Published in final edited form as:

Schizophr Res. 2007 December ; 97(1-3): 206–214.

Neuromagnetic evidence of broader auditory cortical tuning in schizophrenia

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Abstract

Deficits in basic auditory perception have been described in schizophrenia. Previous electrophysiological imaging research has documented a structure-function disassociation in the auditory system and altered tonotopic mapping in schizophrenia. The present study examined auditory cortical tuning in patients with schizophrenia.

Eighteen patients with schizophrenia and 15 comparison subjects were recorded in a magnetoencephalographic (MEG) experiment of auditory tuning. Auditory cortical tuning at 1 kHz was examined by delivering 1 kHz pure tones in conjunction with pure tones at 5 frequencies surrounding and including 1 kHz. Source reconstruction data were examined for evidence of frequency specificity for the M100 component.

There was a significant broadening of tuning in the schizophrenia group evident for the source amplitude of the M100. The frequently reported reduction in anterior-posterior source asymmetry for individuals with schizophrenia was replicated in this experiment. No relationships between symptom severity ratings and MEG measures were observed.

This finding suggests that the frequency specificity of the M100 auditory evoked field is disturbed in schizophrenia, and may help explain the relatively poor behavioral performance of schizophrenia patients on simple frequency discrimination tasks.

Keywords

Magnetoencephalography; Evoked Potentials; Auditory Cortex; Mental Illness; N100; M100

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Contributors D.C.R designed the study, performed the statistical analysis and wrote the manuscript. E.S. contributed data analyses and preliminary statistical analyses. P.D.T. contributed to the design of the experiment and selection of data analytic strategies and M.L.R. had substantial input on clinical aspects of the design, including selection and implementation of schizophrenia diagnostic and clinical measures appearing in the paper. All authors have contributed to and approved the final manuscript.

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Conflict of Interest

All authors declare that they have no conflicts of interest with respect to this manuscript.

2. Introduction

The M100 auditory evoked field has been reported to show anomalous anterior-posterior source location asymmetry in actively psychotic patients with paranoid schizophrenia. In normal adults, the neuroanatomical source of the M100 component is further anterior in the right hemisphere (Baumann et al., 1991). We and others have previously shown that patients with schizophrenia demonstrate disturbed inter-hemispheric asymmetry of the M100 generator location (Reite et al., 1997, Reite et al., 1989, Rockstroh et al., 2001, Tiihonen et al., 1998).

The M100 component appears to be generated by lateral aspects of the transverse gyrus of Heschl and the planum temporale of the superior temporal gyrus (Godey et al., 2001, Reite et al., 1994). Abnormal planum temporale asymmetry has also been implicated as disturbed in schizophrenia (e.g., Shapleske et al., 1999 for a review). In spite of the evident lack of M100 location asymmetry in schizophrenia, however, we published evidence for normal location asymmetry of the gross anatomical correlate for the primary auditory cortices, Heschl's gyri, leading us to speculate that there may be structure-function disassociation and/or changes in cortical organization in the auditory cortex in people with schizophrenia (Rojas et al., 1997).

More recently, we reported MEG data suggesting that tonotopic mapping may be disturbed in patients with schizophrenia for the M100 (Rojas et al., 2002). In that previous study, we reported that, particularly for frequencies below 2 kHz in the left hemisphere, there was a lack of difference in medial-lateral spacing between auditory representations (i.e., a tonotopic gradient) in persons with schizophrenia. Presumably, the coarseness of the spatial gradient over which frequencies are represented in the cerebral cortex is determined in part by the sharpness of frequency tuning curves exhibited by the cells underlying the tonotopically organized fields. The current study was therefore undertaken to measure auditory cortical tuning in patients with schizophrenia. We hypothesized that tuning of the M100 would be broader in patients than in controls.

