γ-Band Auditory Steady-State Responses Are Impaired in First Episode Psychosis

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Background: In chronic schizophrenia and chronic bipolar disorder, γ band (30–100 Hz) auditory steady-state electroencephalogram responses (ASSRs) are reduced in power and phase locking, likely reflecting neural circuit dysfunction. Here we examined whether γ ASSR deficits are also present at first hospitalization for psychosis.

Methods: Subjects were 16 first episode schizophrenia patients (SZ), 16 first episode affective disorder patients (AFF) (13 with bipolar disorder), and 33 healthy control subjects (HC). Stimuli were 20-, 30-, and 40-Hz binaural click trains. The ASSR phase locking and evoked power were analyzed with the Morlet wavelet transform.

Results: At 40-Hz stimulation, SZ and AFF had significantly reduced phase locking compared with HC. This deficit was more pronounced over the left hemisphere in SZ. Evoked power at 40 Hz was also reduced in the patients compared with HC. At 30-Hz stimulation phase locking and evoked power were reduced in both patient groups. The 20-Hz ASSR did not differ between groups, but phase locking and evoked power of the 40-Hz harmonic of the 20-Hz ASSR were reduced in both SZ and AFF. Phase locking of this 40-Hz harmonic was correlated with total positive symptoms in SZ.

Conclusions: The γ ASSR deficit is present at first hospitalization for both schizophrenia and affective disorder but shows a left hemisphere bias in first hospitalized SZ. Some of the neural circuitry abnormalities underlying the γ ASSR deficit might be common to psychoses in general, whereas others might be specific to particular disorders.

The synchronous activity of neurons, mediated by oscillations in the γ band (30–100 Hz) of the electroencephalogram (EEG), has been proposed to play an important role in the linking of neurons into cell assemblies that code information in the brain (1). Abnormalities of γ oscillations in the scalp-recorded EEGs of SZ have been hypothesized to reflect neural circuit abnormalities in this disorder (2–4). Much of this evidence has come from studies of auditory steady-state responses (ASSRs), in which simple auditory stimuli such as clicks are delivered at rapid rates and entrain the EEG at the stimulation frequency (5). The ASSR seems to have a "resonant" frequency at 40 Hz (6), at which frequency the power and phase locking of the ASSR are enhanced compared with other stimulation frequencies. Although it is not thought that the ASSR itself reflects any process related to the formation of cell assemblies, its 40-Hz resonance suggests that the underlying neural circuits preferentially oscillate at this frequency and thus might rely on some of the same circuit and intrinsic neuron properties as non-driven (sensory evoked and cognitive-related) γ oscillations. Chronic SZ show a "γ ASSR deficit" with reduced power and phase locking of ASSRs in the γ band but not at lower frequencies (7–10) compared with healthy individuals. This deficit seems to be most pronounced for 40-Hz stimulation. The γ ASSR deficit has also been reported in chronic bipolar disorder patients (11,12) and early onset psychosis (13), suggesting that it might be a manifestation of a neural circuit disorder (or set of disorders) that is shared by psychoses in general.

However, it has remained unknown whether this deficit appears early in the course of the disorder or only appears later, consistent with reports of progression of the pitch mismatch negativity and gray matter volume loss in Heschl's gyrus (14) or possibly the result of chronic medication. Nor is it known whether this deficit is present in all psychoses or is specific to schizophrenia. This report describes our efforts to address these important questions in the first study (to our knowledge) of the ASSR in first-episode (first hospitalization) patients with schizophrenic and affective (mainly bipolar) psychosis and in healthy control subjects. We examined the ASSR at β (13–29 Hz) and γ stimulation frequencies. The two main aims of this study were: first to determine whether the γ ASSR deficit was present at first hospitalization, and second to determine, if present, whether the γ ASSR deficit was specific to schizophrenic psychosis, thereby providing useful information on commonality or differences between these two psychoses.

Methods and Materials

Subjects

This study was approved by the McLean Hospital Institutional Review Board. After complete description of the study to the subjects, written informed consent was obtained.

