdam, Netherlands). Additional electrodes were placed above and below the left eye and at the outer canthi of both eyes to monitor blinks and eye movements. Each active electrode was measured online with respect to a common mode sense electrode during data collection, forming a monopolar channel. Data were sampled at 1024 Hz at DC to 100 Hz. An additional electrode was placed at the nose tip and all EEG data were re-referenced offline to this electrode.

Data processing was performed using BrainVision Analyzer 2 (Brain Products, Gilching, Germany). Based on visual inspection, bad electrodes, defined as a bad recording for the entire length of the recording, were removed from the recording and a spherical spline interpolation was used to recreate the electrode (Perrin et al., 1989; Picton et al., 2000). Electrodes for 4 patients (average of 1.5 per patient) and 2 controls (average of 2 electrodes per control) were interpolated. Eyeblinks were removed from the data using a regression-based algorithm (Gratton et al., 1983). Continuous data were then epoched at -100 to 600 ms relative to stimulus onset; data were then baseline corrected using the average activity of the 100 ms prestimulus interval. Epochs were high-pass filtered at 1 Hz and low-pass filtered at 30 Hz (zero phase shift, 24 dB/octave rolloff) to remove any residual high-frequency artifact. Epochs that contained activity exceeding $\pm 75 \mu\text{V}$ at any electrode site were automatically rejected. For patients, a mean (SD) of 52.7 (10.0) trials were accepted for each condition (A, V, and AV); for controls, 53.2 (8.4) trials were accepted for each condition.

We considered four ERP waveforms. Auditory N100 and P200 amplitudes were measured as the mean voltages in the 127-177 and 218-308 ms latency range, respectively. Visual P100 and N160 were measured as the mean voltages in the 80-120 and 130-180 ms latency range, respectively. Windows were centered on the peak latency seen for each component. The 2 auditory ERP responses were averaged over 6 frontocentral electrodes where activity, based on visual inspection, was largest: C1, C2, Cz, FC1, FC2, FCz. The 2 visual ERP responses were averaged over 4 left (P5, P7, P9, PO7) and 4 right (P6, P8, P10, PO8) parieto-occipital electrodes where activity, based on visual inspection, was largest.

Statistical Analyses

Independent samples t-tests and chi-square tests were used to assess group differences for continuous and categorical demographic variables, respectively. Behavioral data were analyzed in two ways. First, we examined the hit rate and RTs using $2 (\text{group}) \times 3 (\text{condition})$ repeated measures ANOVAs; false alarm rates to the catch trials were analyzed with an independent samples t-test. Next, we examined violations of the race model with the RMITest program (Ulrich, et al., 2007). A CDF was generated for each subject and each condition using raw RTs. The race model CDF was calculated by summing the CDFs of the unisensory conditions (A + V). CDFs were calculated for twenty different percentiles, ranging from 0.03-0.98. The percentile value determines the upper RT limit for that percentile: e.g., an RT value of 500 ms at the 0.50 percentile means that 50% of the trials for the particular condition are 500 ms or faster. Violations of the race model at the group level were examined with paired t-tests at each of the 20 percentiles. Violations of the race model for each individual subject were also examined by counting the number of instances at any given percentile where the RT to the AV condition was faster than the RT to the race model prediction. Between group differences in the number of violations of the race model counted for each subject were examined using an independent sample t-test.

To examine group differences in unisensory auditory ERPs, we conducted a one-way ANOVA with group as the main factor; for unisensory visual ERPs, we conducted a $2 (\text{group}) \times 2 (\text{hemisphere})$ repeated measures ANOVA. To examine MSI effects on ERPs, we compared the AV condition to the sum of the unisensory conditions (A + V) for the same set of electrodes, within each group. We analyzed each of the four ERP components separately using a $2 (\text{group}) \times 2 (\text{AV vs. A+V})$ repeated measures ANOVA. For all repeated measures ANOVAs resulting in more than one degree of freedom we used Greenhouse-Geisser correction factors (ϵ) to account for the effects of sphericity. We report the uncorrected degrees of freedom, the corrected p-values, and the correction factor.

Results

Demographics

Demographic information is presented in Table 1. Patients were clinically stable with relatively low levels of symptoms. Groups did not differ on age or gender, though there were significant differences in personal education.