To derive a measure of tuning, we capitalized on the stimulus-specific refractory behavior of the M100. The amplitude of the M100 to repeated sounds identical in their physical characteristics (e.g., frequency, duration, amplitude) is related to the rate at which the stimuli are repeated; the slower the repetition rate, the larger the M100 amplitude, where the growth in amplitude approaches an asymptote as the repetition rate approaches .25 Hz (Hari et al., 1982, Lu et al., 1992). We reasoned that by holding the repetition rate constant and varying only the frequency of alternate tones in a train of pure tones, changes in M100 amplitude to the standard tone would reflect the degree of tuning of the M100 population to that frequency. We adopted a method first introduced by Naatanen et al. (1988), who employed a similar strategy to demonstrate that N100 (the EEG analog of M100 plus its non-temporal generators) amplitudes were highly sensitive to both frequency and spatial location.

3. Methods

3.1 Subjects

Eighteen participants with DSM-IV schizophrenia diagnoses were recruited for the study (7 female) as well as 15 participants (5 female) with no history of psychiatric or neurological illness meeting Research Diagnostic Criteria for never mentally-ill (Spitzer et al., 1978).

The schizophrenia and comparison groups did not differ in age or parental socioeconomic status. Comparison subjects had more years of formal education as well as significantly higher full scale IQ scores on the WAIS-III (see Table 1).

Persons with schizophrenia were re-diagnosed for the study using the Structured Clinical Interview for the DSM-IV (SCID) (First et al., 1994). To further assess clinical presentation, we also administered the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987). Eleven of the schizophrenia participants met paranoid subtype criteria and the remaining subjects were classified as undifferentiated. Control subjects were first screened using the SCID Screen Patient Questionnaire – Extended (First et al., 1999) and subjects whose responses needed further clarification were administered that portion of the full SCID interview still in question. In addition, both the schizophrenia and comparison subjects were administered a Wechsler Adult Intelligence Scale, 3rd Edition (WAIS-III) to assess intellectual capabilities (Wechsler, 1997). All persons with schizophrenia except 1 were using antipsychotic medications at the time of the interview (Gueguin et al., 2007) and subsequent MEG recordings. Nine of the schizophrenia group participants were medicated with atypical antipsychotics, 4 with conventional antipsychotics and 1 was taking both a conventional and an atypical antipsychotic. For those medications with reported chlorpromazine equivalency, the mean daily dose was 530.31 ± 485.15 mg. All participants gave informed consent to participate in this research consistent with the requirements of the Colorado Multiple Institutional Review Board and the principles for ethical research contained in the Declaration of Helsinki.

3.2 Stimulus delivery and MEG recordings

MEG recordings were made to monaural, contralateral ear stimulus presentations of pure tone acoustic stimuli 200 ms in duration with 10 ms rise and fall. Stimuli were delivered via foam insert earphones (E.A.R., Cabot Safety Co., Indianapolis, IN). Prior to MEG recording, a hearing threshold test was administered to each participant, and the level of presentation for each frequency was adjusted individually to 50 dB above hearing threshold to control for the effect of stimulus frequency on perceived loudness. No differences were detected in hearing threshold at any frequency between schizophrenia and comparison subjects ($P > .2$ for all 5 frequencies). Five separate stimulus blocks per ear were delivered in random order to each subject. For each block, a 1000 Hz pure tone was alternated with a stimulus of another frequency: a) 690, b) 930, c) 1000, d) 1070 and e) 1310 Hz. The inter-stimulus interval was fixed at 1.5 s throughout each block. Three-hundred discrete stimulus trials were delivered per ear and frequency during the experiment, yielding 150 stimuli for each of the two frequencies present in each block (see Figure 1).

MEG data were acquired with a 4D-Neuroimaging (San Diego, CA) Magnes I neuromagnetometer system with 37 axially-wound, first-order gradiometers with 5 cm baselines and 2 cm coil diameters. Recordings were made inside a custom-built magnetically-shielded room with 35 dB reduction at DC and 55 dB reduction at 60 Hz. Participants were recorded while lying on their sides in a comfortable recording bed, and were allowed to view a silent video of their choice during recording sessions on a monitor 4 m away. Each hemisphere was recorded separately in random order between subjects. The dewar was positioned over each side of the head so that the center channel of the hexagonal array would be centered between the minima and maxima for the M100 (approximately the C3/C4 electrode location for the 10–20 International Electrode System).