Subjects were 32 first-episode psychosis patients and 34 healthy control subjects (HC; 14 female) paid for their participation. The HC were recruited from the local community through newspaper advertisements and were free of Axis I or II disorders (Structured Clinical Interview for DSM-III-R Non-Patient Edition [SCID-NP], 15; Structured Clinical Interview for DSM-IV Axis II Personality Disorders [SCID II], 16) as well as a history of Axis I disorders in first-degree relatives. One HC was classified as an outlier, and his data were excluded, because his 40-Hz evoked

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power was > 4 SDs above the group mean and his 30-Hz evoked power and 40-Hz phase locking values were > 2 SD above the respective group means. This exclusion did not meaningfully change the pattern of results. The final HC sample consisted of 33 subjects (14 female).

Patients were diagnosed with schizophrenia (SZ; $n = 16$; 4 female) or affective disorder (AFF; $n = 16$; 5 female) according to DSM-IV criteria (SCID, 17). The diagnostic composition of the SZ group was: 12 paranoid, 3 schizoaffective, and 1 disorganized. The AFF group consisted of 13 patients (4 female) with bipolar disorder and 3 patients (1 female) with major depression, all with psychotic features. Diagnoses were confirmed at a follow-up interview at least 6 months after the initial hospitalization when possible (6 SZ, 4 AFF). Psychosis patients participated in the study at 13.6 ± 10.8 (mean $\pm$ SD) days after admission. The time from admission to the EEG recording session did not differ between the patient groups (Table 1).

Subjects were selected without regard for ethnicity and met our standard inclusion criteria: 1) right-handed as assessed by the Edinburgh Handedness Inventory (18); 2) no history of electro-convulsive treatment; 3) no history of neurological illness, including epilepsy; 4) no alcohol or drug dependence or history of a "detox" admission within the last 5 years (DSM-IV criteria); 5) no present medication for medical disorders that would have deleterious EEG, neurological, or cognitive functioning consequences; and 6) estimated verbal IQ above 75.

Parental socioeconomic status was assessed with the Hollingshead two-factor index (19). The Mini-Mental State Examination (MMSE) was performed with all participants to rule out any dementia or delirium. The information subscale of the Wechsler Adult Intelligence Scale—Revised (WAIS-R) was used to estimate general fund of information. The Global Assessment Scale (GAS) (20) was administered to all patients to evaluate severity of illness and general level of functioning. Psychotic symptoms were rated with the Positive and Negative Syndrome Scale (PANSS) (21). Demographic and clinical data and inter-group comparisons

are summarized in Table 1. The groups did not differ on age, gender proportion, handedness, parental socioeconomic status, or WAIS-R score. There was a significant effect of Group on MMSE score, with SZ scoring slightly lower than HC. The SZ had significantly higher PANSS negative symptom ratings than AFF, and there was a trend for them to have higher general symptom ratings as well.

All patients received atypical antipsychotic drugs, and 2 SZ and 2 AFF also received typical antipsychotic drugs. Antipsychotic medication dosage was calculated in terms of chlorpromazine equivalents (22,23). There was a trend for SZ to have a higher average medication dosage than AFF (Table 1). Within each group, the following numbers of subjects received additional medications: mood stabilizers: 4 SZ, 10 AFF; anti-depressant drugs: 6 SZ, 9 AFF; anti-anxiolytic drugs: 4 SZ, 2 AFF.

Stimuli and Experimental Design

Subjects were seated in a quiet room in a comfortable chair 1.1 m in front of a computer monitor. Stimuli were presented through headphones (55 dB sound pressure level) in three blocks of stimuli (150/block): 20-Hz, 30-Hz, and 40-Hz stimulation rates. Stimuli consisted of trains of 1-msec white noise clicks (500-msec duration, 1100-msec stimulus onset asynchrony). Subjects were instructed to look at the fixation cross on the monitor and listen to the stimuli. The order of blocks was counterbalanced across subjects.

Electrophysiological Recording and Analysis

The EEG was recorded with Neuroscan Synamp 1 amplifiers (.01–100-Hz, 500-Hz digitization) with sintered Ag/Ag-Cl electrodes in an electrode cap at 60 scalp sites, nosetip, and left mastoid, referenced to the right mastoid. The forehead (AFz) served as ground. Bipolar vertical and horizontal electro-oculograms were recorded from electrodes above and below the right eye and at the left and right outer canthi, respectively. Electrode impedances were <5 kΩ.