Behavioral Data

Behavioral data were not available for 1 healthy control due to equipment malfunction. One patient had too few hits (16/60) in the visual condition (V) and thus could not be included in the race model analysis. Therefore, both participants' data were not included in the ERP analyses.

Hit Rate, False Alarm Rate and Reaction Time—Both groups showed a high hit rate for each of the three conditions and a low false alarm rate for the catch trials. Hit rates showed only a significant main effect of condition, $F(2, 120) = 15.561, p < 0.001, \varepsilon = 0.64$. Follow-up contrasts revealed significant differences in hit rate among all three conditions: $AV > A > V, p's < 0.01$. For false alarm rates for catch trials, the range was 0-5; there was no significant difference between schizophrenia patients, 0.44 (1.11), and healthy controls, 0.28 (0.80), $t(61) = 0.67, p > 0.50$. For RT, there was a significant main effect only for condition, $F(2, 120) = 143.3, p < 0.001, \varepsilon = 0.70$. The group main effect and the interaction were not significant. Follow-up contrasts revealed significant differences, $p's < 0.001$, in RT among all three conditions, such that $AV < V < A$. Average hit rates and RT for each condition for both groups can be seen in Table 2.

Race Mode—The results of the race model analysis are displayed in Figure 2 as average CDFs for both groups. At the group level, healthy controls showed significant violations of the race model for 12 of the percentiles (0.03-0.58 percentiles). Schizophrenia patients showed significant violations of the race model for 9 of the percentiles (0.08-0.48 percentiles). Violations of the race model at the individual level were also examined: controls had 13.3 (5.6) and patients had 11.9 (5.4) violations, a non-significant difference, $t(59) = 1.02, p < 0.32$.

Unisensory ERP Analysis

Means and standard deviations for each of the four ERP components of interest for the A, V, AV and the A+V conditions can be seen in Table 3 and Figure 3.

Auditory—For the N100, controls, $-4.97 (2.28) \mu V$, had significantly larger responses compared to patients, $-3.68 (2.01) \mu V, t(59) = 2.34, p < 0.05$. There were no significant between group differences for the P200.

Visual—There were no main effects or interactions for the P100. For the N160, controls, $-4.45 (2.34) \mu V$, had significantly larger responses compared to patients, $-3.17 (2.55) \mu V$, in the left hemisphere, $t(59) = 2.21, p < 0.05$; there was no between group difference in the right hemisphere.

Multisensory ERP Analysis

Auditory—For the N100, there was a significant main effect of group, $F(1, 59) = 5.46, p < 0.05$, and a marginal group $\times$ condition interaction, $F(1, 59) = 3.38, p < 0.08$. Controls, $-3.64 (3.25) \mu V$, had an overall larger N100 compared to patients, $-2.08 (1.86) \mu V$. For the P200, there was a significant main effect of condition, $F(1, 59) = 9.55, p < 0.01$. The P200

was larger for AV, 1.33 (3.22) μ V, compared to A+V, 0.59 (3.79) μ V, responses. The group main effect and interaction with group were not significant (see Table 3 and Figure 4)

Visual—There were no significant main effects or interactions for the P100. For the N160 there was only a marginal group $\times$ condition $\times$ hemisphere interaction, $F(1, 59) = 2.80, p < 0.10$. This interaction was due to controls showing larger responses to AV versus A+V stimuli in the right hemisphere, while patients showed larger responses to A+V versus AV stimuli; there were no differences between either condition in either group in the left hemisphere (see Table 3 and Figure 5). However, these differences in the right hemisphere were not statistically significant.

Correlations between Behavior and Clinical Symptoms

We examined correlations between behavior and clinical symptoms in the schizophrenia patients, and correlations between age and behavior separately in both groups. Unsurprisingly, in patients avolition was positively correlated with RT to auditory, visual, and AV stimuli, r 's of 0.42, 0.56, and 0.43, respectively, p 's < 0.02 . Avolition was also significantly negatively correlated with hits to AV stimuli, $r = -0.39, p < 0.03$. In patients, age was only significantly correlated with hit to visual stimuli, $r = 0.36, p < 0.05$. In controls, age was significantly correlated with hits to AV stimuli and number of race model violations, both r 's = 0.38, p 's < 0.05 .