Prior to MEG recording, the location and orientation of the MEG coils relative to each subject's head were determined by digitizing a set of fiducial reference points on the head using a magnetic digitizer (Polhemus 3SPACE, Colchester, VT). The left and right preauricular points (LPA and RPA) and the nasion were used to establish a right-handed Cartesian coordinate system, where the line between LPA and RPA is the y-axis (positive out the left ear). The x-axis is the line normal to the y-axis at the midpoint (origin), with positive x exiting through the front of the head at the nasion, and the z-axis is normal to x and y at the origin (positive z exits at the top of the head).

MEG data were digitized at 16-bits quantization at a sampling rate of 1041.7 Hz within an epoch window of 450 milliseconds (200 ms pre-stimulus and 250 ms post-stimulus) triggered by the onset of each sound. A pass band between 1 and 200 Hz was used during acquisition.

3.3 Data processing and magnetic source localizations

After acquisition, further data reduction and source analyses were accomplished using the Brain Electrical Source Analysis (BESA) software package, version 5.1 (Megis GmBH, Germany). All data epochs with values exceeding ± 2000 fT were rejected from further analysis to exclude trials with non-physiological artifacts (e.g., movement). Noisy channels (those whose values consistently exceeded 2000 fT during recording) were removed from analysis. Two participants in the control group and one in the schizophrenia group had a single channel removed from the array prior to the remaining analyses. The remaining epochs were inspected visually for any remaining artifact, and signal averaged separately for each hemisphere to produce an averaged auditory evoked magnetic field. Between 119 and 147 artifact-free trials were used in each average out of the possible 150 per block. Averages were baseline corrected using the 200 ms pre-stimulus window and were digitally low-pass filtered (24 dB/octave, phase invariant Butterworth) at 20 Hz. For the block with only 1000 Hz stimuli, every other stimulus was used to produce an average methodologically comparable to the averages for the four additional blocks. The resulting numbers of trials in each grand average did not differ between groups for the left (control: 683.93 $\pm$ 107.67; schizophrenia: 684.39 $\pm$ 93.55 trials, $t(31)=.01$, $p>.05$) or the right (control: 677.80 $\pm$ 98.04; schizophrenia: 686.67 $\pm$ 78.38 trials, $t(31)=.29$, $p>.05$) hemispheres.

A best fitting conductive sphere model was constructed from the intracranial surfaces of the T1-weighted MRI scans of subjects enrolled in the study (see Rojas et al. (1997) for details of MRI pulse sequence and Teale et al. (2002) for a description of the spherical model). Dipole fitting was performed on the average data for all 1000 Hz stimulus presentations for all 5 blocks (i.e., 750 possible trials before artifact rejection), for each hemisphere separately. A single equivalent current dipole (ECD) was then fit separately for left and right hemispheres using a spatiotemporal model to the observed data in the post-stimulus window between 60–120 ms, yielding parameter estimates of the x, y, and z ECD position information, as well as dipole orientation and magnitude over time (see Figure 2a). The x, y, and z location parameters from the grand average dipole fit were then saved and applied to each of the 1 kHz averages from the 5 blocks per hemisphere in a second fitting procedure where only orientation and magnitude were allowed to vary. This procedure was designed to reduce the impact that location (particularly depth) might exert on the strength parameter by fixing the location for each block according to the overall grand average fit. The point on each M100 waveform selected for statistical treatment corresponded with the source waveform peak between 60 and 120 ms post-stimulus with dipole fits having residual errors less than or equal to 10% (Figure 2b). To reduce the considerable inter-subject variability in source amplitude, the measure was range normalized between 0 and 1 separately for each hemisphere, such that, for example, the trial block with the largest amplitude was assigned a 1, the smallest amplitude a zero, and the remaining 3 blocks proportionally intermediate values. Source location estimates from the left and right grand averages and normalized source amplitudes and latencies from the block fits were used as dependent measures in further statistical analyses (see Table 2 for raw mean amplitude and latency data). The model goodness of fit did not differ between groups for the left (control: .94 $\pm$.01; schizophrenia: .93 $\pm$.04, $t(31)=.89$, $p>.05$) or the right (control: .94 $\pm$.01; schizophrenia: .94 $\pm$.01, $t(31)=.78$, $p>.05$) hemispheres.