Table 1. Subject Demographic and Clinical Data

	HC	SZ	AFF	Statistic	p
% Female Subjects	42.4	25.0	31.3	$\chi^2(2) = 1.59$	.452
Age (yrs)	27.5 ± 8.7	25.5 ± 8.1	24.4 ± 7.4	$F(2,62) = .850$	.432
Parental Socioeconomic Status	$1.6 \pm .8$	1.8 ± 1.1	$1.4 \pm .6$	$F(2,56) = 1.06$	.353
Handedness	$.76 \pm .14$	$.78 \pm .21$	$.76 \pm .12$	$F(2,52) = .075$	.928
MMSE	$29.3 \pm .7$	28.3 ± 1.8	28.8 ± 1.0	$F(2,52) = 4.35$	.018*
WAIS-R Information Subscale	13.9 ± 2.2	12.8 ± 2.3	12.9 ± 2.0	$F(2,52) = 1.77$	.180
Days From Admission		14.9 ± 11.9 range 3–42	12.3 ± 9.8 range 4–37	$F(1,29) = .404$	.530
Duration of Continuous Antipsychotic Medication (days)		14.7 ± 12.1 range 2–42	12.3 ± 9.8 range 4–37	$F(1,29) = .354$	.557
Medication Dosage (CPZ equivalents)		338 ± 196 range 50–800	220 ± 125 range 75–556	$F(1,25) = 3.54$	.072
Global Assessment Scale		34.8 ± 7.2	38.2 ± 6.0	$F(1,25) = 1.82$	.189
PANSS Total		80.9 ± 12.1	72.3 ± 16.0	$F(1,29) = 2.84$	.103
PANSS: Positive Symptom Total		20.9 ± 4.5	20.9 ± 7.2	$F(1,29) = .00$	.997
PANSS: Negative Symptom Total		17.8 ± 5.5	13.2 ± 5.1	$F(1,29) = 5.83$	.022*
PANSS: General Symptom Total		37.7 ± 7.0	32.9 ± 6.5	$F(1,29) = 3.91$	.058
# Trials: 20 Hz	145 ± 8	145 ± 7	142 ± 13	$F(2,62) = .590$	.557
# Trials: 30 Hz	142 ± 12	145 ± 7	145 ± 6	$F(2,62) = .733$	.485
# Trials: 40 Hz	145 ± 7	144 ± 6	146 ± 7	$F(2,62) = .252$	.778