Discussion

We examined MSI using both behavioral and EEG methods and found that schizophrenia patients were generally similar to healthy controls. At the behavioral level, both groups had faster reaction times in the MSI condition compared to the unisensory conditions. Patients had fewer violations of the race model relative to healthy controls, but not significantly so. At the neural level, there were no significant differences between groups on any of the ERP measures of MSI. This lack of difference on MSI measures was in contrast to the observed group differences (smaller amplitude in patients) on two of the unisensory ERPs that were examined.

Our study failed to replicate the behavioral results of Williams et al. (2010) who found significantly fewer violations of the race model in patients. The patient sample characteristics (e.g., age, gender, length of illness) were similar in the two studies, and we modeled our procedures on that study (e.g., type and number of stimuli), so the reasons for the discrepant findings are unclear.

Our findings are also inconsistent with the results found in Stone et al. (2011) and Stekelenburg, et al. (2013). In Stone et al. patients had a heightened MSI effect compared to controls as indexed by both behavior and ERP. However, in Stekelenburg et al. patients failed to show ERP evidence of MSI compared to healthy controls. There were notable methodological differences between these two studies and the current study. Stone et al. used complex visual and auditory stimuli while Stekelenburg et al. used congruent and incongruent audiovisual stimuli. Our stimuli were very simple and were presented

simultaneously. The paradigm differences among these studies and the current study might account for the discrepant findings.

Although there were no significant group differences in MSI, there were some subtle hints of abnormalities. For example, patients showed a reduction (not augmentation) of the right hemisphere visual N160 in the AV versus A+V conditions, but this finding did not reach significance. They also had slightly fewer violations of the race model. However, MSI at the behavioral level occurred as both groups exhibited violations of the race model, which is considered a good way to determine if multisensory processing results in integration of stimuli rather than simple additive effects. MSI at the neural level also occurred as both groups showed larger auditory P200 responses to AV vs. A+V conditions. Therefore the MSI paradigm appeared to be working correctly in the current study, even though we did not find significant group differences.

We intentionally selected very simple stimuli to try to assess the basic MSI phenomenon. Importantly, our paradigm did not necessarily rely on *integration*; rather we focused on the *processing* of multisensory stimuli and its facilitatory effects on behavioral and neural responses. Most studies of MSI in schizophrenia have used more complex stimuli or paradigms that require integration of auditory and visual stimuli. For example, de Gelder, et al. (2005) and de Jong, et al. (2009) have used audiovisual speech and found deficits in schizophrenia patients. In paradigms that manipulate the synchrony of auditory and visual stimuli (e.g., multisensory stimuli that are either synchronous or asynchronous), schizophrenia patients show normal performance when stimuli are perfectly synchronous (as in the current study) but deficits when there is some level of asynchrony (e.g., Foucher, et al., 2007; Martin, et al., 2013; Tschacher & Bergomi, 2011). It may be possible that the processing of multisensory stimuli is intact when stimuli are simple and synchronous. However, MSI appears to be deficient in schizophrenia when stimuli need to be integrated or when stimuli are slightly asynchronous. It is possible that more complex stimuli and an examination of asynchronous/synchronous stimuli might have resulted in larger behavioral and neural deficits in the patients in the current study.

In conclusion, our results show that schizophrenia patients exhibit relatively intact MSI, though with some subtle (non-significant) differences at the neural and behavioral levels. Our findings are inconsistent with most (but not all) of the previous studies of MSI in schizophrenia that have reported MSI deficits. Patients with schizophrenia clearly have well-established problems in unisensory processing. Our results suggest that specific neural processes associated with MSI of simple auditory and visual stimuli are not an additional source of impairment in schizophrenia.