3.4 Statistical Analyses

Statistica 6.1 (Statsoft, Tulsa, OK) was used for all statistical computations. All significance tests were two-tailed and conducted at .05 alpha. Type III sums of squares were used in all

ANOVA designs, which were implemented using the general linear model module. Hemisphere and frequency effects, where specified in ANOVA designs, were treated as repeated measures variables. To test a priori hypotheses, single degree of freedom contrasts were specified in ANOVA designs where applicable. Unplanned or secondary analyses were conducted using post-hoc Fisher's LSD tests. The homogeneity of variance assumption was examined using Cochran's C statistic.

4. Results

4.1 Sample Characteristics

To determine whether differences in group demographics (i.e., education and IQ) could interact with the dependent variables of interest in the study, Pearson r correlation coefficients were calculated between education, IQ and the MEG variables analyzed in the study. No significant correlations between these variables were observed, corrected multiple comparisons using the Bonferroni procedure, and they were not given further consideration. Only 1 correlation was significant prior to Bonferroni correction, IQ and right M100 source latency in the 1 kHz condition ($r = -.38$, $p < .04$). The remaining correlations ranged between $-.33$ and $.32$.

4.2 M100 Source Amplitude

To assess neighboring frequency effects on 1 kHz source amplitude, the range normalized source amplitudes were entered into a $2 \times 2 \times 5$ mixed model ANOVA (group by hemisphere by frequency), where hemisphere and frequency were treated as within subjects variables. The frequency effect term was polynomially contrast-coded to examine the predicted quadratic tuning shape in the group by frequency interaction. The group main effect was significant, $F(1,31) = 7.71$, $P < .01$, indicating that the schizophrenia patients had higher source amplitudes. A main effect of frequency was also observed, $F(4,124) = 10.43$, $p < .001$, suggesting that the farther the neighboring frequency was from 1 kHz, the larger the source amplitude for the M100 to the 1 kHz sound became. A significant diagnosis by contrast-coded frequency interaction term, $F(1,31) = 5.91$, $p < .05$, suggested that the shapes of the frequency effect differed between groups (Figure 3). No other significant main effects (i.e., hemisphere) or interactions (group by hemisphere by frequency) were observed in this analysis.

Post-hoc between-group Fisher LSD tests indicated that the groups differed at the 690 Hz ($p = .007$), 930 Hz ($p = .009$) and 1000 Hz ($p < .0001$) levels, but not at the 1070 Hz ($p = .84$) and 1310 Hz ($p = .70$) levels. Within the schizophrenia group, post-hoc differences between frequencies were observed between the 1310 Hz tone and the 930 and 1000 Hz tones ($p = .02$ and $.009$, respectively). For the control group, the 1000 Hz tone differed from the 690, 1070 and 1310 Hz tones ($p = .00001$, $.002$ and $.0000003$). Additionally, the 690 Hz tone differed from the 930 and 1070 Hz tones ($.0003$ and $.04$), the 930 Hz tone was significantly different from the 1310 Hz tone ($p = .001$). All ten dependent variables in these analyses (5 frequencies, left and right hemispheres) met the homogeneity of variance assumption of ANOVA. Cochran's Cs ranged from $.53$ to $.73$, all $p > .05$.