Mean $\pm$ SD are listed for each group. Asterisks (*) indicate statistically significant results. HC, control subjects; SZ, schizophrenia patients; AFF, affective disorder patients; MMSE, Mini-Mental State Examination; WAIS-R, Wechsler Adult Intelligence Scale—Revised; CPZ, chlorpromazine; PANSS, Positive and Negative Syndrome Scale.
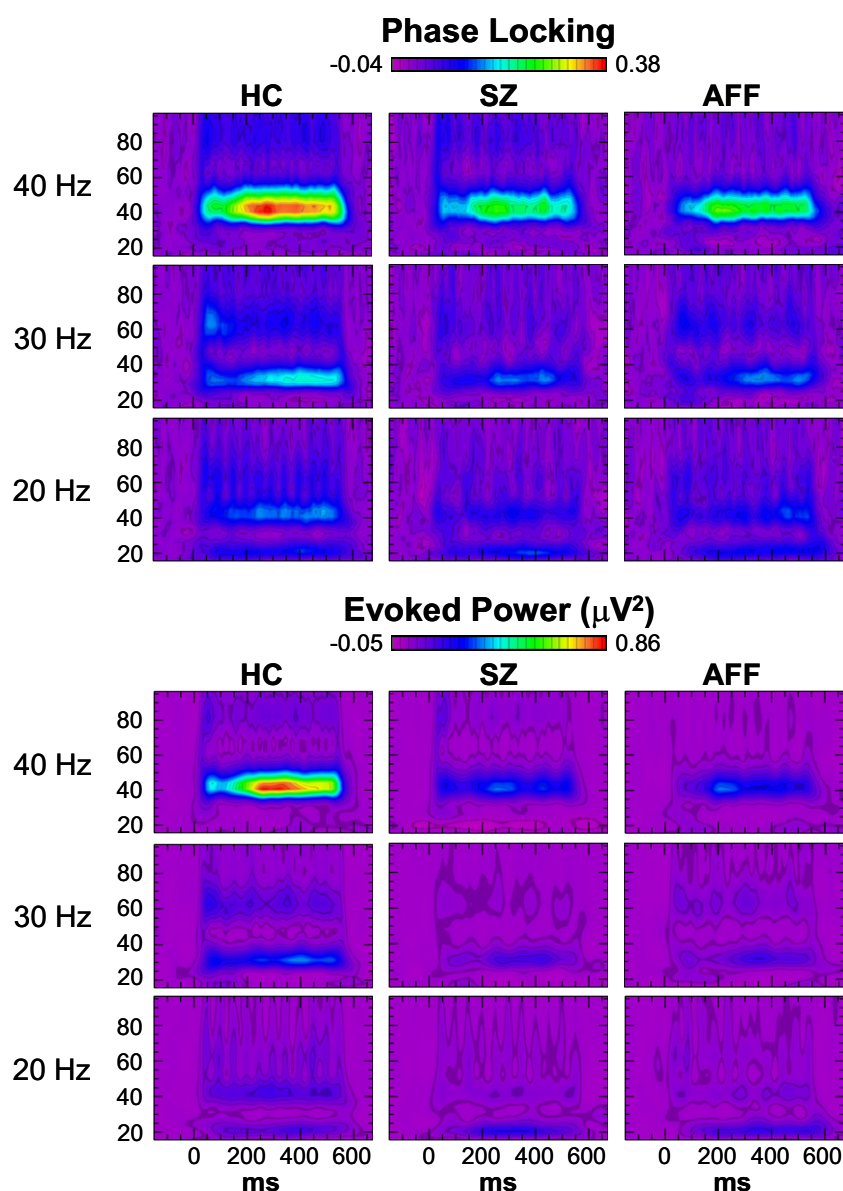
Figure 1. Time-frequency maps of auditory steady-state electroencephalogram response phase locking (top) and evoked power (bottom) at electrode Cz for each subject group for 20-, 30-, and 40-Hz stimulation. Subject groups are healthy control subjects (HC), schizophrenia patients (SZ), and affective disorder patients (AFF).

The epoching of continuous EEG files and artifact-related processing were performed with BrainVision Analyzer (Brain Products GmbH). Single-trial epochs were extracted from −250 to 850 msec relative to stimulus onset and corrected for eye movements and blinks (24). Next, epochs containing artifacts were removed. The artifact criteria were: 1) > ±100 μV change in one time point; 2) amplitude range within an epoch exceeding 300 μV; and 3) > 100-msec flat EEG (±.5 μV range). These criteria were visually tested and verified. Finally, artifact-free single epochs were re-referenced to averaged mastoids. There were no differences between the subject groups in the number of trials/condition after artifact rejection (Table 1).

Averaging and time-frequency analyses were performed with custom software written in the IDL programming environment (ITT Visual Information Solutions, Boulder, Colorado). Event-related potentials (ERPs) were averaged for each driving stimulus frequency. For ASSR analyses, the Morlet wavelet transform was applied to the single epochs in the 20–100-Hz frequency range of the EEG from −250 to 772 ms. Event-related spectral measures were computed on the wavelet-transformed epochs for each stimulus condition at each time point and wavelet frequency to yield time-frequency maps (25). Phase locking measures the variance of phase across single trials and is mathematically independent of power. Phase locking is computed as 1 − the circular variance of phases and ranges from 0 (random distribution of phases) to 1 (perfect phase locking). Evoked power measures the power of the average ERP, in which the contribution of non–stimulus-locked activity is minimized.

Average baseline values were subtracted from each time-frequency map (−150−−50 msec; there were no significant effects on baseline values for either spectral measure). Average spectral measures were computed at the time points (30–530 msec), electrodes (Fp1/2, F1/2, F3/4, FC1/2, FC3/4, C1/2, C3/4), and wavelet frequencies (20 Hz: 20.3–22.1 Hz; 30 Hz: 31.3–34.1 Hz; 40 Hz: 40.5–44.1 Hz) where both ASSR phase locking and evoked power were maximal. Latency effects are not reported here, because inspection of the data and preliminary analyses indicated that the observed group differences did not vary
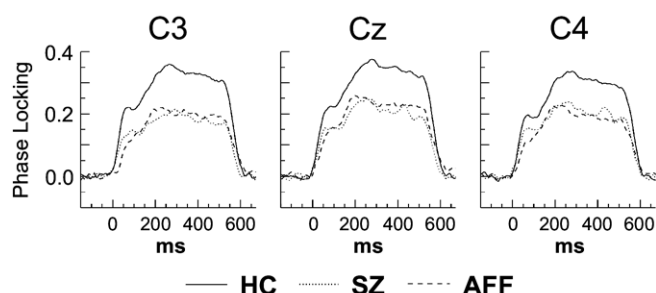
Figure 2. Phase locking time series from the 40-Hz auditory steady-state electroencephalogram response at left hemisphere (C3), midline (Cz), and right hemisphere (C4) electrodes. The time series were extracted from the frequency bands of the maximal response in Figure 1 (40.5–44.1-Hz wavelet center frequencies).