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References

- Bell AH, Meredith MA, Van Opstal AJ, Munoz DP. Crossmodal integration in the primate superior colliculus underlying the preparation and initiation of saccadic eye movements. *Journal of Neurophysiology*. 2005; 93:3659–3673. [PubMed: 15703222]
- Butler PD, Javitt DC. Early-stage visual processing deficits in schizophrenia. *Current Opinions in Psychiatry*. 2005; 18:151–157.
- Calvert GA, Campbell R. Reading speech from still and moving faces: The neural substrates of visible speech. *Journal of Cognitive Neuroscience*. 2003; 15:57–70. [PubMed: 12590843]
- Chen Y, Levy DL, Sheremata S, Holzman PS. Compromised late-stage motion processing in schizophrenia. *Biological Psychiatry*. 2004; 55:834–841. [PubMed: 15050865]
- de Gelder B, Vroomen J, Annen L, Masthof E, Hodiament P. Audio-visual integration in schizophrenia. *Schizophrenia Research*. 2003; 59:211–218. [PubMed: 12414077]
- de Gelder B, Vroomen J, de Jong SJ, Masthoff ED, Trompenaars FJ, Hodiament P. Multisensory integration of emotional faces and voices in schizophrenics. *Schizophrenia Research*. 2005; 72:195–203. [PubMed: 15560964]
- de Jong JJ, Hodiament PPG, Van den Stock J, de Gelder B. Audiovisual emotion recognition in schizophrenia: Reduced integration of facial and vocal affect. *Schizophrenia Research*. 2009; 107:286–293. [PubMed: 18986799]
- Dhamala M, Assisi CG, Jirsa VK, Steinberg FL, Kelso JA. Multisensory integration for timing engages different brain networks. *Neuroimage*. 2007; 34:764–773. [PubMed: 17098445]
- Diederich A, Colonius H. Intersensory facilitation in the motor component? A reaction time analysis. *Psychological Research*. 1987; 49:23–29.
- Fiszdon JM, Bell MD. Effects of presentation modality and valence on affect recognition performance in schizophrenia and healthy controls. *Psychiatry Research*. 2010; 176:120–125. 10.1016/j.psychres.2008.11.014 [PubMed: 20202689]
- Ford JM. Schizophrenia: The broken P300 and beyond. *Psychophysiology*. 1999; 36:667–682. [PubMed: 10554581]
- Foucher JR, Lacambre M, Pham B-T, Giersch A, Elliott MA. Low time resolution in schizophrenia: Lengthened windows of simultaneity for visual, auditory and bimodal stimuli. *Schizophrenia Research*. 2007; 97:118–127. [PubMed: 17884350]
- Giard MH, Peronnet F. Auditory-visual integration during multimodal object recognition in humans: A behavioral and electrophysiological study. *Journal of Cognitive Neuroscience*. 1999; 11:473–490. [PubMed: 10511637]
- Green MF, Nuechterlein KH, Mintz J. Backward masking in schizophrenia and mania: II. Specifying the visual channels. *Archives of General Psychiatry*. 1994; 51:939–944. [PubMed: 7979881]
- Kopelowicz A, Ventura J, Liberman RL, Mintz J. Consistency of brief psychiatric rating scale factor structure across a broad spectrum of schizophrenia patients. *Psychopathology*. 2008; 41:77–84. [PubMed: 18033976]
- Levy DL, Holzman PS, Matthyse S, Mendell NR. Eye tracking dysfunction and schizophrenia: A critical perspective. *Schizophrenia Bulletin*. 1993; 19:461–536. [PubMed: 8235455]
- Martin B, Giersch A, Huron C, van Wassenhove V. Temporal event structure and timing in schizophrenia: Preserved binding in a longer “now”. *Neuropsychologia*. 2013; 51:358–371. [PubMed: 22813430]
- Miller J. Divided attention: Evidence for coactivation with redundant signals. *Cognitive Psychology*. 1982; 14:247–279. [PubMed: 7083803]
- Molholm S, Ritter W, Murray MM, Javitt DC, Schroeder CE, Foxe JJ. Multisensory auditory-visual interactions during early sensory processing in humans: A high-density electrical mapping study. *Cognitive Brain Research*. 2002; 14:115–128. [PubMed: 12063135]
- Pearl D, Yodashtkin-Porat D, Katz N, Valevski A, Aizenberg D, Sigler M, Kikinzon L, et al. Differences in audiovisual integration, as measured by McGurk phenomenon, among adult and adolescent patients with schizophrenia and age-matched healthy controls groups. *Comprehensive Psychiatry*. 2009; 50:186–192. 10.1016/j.comppsy.2008.06.004 [PubMed: 19216897]