4.3 M100 Source Latency

We also examined the effects of neighboring frequency on M100 source latency in a separate $2 \times 2 \times 5$ mixed model ANOVA (group by hemisphere by frequency). A significant main effect of hemisphere was found for the latency of the 1 kHz M100, $F(1,31) = 8.20$, $p < .01$, indicating that the left hemisphere latency (90.80 ± 1.42 ms) was slightly longer than the right hemisphere latency (87.31 ± 1.65 ms). A significant frequency main effect was also observed, $F(4, 124) = 3.39$, $p < .05$, suggesting that 1 kHz M100 latency increased as the neighboring frequency became further from 1 kHz. There was not a significant group main effect or group by hemisphere by frequency interaction term, but the group by frequency interaction term

approached significance, $F(4,124) = 2.19$, $p = .07$, which may suggest that the frequency effects are attributable primarily to the control group. Post-hoc Fisher LSD tests, however, did not reveal significant group differences in latency at any neighbor frequency (all $p > .20$).

4.4 M100 Source Location

The M100 source location parameters from the 1 kHz grand averages (x, y and z, or anterior-posterior, medial-lateral and inferior-superior) were entered into separate 2×2 mixed model ANOVAs (group by hemisphere). For the x-coordinate (anterior-posterior), the diagnosis main effect was non-significant, but the hemisphere main effect was significant, $F(1,31) = 10.00$, $p < .004$, indicating that sources in the right hemisphere were located anterior to sources in the left. However, the diagnosis by hemisphere interaction term was also significant, $F(1,31) = 7.26$, $p < .02$, suggesting that the left-right asymmetry was not present, or reduced, in the schizophrenia group (see Table 2 for mean source location data). Post-hoc testing confirmed that for controls, the left and right hemisphere x-locations were significantly different from each other ($p = .0004$) and also that the control left x-location was significantly posterior to that of the schizophrenia location ($p = .01$). The schizophrenia group's left and right x-locations did not differ significantly from each other ($p = .73$). For the y-coordinate, since the sign of the coordinate changes as a function of hemisphere, the absolute value of the coordinate was entered into the ANOVA to avoid a trivially significant hemisphere main effect in medial-lateral value. No significant main effects or interactions were observed for the y-coordinate. For the z-coordinate (inferior-superior), no significant main effects or interaction terms were noted, except that a possible trend for the sources in the right hemisphere to be slightly more superior than those on the left, $F(1,31) = 3.37$, $p = .08$.

4.5 Relationships to Symptoms and Medications

To examine how clinical ratings of symptom experience in schizophrenia might relate to the dependent measures, PANSS summary scores (positive, negative, and general) were correlated with the normalized source amplitudes and latencies for the M100. Additionally, the chlorpromazine equivalency measure was correlated with each dependent measure. To protect family-wise type I error and reflect that no a priori hypotheses were proposed for symptom – MEG relationships, a Bonferroni corrected p-value of .000625 was employed for each test (number of correlations = 80). None of the symptom or medication correlations reached significance after correction. Before correction, the PANSS positive score was correlated with the left M100 source amplitude in the 930 Hz condition ($r = .68$, $p = .002$) and the PANSS negative score was correlated with the right hemisphere M100 source amplitude in the 1310 Hz condition ($r = .51$, $p = .03$). All other non-significant correlation coefficients ranged from $-.35$ to $.40$.

5. Discussion

The present study investigated the frequency specificity of the M100 component in participants with schizophrenia. Bearing in mind that the M100 component likely reflects the population synaptic activity of ~50,000–100,000 synchronous cells (Hamalainen et al., 1993, Murakami and Okada, 2006), and is therefore a spatially coarse metric of tuning, the results of the study suggest that people with schizophrenia exhibit less frequency specificity for this neuronal population.