strongly with latency, consistent with the findings of Light *et al.* (10).

Statistical Analysis

Dependent variables (phase locking and evoked power) were analyzed with analysis of variance (ANOVA) in the design Group (SZ/AFF/HC) × Hemisphere (Left/Right) × Site (7/hemisphere). Separate ANOVAs were performed for each stimulation frequency (20, 30, and 40 Hz as well as the 40-Hz harmonic of the 20-Hz ASSR). The Greenhouse-Geisser correction for inhomogeneity of variance (26) is reflected in the reported p values. Dunnett's t was used for post hoc comparisons, testing that SZ and AFF values were < HC values and correcting for multiple comparisons. Spearman's ρ was used for correlation analyses (2-tailed). For all statistical analyses, $\alpha = .05$ (unless otherwise noted).

Results

The ASSR was maximal—as is typical—for 40-Hz stimulation in both the phase locking and evoked power data (Figure 1). Also, during 20-Hz stimulation a robust harmonic was apparent at 40 Hz.

Phase Locking

During 40-Hz stimulation the phase locking aspect of the ASSR was reduced in SZ and AFF compared with HC. The main effect of Group was significant [$F(2,62) = 4.09, p < .05$], as were post hoc comparisons between SZ and HC ($p < .05$) and AFF and HC ($p < .05$). In addition, the Group × Hemisphere interaction was significant [$F(2,62) = 3.49, p < .05$]. When the analysis was repeated for each patient group compared with the HC separately, the Group × Hemisphere interaction was significant for SZ [$F(1,47) = 6.41, p < .05$) but not AFF [$F(1,47) = 1.63, p = .208$]. This pattern of effects reflected a larger reduction of phase locking in SZ over the left hemisphere (HC − SZ = .114, $p < .05$) compared with the right hemisphere (HC − SZ = .091, $p < .05$) (Figure 2).

For 30-Hz stimulation there was a significant reduction of phase locking in patients [$F(2,62) = 3.25, p < .05$]. Post hoc tests found that this reduction was significant for SZ ($p < .05$) and marginally significant for AFF ($p = .053$). The Group × Hemisphere interaction was not significant [$F(2,62) = .152, p = .859$].

During 20-Hz stimulation the ASSR at 20 Hz did not differ between groups [$F(2,62) = .029, p = .972$]. The Group × Hemisphere interaction also was not significant [$F(2,62) = .095, p = .909$]. In contrast, there was a significant effect of Group on

the 40-Hz harmonic of the 20-Hz ASSR [$F(2,62) = 3.26, p < .05$]. Post hoc comparisons found that the 40-Hz harmonic was significantly reduced in SZ compared with HC ($p < .05$). In AFF the reduction compared with HC was marginally significant ($p = .051$). The Group × Hemisphere interaction for the 40-Hz harmonic was not significant [$F(2,62) = 1.48, p = .235$].

Evoked Power

Although ASSR evoked power during 40-Hz stimulation seemed to be reduced in SZ and AFF compared with HC, the main effect of Group only approached significance [$F(2,62) = 2.63, p = .080$], and the Group × Hemisphere interaction was not significant [$F(2,62) = .473, p = .626$]. Because the reduction of 40-Hz evoked power has been a consistent finding of ASSR studies of psychosis, we examined this measure further. In post hoc tests the reduction approached significance in SZ ($p = .075$) and was marginally significant in AFF ($p = .052$). Inspection of the distributions of individual values (Figure 3, top plots) revealed outliers in the SZ and HC groups. In the other measures these subjects' values were not outliers, so we decided not to exclude them from analyses (unlike the HC subject described in the Subjects section). Therefore, to reduce the influence of these outliers, we analyzed the Group effect with the nonparametric Kruskal-Wallis χ^2 test and found a significant effect [$\chi^2(2) = 10.3, p < .01$]. In paired comparisons with the Mann-Whitney U test, 40-Hz evoked power was significantly reduced in SZ ($U = 136, p < .05$) and AFF ($U = 149, p < .05$) compared with HC (correcting for multiple comparisons).