- Raab DH. Statistical facilitation of simple reaction times. *Transactions of the New York Academy of Sciences*. 1962; 24:574–590. [PubMed: 14489538]
- Rowland B, Quessy S, Stanford TR, Stein BE. Multisensory integration shortens physiological response latencies. *Journal of Neuroscience*. 2007; 27:5879–5884. [PubMed: 17537958]
- Senkowski D, Saint-Amour D, Höfle M, Foxe JJ. Multisensory interactions in early evoked brain activity follow the principle of inverse effectiveness. *NeuroImage*. 2011; 56:2200–2208. [PubMed: 21497200]
- Stein BE, London N, Wilkinson LK, Price DD. Enhancement of perceived visual intensity by auditory stimuli: A psychophysical analysis. *Journal of Cognitive Neuroscience*. 1996; 8:497–506. [PubMed: 23961981]
- Stein BE, Meredith MA, Huneycutt WS, McDade L. Behavioral indices of multisensory integration: Orientation to visual cues is affected by auditory stimuli. *Journal of Cognitive Neuroscience*. 1989; 1:12–24. [PubMed: 23968407]
- Stein BE, Stanford TR. Multisensory integration: Current issues from the perspective of the single neuron. *Nature Reviews: Neuroscience*. 2008; 9:255–266.
- Stekelenburg JJ, Maes JP, Van Gool AR, Sitskoorn M, Vroomen J. Deficient multisensory integration in schizophrenia: An event-related potential study. *Schizophrenia Research*. 2013; 147:253–261. [PubMed: 23707640]
- Stone DB, Urrea LJ, Aine CJ, Bustillo JR, Clark VP, Stephen JM. Unisensory processing and multisensory integration in schizophrenia: A high-density electrical mapping study. *Neuropsychologia*. 2011; 49:3178–3187. [PubMed: 21807011]
- Surguladze SA, Calvert GA, Brammer MJ, Campbell R, Bullmore ET, Giampietro V, David AS. Audio-visual speech perception in schizophrenia: An fMRI study. *Psychiatry Research: Neuroimaging*. 2001; 106:1–14.
- Szyck GR, Munte TF, Dillo W, Mohammadi B, Samii A, Emrich HM, Dietrich DE. Audiovisual integration of speech is disturbed in schizophrenia: An fMRI study. *Schizophrenia Research*. 2009; 110:111–118. [PubMed: 19303257]
- Tschacher W, Bergomi C. Cognitive binding in schizophrenia: Weakened integration of temporal intersensory information. *Schizophrenia Bulletin*. 2011; 37:S13–S22. [PubMed: 21860043]
- Turetsky BI, Bilker WB, Siegel SJ, Kohler CG, Gur RE. Profile of auditory information-processing deficits in schizophrenia. *Psychiatry Research*. 2009; 165:27–37. [PubMed: 18990453]
- Ulrich R, Miller J, Schroter H. Testing the race model inequality: An algorithm and computer programs. *Behavior Research Methods*. 2007; 39:291–302. [PubMed: 17695357]
- Ventura J, Liberman RP, Green MF, Shaner A. Training and quality assurance with the Structured Clinical Interview for DSM-IV. *Psychiatry Research*. 1998; 79:163–173. [PubMed: 9705054]
- Ventura J, Lukoff D, Nuechterlein KH, Liberman RL, Green MF, Shaner A. Brief Psychiatric Rating Scale (BPRS). *International Journal of Methods in Psychiatric Research*. 1993; 3:227–243.
- Williams LE, Light GA, Braff DL, Ramachandran VS. Reduced multisensory integration in patients with schizophrenia on a target detection task. *Neuropsychologia*. 2010; 48:3128–3136. [PubMed: 20600181]
- Wynn JK, Sugar CS, Horan WP, Kern RS, Green MF. Mismatch negativity, social cognition, and functioning in schizophrenia patients. *Biological Psychiatry*. 2010; 67:940–947. [PubMed: 20074704]

Figure 1.