The M100 component probably has at least two generator locations per hemisphere located in close proximity in auditory regions of the superior temporal gyrus (Godey et al., 2001, Liegeois-Chauvel et al., 1994, Teale et al., 2000, Teale et al., 1998). Based on depth electrode recordings, Liegeois-Chauvel et al. (1994) suggested that activity from lateral portions of Heschl's gyrus and the planum temporale are responsible for the M100. These regions are not

likely to contain significant portions of primary auditory cortex (Morosan et al., 2001, Rademacher et al., 1993). While some regions of secondary, or belt, auditory cortex exhibit frequency tuning, tuning is often more complex or less specific in these regions (i.e., preference for broadband rather than pure tone stimuli (Kosaki et al., 1997)). Indeed, even within AI it has been shown in cats that several distinct tuning shapes may be characterized among the principal cells (Sutter, 2000). Therefore, the M100 response is likely a combination of differently tuned auditory cortical regions, and the change we observed in schizophrenia may either be a strict reduction in the number of tuned units responding across the regions, a change in the balance of contributions from tuned and non-tuned regions, and/or a broadening in the frequency specificity of tuned populations. Because of intrinsic limitations in MEG spatial resolution, MEG probably will not be able to provide substantial insight into which of these mechanisms, if any, may contribute to the observed deficit. However, there are components in the auditory evoked magnetic field that are generated by primary auditory cortex (Lutkenhoner et al., 2003, Pantev et al., 1995, Yvert et al., 2001). A future study focusing on such signals could therefore examine population frequency tuning of units that are more likely to have sharper tuning curves, at least in healthy individuals.

The observed change in M100 frequency specificity does not necessarily imply a static alteration in the underlying population of cells. Cortical tuning is dynamic and can be rapidly altered by experience (Kilgard et al., 2001, Recanzone et al., 1993). Experience-dependent plasticity in auditory responses is found even in averaged evoked responses from human MEG recordings (Cansino and Williamson, 1997, Pantev and Lutkenhoner, 2000). For example, Pantev et al. (Pantev et al., 1999) observed that laboratory induced deprivation of selective frequencies over a 3 hour period changed the response amplitude of that frequency in a post-deprivation recording compared to pre-deprivation. It is therefore possible that the type of tuning observed here is paradigm dependent and that the group difference reflects a difference in the ability of the M100 neuronal population to adapt over the course of the stimulus blocks.

Since the frequency specificity of the M100 in this experiment depends on the refractory behavior of the component, it is possible that selective deficits in refractory behavior could also explain the findings (e.g., patients may have longer refractory periods). Some evidence for this exists in the EEG literature on N100, the electric potential analog of the M100. Several reports of ISI dependent amplitude reductions in the EEG measured N100 component in schizophrenia have been reported (Roth et al., 1991, Roth et al., 1980, Shelley et al., 1999). It should be noted, however, that a deficit in refractory behavior would have to be frequency specific to produce the group differences noted in the current study. A generalized prolongation of the refractory period would be predicted to decrease source amplitudes across all 5 neighboring frequency blocks in the experiment, while a generalized decrease would have the opposite effect across the frequencies.

Taken together with our earlier finding of altered tonotopic representation (Rojas et al., 2002), there appear to be fundamental changes in the representation of frequency in the auditory cortex in schizophrenia. This may partially explain the pitch perception problems in persons with schizophrenia (e.g., Holcomb et al. (1995) and Rabinowicz et al. (2000)). Poorer tuning could account for the reduction in inter-frequency distance in brain space observed in the prior tonotopy study of Rojas et al. (2002) and perceptual distance is presumably a function, in part, of cortical representation distance.

There are several limitations to the current work. Since the majority of our subjects with schizophrenia were medicated, the effects of antipsychotic agents could be confounds to our interpretation of the findings. Extension of the findings to medication naïve individuals and correlation with psychoacoustic data in future studies is warranted. Given the modest sample size and large heterogeneity observed in schizophrenia, future experiments could benefit from

an expansion of the sample and more detailed clinical evaluation. Finally, we do not address the specificity of the findings to schizophrenia in the current paper. Adding a clinical control group such as bipolar disorder, with or without psychosis, would assist with specificity of the deficit to schizophrenia or to psychosis more broadly conceived.

Acknowledgements

The authors would like to thank Mr. Jeff Russ for conducting some of the early MRI and MEG preprocessing.

Role of the Funding Source

The funding for this study was provided by NIMH Grant MH60214; the NIMH had no role in study design, data collection and analysis, interpretation of the findings or in the decision to submit the paper for publication.

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Figure 1.