During 30-Hz stimulation evoked power was reduced in SZ and AFF compared with HC [Group: $F(2,62) = 3.74, p < .05$; post hoc tests: p values < .05]. The Group × Hemisphere interaction was not significant [$F(2,62) = .672, p = .514$].

For 20-Hz stimulation, evoked power at 20 Hz seemed to be larger in SZ than AFF and HC, but the main effect of Group was not significant [$F(2,62) = .192, p = .826$]. The increase in power for SZ and AFF was due to the presence of outliers who also had extremely large phase locking scores (Figure 3). The Group × Hemisphere interaction was not significant [$F(2,62) = .064, p = .938$]. The 40-Hz harmonic of the 20-Hz ASSR was significantly reduced in both patient groups [Group: $F(2,62) = 3.18, p < .05$; post hoc tests: p values < .05]. The Group × Hemisphere interaction for the 40-Hz harmonic was not significant [$F(2,62) = .051, p = .950$].

Correlations with Demographic and Clinical Variables

To rule out confounding effects, correlations were calculated between ASSR measures of interest and demographic variables. The ASSR measures of interest (those that differed between groups) were phase locking and evoked power at 40 Hz, 30 Hz, and the 40-Hz harmonic of the 20-Hz ASSR, averaged across the fronto-central electrodes (see Methods). In no group were there correlations with age, parental socioeconomic status, handedness, medication dosage, or time from admission.

Next we conducted exploratory correlations between the ASSR measures of interest and clinical symptom ratings on the PANSS. We examined correlations with the PANSS Positive, Negative, and General Symptom subtotals, applying a Bonferroni correction with $\alpha = .05$ (6 ASSR measures × 3 symptom totals = 18 correlations/group). No significant correlations were found in the AFF group. In the SZ group, phase locking of the 40-Hz harmonic of the 20-Hz ASSR was correlated with the Positive Symptom Total ($n = 15, \rho = .72, p < .05$ [$p = $
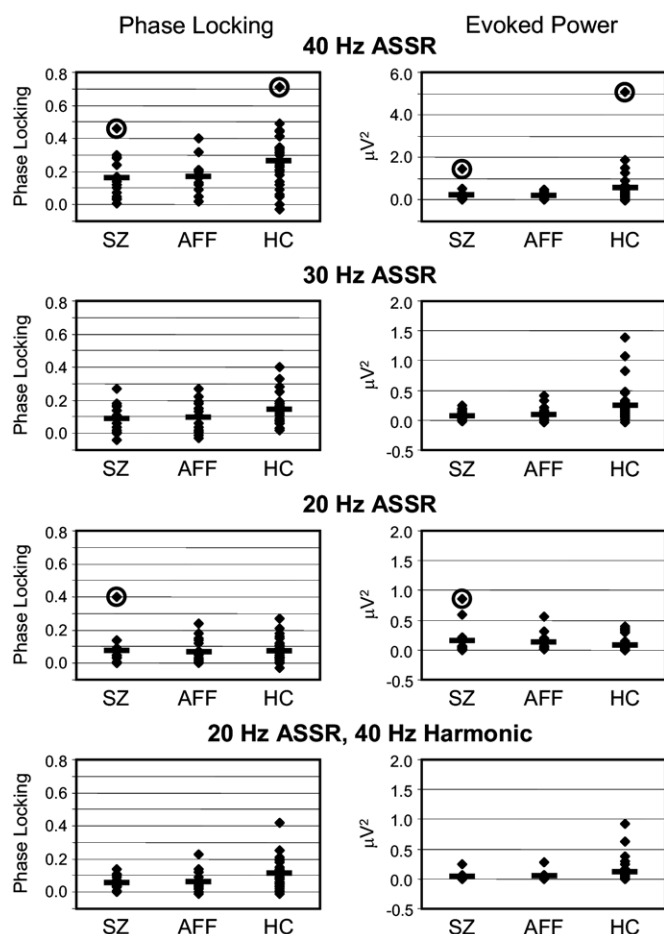
Figure 3. Scatterplots illustrating intersubject variability in phase locking and evoked power, measured at fronto-central electrodes. Horizontal bars indicate the mean values for each group for comparison with the individual values. Outliers are circled for both measures. Note that the y-axis on the 40-Hz auditory steady-state electroencephalogram response (ASSR) evoked power plot has a different scale than the other plots to accommodate the outlying values. Other abbreviations as in Figure 1.