Hypothetical cumulative density functions (CDF) and race model data. Hypothetical CDFs for CDFs for auditory (blue), visual (red), race model (green), and MSI (purple) are shown. Multisensory integration is thought to occur when CDFs for the AV condition are faster (i.e., appear lower) than that for the predicted race model CDF (left panel). Multisensory integration has not occurred when CDFs for the AV condition are slower (i.e., appear higher) than that for the predicted race model CDF (right panel).

Figure 2.

Cumulative density functions (CDF) and race model data for healthy controls (left) and schizophrenia patients (right). CDFs for auditory (blue), visual (red), race model (green), and MSI (purple) are shown. Asterisks at individual percentiles indicate significant differences in RT between MSI and the race model.

Figure 3.

ERPs to unisensory (auditory or visual only) stimuli for controls (in black) and patients (in red). A) ERPs to auditory stimuli over fronto-central electrodes; B) ERPs to visual stimuli over left parieto-occipital electrodes; and C) ERPs to visual stimuli over right parieto-occipital electrodes. Arrows show the auditory N100 and P200 and visual P100 and N160 peaks.

Figure 4. Auditory ERPs to the sum of unisensory stimuli (A+V, in red) and MSI stimuli (in black) for controls (left) and patients (right). ERPs over fronto-central electrodes were used to examine auditory N100 and P200.

Figure 5.

Visual ERPs to the sum of unisensory stimuli (A+V, in red) and MSI stimuli (in black) for controls (left) and patients (right). ERPs over left and right parieto-occipital electrodes were used to examine visual P100 and N160.

Table 1

Demographic information and symptom ratings.

	<u><i>Patients</i></u> <i>(n = 33)</i>		<u><i>Normal Controls</i></u> <i>(n = 30)</i>	
	Mean	SD	Mean	SD
Age	48.4	9.0	48.0	8.1
Education *	12.5	1.9	14.5	1.5
Parental Education	12.9	4.1	14.8	2.8
Male:Female	23:10	----	21:9	----
BPRS				
Total Score	36.7	10.0		
Factors (mean score per item)				
Depression/Anxiety	1.7	0.7		
Positive Symptoms	1.7	0.7		
SANS Global Scores				
Affective Flattening	2.0	1.5		
Alogia	0.6	0.9		
Avolition	2.8	0.8		
Anhedonia	2.2	1.1		

* p < 0.05 difference between groups

Table 2

Hit rates and reaction times for each stimulus condition and number of race model violations for both groups.

	Schizophrenia Patients	Healthy Controls
Hit Rate (# out of 60)		
Auditory	57.2 (4.9)	59.1 (1.5)
Visual	55.2 (8.4)	55.0 (6.4)
Auditory-Visual	59.1 (1.9)	59.5 (1.0)
Reaction Time (ms)		
Auditory	599 (148)	547 (110)
Visual	499 (112)	460 (75)
Auditory-Visual	428 (115)	400 (77)
# Race Model Violations	11.9 (5.4)	13.3 (5.6)

Table 3

Means (SD) for unisensory and multisensory ERPs.

	Unisensory		Patients		Controls	
	Patients	Controls	Multisensory		Multisensory	
			AV	A+V	AV	A+V
Auditory						
N100	-3.68 (2.01)	-4.97 (2.28) *	-1.94 (2.20)	-2.22 (2.10)	-3.99 (3.53)	-3.30 (3.24)
P200	1.29 (2.45)	2.14 (3.17)	1.03 (2.78)	0.24 (3.26)	1.66 (3.66)	0.98 (4.33)
Visual						
Left P100	1.78 (1.57)	2.06 (1.92)	1.25 (1.52)	1.41 (1.66)	1.67 (1.41)	1.62 (1.92)
Right P100	1.75 (1.67)	1.99 (1.74)	1.47 (1.46)	1.30 (1.73)	1.92 (1.59)	1.70 (2.14)
Left N160	-3.17 (2.55)	-4.45 (2.34) *	-3.04 (2.39)	-2.78 (2.98)	-4.67 (2.86)	-4.40 (2.91)
Right N160	-3.69 (2.73)	-4.03 (2.53)	-3.30 (2.65)	-3.76 (3.23)	-4.48 (3.55)	-4.01 (3.06)

* p < 0.05 difference between patients and controls