Top panel: Experimental design. Time increases from left to right. The 690 Hz condition is illustrated. The double arrows indicate the stimulus onset asynchrony between tones of varying frequency (1.5 s) and tones of identical frequency (3.0 s). The dotted lines indicate the trials used for averaging to produce the average evoked response in the bottom panel. Bottom panel: Overlap of all 37 waveforms from M100 to 1 kHz tone. The grand average across all 5 trial blocks for the right hemisphere (left ear stimulus) is illustrated and corresponds to the data used for source analysis.

Figure 2.

A. Partially inflated cortical surface from single subject illustrating source location for M100 response. The same subject and source localization corresponding to Figure 2 are shown. B. Source waveforms to the 1 kHz stimulus condition across all 5 neighbor frequency blocks are shown for right hemisphere of same subject in 2A.

Figure 3. Mean (+/- SD) normalized source amplitude of the M100 to 1 kHz stimulation as a function of neighboring frequency.

Table 1Sample Characteristics (mean $\pm$ SD).

	Schizophrenia	Control
Age (y)	40.99 $\pm$ 8.17	43.01 $\pm$ 4.59
Education (y)	13.13 $\pm$ 1.79 *	15.6 $\pm$ 1.84
Parental SES [§]	33.18 $\pm$ 20.26	35.61 $\pm$ 7.18
Full Scale IQ	93.59 $\pm$ 14.92 *	113.75 $\pm$ 17.73
PANSS Positive	18.39 $\pm$ 8.39	n.a.
PANSS Negative	13.72 $\pm$ 3.92	n.a.
PANSS General	32.33 $\pm$ 6.93	n.a.

|| P < .001

* P < .05

[§] Hollingshead's 4-factor Index of Social Position (Hollingshead, 1975), based on parental education and occupational status.

Table 2

Raw M100 source amplitude and latency data

Frequency	Measure	Schizophrenia		Control	
		Left Hemisphere	Right Hemisphere	Left Hemisphere	Right Hemisphere
690 Hz	Amplitude (nA-m)	10.99 ± 8.32	11.36 ± 7.98	9.79 ± 5.87	9.20 ± 5.56
	Latency (ms)	90.05 ± 13.21	85.48 ± 11.53	97.70 ± 13.50	92.86 ± 15.79
930 Hz	Amplitude (nA-m)	9.64 ± 7.36	10.68 ± 6.44	7.95 ± 5.68	8.10 ± 4.89
	Latency (ms)	88.91 ± 14.05	85.86 ± 12.62	92.67 ± 13.83	84.57 ± 14.01
1000 Hz	Amplitude (nA-m)	10.31 ± 8.21	10.62 ± 6.49	7.57 ± 5.20	7.56 ± 4.96
	Latency (ms)	88.91 ± 14.99	85.70 ± 13.11	86.66 ± 13.12	84.63 ± 15.89
1170 Hz	Amplitude (nA-m)	10.65 ± 6.91	11.09 ± 7.32	9.00 ± 6.38	8.68 ± 5.71
	Latency (ms)	88.14 ± 11.88	86.08 ± 13.60	89.01 ± 12.89	89.47 ± 15.74
1310 Hz	Amplitude (nA-m)	10.36 ± 5.64	11.58 ± 7.03	9.43 ± 6.03	9.20 ± 5.24
	Latency (ms)	93.48 ± 12.36	83.74 ± 11.35	92.47 ± 14.05	94.56 ± 14.43

Table 3Mean 1 kHz M100 Source Locations ($\pm$ SD).

	Control		Schizophrenia	
	Left	Right	Left	Right
Medial-lateral (mm)	-40.83 ± 18.95	43.88 ± 22.23	-45.11 ± 9.22	47.27 ± 5.94
Anterior-posterior (mm)	-10.20 ± 15.53	2.52 ± 5.89	-96 ± 6.67	$.06 \pm 6.36$
Superior-inferior (mm)	47.18 ± 10.80	51.46 ± 6.51	46.32 ± 8.24	49.63 ± 8.21