.0026 uncorrected]) (Figure 4). The correlation between 40-Hz harmonic phase locking and the Hallucinations symptom score seemed to make the largest contribution to the overall positive symptom correlation but was not significant at the corrected p level ($n = 15$, $\rho = .67$, $p = .123$ [$p = .0068$ uncorrected]).

Discussion

This study demonstrates that the γ ASSR deficit is present at first hospitalization for both schizophrenia and affective disorder, particularly bipolar disorder (we note that the effects reported for the AFF group did not change appreciably when the non-bipolar patients were removed from the analyses). Thus, the γ ASSR deficit that has been observed in chronic psychosis patients does not seem to be due to brain abnormalities that only arise because of the chronic state, although progressive changes in severity might still occur. Nor does the γ ASSR deficit seem to be due to long-term consequences of antipsychotic medication.

Although both the SZ and AFF groups showed reduced γ-frequency ASSRs compared with HC, there were differences between the groups in the expression of the γ ASSR deficit. First,

for 40-Hz phase locking the γ ASSR deficit was more pronounced over the left hemisphere in SZ. The lateralization of the γ ASSR deficit to the left hemisphere in SZ is consistent with a large body of evidence for structural and functional abnormalities of the left hemisphere in schizophrenia (27–31). The current data suggest that schizophrenia is characterized by left hemisphere pathology, particularly during the early phase of the disease. In contrast, the deficit in affective psychosis patients is bilateral.

Second, the SZ demonstrated a correlation between symptom ratings and the ASSR, whereas no correlations were found for the AFF. This correlation was counterintuitively in the positive direction, indicating that the ASSR was more normal in SZ who were more symptomatic. In the scatterplot of the Positive Symptom Total versus 40-Hz harmonic phase locking values in Figure 4, the mean phase locking values for each group are indicated to demonstrate how the intersubject variability relates to the overall between-group differences. The SZ with the highest symptom ratings have phase locking values near the HC mean, whereas the majority of SZ have much lower phase locking values.

A similar pattern was also found in our second study of Gestalt perception, in which the phase locking of a β oscillation associated with visual object perception was positively correlated in SZ with positive symptoms such as visual hallucinations and thought disorder (3). Here positive symptoms were again involved. We have hypothesized that such positive correlations, particularly involving positive symptoms, might reflect a propensity for a dysfunctional cortical network to synchronize inappropriately in psychosis (3,32). However, given the unusual nature of this correlation, replication of this finding is crucial. Another important question is why this correlation was found for the 40-Hz harmonic of the 20-Hz ASSR but not for the 40-Hz ASSR itself. Longitudinal testing of this cohort should determine whether this positive correlation remains or whether patients that remain psychotic begin to show less synchronous activity.

In the present study the 30-Hz ASSR was reduced in both patient groups compared with HC. In reviewing the ASSR studies in schizophrenia and bipolar disorder to date that tested the ASSR at approximately 30 Hz, it seems that the occurrence of deficits at this frequency is variable. Brenner *et al.* (7) and Light *et al.* (10) reported 30-Hz deficits in schizophrenic subjects, whereas Kwon *et al.* (9) and Hong *et al.* (8) did not. In bipolar disorder, O'Donnell *et al.* (12) found a 30-Hz ASSR deficit, whereas O'Donnell *et al.* (11) did not. Furthermore, Brenner *et al.* (7) and O'Donnell *et al.* (12) found
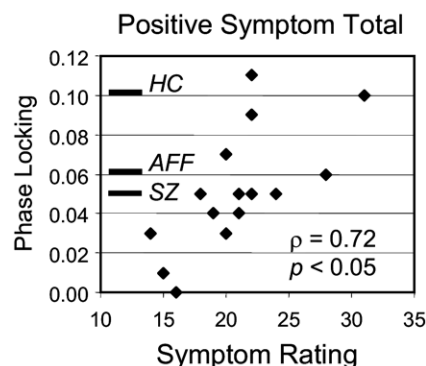
Figure 4. Scatterplot illustrating the correlation between the Positive and Negative Syndrome Scale (PANSS) Positive Symptom Total score and phase locking of the 40-Hz harmonic of the 20-Hz ASSR in SZ. The mean phase locking values for each group are indicated with horizontal bars. Note that only the SZ with the most positive phase locking values were near the mean of the HC group. Other abbreviations as in Figures 1 and 3.

ASSR deficits across a wide range of frequencies (although the deficits seemed greatest in the γ band). As more ASSR studies are conducted (hopefully with a wider range of frequencies), it will be important to determine whether the frequency range of ASSR deficits reflects factors such as symptom patterns or medication type.

Finally, in the present study we observed an outlier in the SZ group with extremely large (> 2 SD) 20-Hz phase locking and evoked power values (Figure 3). This subject caused the SZ group to have a larger 20-Hz evoked power ASSR than the HC group, although the difference was not significant. Similarly, Kwon *et al.* (9) reported that 20-Hz ASSR evoked power in chronic SZ was nonsignificantly larger than in HC (as well as a 20-Hz subharmonic during 40-Hz stimulation that we did not observe), as did Light *et al.* (10). In examining the outlier's demographic and clinical data, we could not find any particular measures that distinguished this patient from the rest of the SZ group. Individual patients with extremely large 20-Hz ASSRs have not been reported in the three other published ASSR studies of SZ (7,8,10). Further research will be necessary to determine whether these patients might in fact represent a particular subtype of schizophrenia.

These data demonstrate that the γ driving deficit is already present at first hospitalization for psychosis in both schizophrenia and affective disorder, but they also raise the issue of diagnostic specificity. Both patient groups evinced similar patterns of responses across frequencies, suggesting that the same neural circuit abnormalities to which the ASSR is sensitive are present in schizophrenia and affective psychosis. This would not be a surprising result, because there is a considerable degree of overlap in inhibitory interneuron-related neural circuit abnormalities in schizophrenia and bipolar disorder (33–37). However, we are not aware of studies that have examined neural circuitry in the auditory cortex of affective disorders, and to date little work has been done in schizophrenia, so it remains to be determined whether auditory cortical abnormalities at the microcircuit level are the basis for similarities in the γ driving deficit. Conversely, this study demonstrates that the γ driving deficits are not identical, because the difference in the laterality of the deficit clearly differentiates schizophrenia (left-sided) and affective psychosis (bilateral) and therefore provides diagnostic specificity. In addition, because the γ driving deficit in bipolar disorder seems to be state-dependent (11), it is possible that the deficits in schizophrenia and bipolar disorder might be differentiated by their state versus trait dependence. The disorders might also be distinguished by the presence of individuals with extremely large 20-Hz responses in schizophrenia but not in affective psychosis.

To date, two other studies have examined γ oscillations in first-episode SZ. In these studies, subjects performed auditory oddball tasks. Gallinat *et al.* (38) observed a reduction in the power of a late evoked γ oscillation but did not find any differences in the power of the early stimulus-evoked oscillation. In contrast, Symond *et al.* (39) found that a measure of inter-electrode phase synchrony was reduced in first episode patients compared with HC, as in chronic patients (40). Taken together, the results of the present study and those of Gallinat *et al.* and Symond *et al.* imply that stages of auditory processing are differentially affected in early-stage psychosis.

In conclusion, the present findings demonstrate that the γ ASSR deficit is present at first hospitalization for psychosis in patients with schizophrenia and affective psychoses. The phase locking aspect of the deficit is more pronounced at left hemisphere electrode sites in SZ. These results suggest that schizo-phrenia and affective psychosis might share some common neural circuitry abnormalities that are expressed in the γ ASSR deficit, but the differing patterns of expression of this deficit (such as lateralization and correlations with clinical variables) imply that it is related to different aspects of psychosis. However, we note that to the extent to which medication effects might be responsible for the present results, similarities in the γ ASSR deficit between schizophrenic and affective psychosis patients might be due to the use of the same medications.

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